Posters

SERUM CALCIUM LEVEL IS ASSOCIATED WITH METABOLIC SYNDROME (METS) - A POPULATION BASED EPIDEMIOLOGIC STUDY

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Background: It has been shown that serum calcium homeostasis is associated with disturbances in glucose metabolism. The aim of our study was to examine the possible association between serum calcium and metabolic syndrome.

Material and methods: As a part of the national development strategy for the prevention of diabetes in Finland (D2D-programme) a study population of 4500 middle-aged men and women were recruited. A 2-hour glucose, serum calcium, and serum lipids were measured and antropometric measurements were performed by a trained nurse. The metabolic syndrome (MetS) was defined according to the criteria of NCEP. For analyzing serum calcium a calorimetric method based on arsenatso-III-calourstuff was used.

Results: Altogether 2896 individuals, 1396 men (62% of men invited) and 1500 women (66,7% of women invited), participated in the study. The mean age of men was 60,3 (8,3) and that of women 59,8 (8,5) years. BMI (kg/m^2) was 27,7 (4,1) for men and 27,7 (5,2) for women. The prevalence of NCEP-MetS increased according to the serum calcium quartiles in a linear trend (p-value < 0.001) in both men´s and women´s groups, even in the case when age, physical activity, alcohol intake and smoking were adjusted.

Discussion: The result of this large-scale population-based study supports the previous notion of the association of serum calcium level and MetS. Attention should be paid to the even mildly elevated values, because the risk of MetS increases with the elevating level of serum calcium.

CAN THE METABOLIC SYNDROME, THE HUMAN EQUIVALENT OF "GLOBAL WARMING", BE REVERSED BY USE OF A "GREEN" DIET?

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Aims: Global Warming and the Metabolic Syndrome (MS) share many similar features. They both may occur from over utilization of fuels, which result in global changes to the planet and multifactorial changes within the human organism. We studied whether the application of "green" thinking might have the same effect on human ecology, as it appears to have on the earth's ecology.

Methods: We studied in 800 pts with MS, a diet (Diet Evolution) that consists of replacing energy dense fuels, defined as refined or whole grains, pulses, potatoes, and beans, with low energy dense green fuels, particularly salads, leaves and vegetables, supplemented with controlled amounts of green based oils, nuts, seeds, and grass-fed animal products (a grain-limited Mediterranean diet). Pts have been followed from 6 months to 6 years (mean 2.5 years), with blood work sent to a Core Lab (Berkeley Heart Labs, Alameda, CA).

Results: Compliance is 80%. Weight loss ranged from 8 lbs to 85 lbs (mean 30 lbs)

Systolic Blood pressure fell from 140 ± 20 to 110±8 mmHg over the 1st year. Triglycerides fell from 178±30 to 65± 20 mg/dl. Insulin fell from 17 ±10 to 8±6 uU/dl. Hs-CRP (body Inflammation or "warming") fell from 4.5 to 1.0+/-0.5 mg/dl. fibrinogen levels fell from 568±55 to 387±24 mg/dl.

Conclusions: Applying the same "green" thinking that combats Global Warming can eliminate The Metabolic Syndrome, a perfect example of human excess fuel utilization.Pt acceptance is high and the results remarkable. A green diet effectively reverses human "climate change."

TRIGLYCERIDE TO HDL-C RATIO AS PREDICTOR OF NEW ONSET DIABETES IN GENERAL POPULATIONS; A LONGITUDINAL DATABASE ANALYSIS

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Background: Triglyceride to HDL-C Ratio (TG/HDL-C)has been associated with insulin sensitivity and insulin resistance in general populations. We sought to determine whether TG/HDL-C predicts new onset diabetes.

Method: The study population comprised 1.47 million patients enrolled in the GE Centricity Electronic medical Records Database from Jan 31 2001 to Dec 31 2005. The follow-up period was defined as time from first recorded TG/HDL-C measure to new onset diabetes (NODM via ICD-9 code; prevalent cases were excluded). Cox Proportional Hazards Regression was used to estimate hazard ratios for categories of TG/HDL and NODM. Analyses were adjusted for age and gender.

Results: Fifty-five percent of the population were female. Median age was 55 years. Adjusted HRs (+/- 95%CI) for NODM for each TG/HDL-C category were as follows: >1-2 = 1.413(1.374-1.452); >2-3 = 2.055(2.00-2.112); >3-4=2.643(2.571-2.171); >4-5=3.078(2.991-3.168); >5-6 = 3.447(3.345-3.55); >6-10 = 4.121(4.007-4.237); >10 = 5.793(5.624-5.967).

Conclusions: TG/HDL-C is a strong predictor of NODM in general populations. Ratios of 4 or greater are associated with a threefold or greater increase in the hazard for NODM.

THE METABOLIC SYNDROME AS AN INDEPENDENT PREDICTOR OF DIABETES, CARDIOVASCULAR DISEASE AND ALL CAUSE MORTALITY; A META-ANALYSIS OF RECENT STUDIES

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Background: Controversy remains as to whether the metabolic syndrome, however defined, is an independent prognostic marker for diabetes and cardiovascular events. Further, its utility beyond Western European populations has been questioned. We conducted a review and meta-analysis of recent global epidemiologic studies relating metabolic syndrome to diabetes, cardiovascular events and all cause mortality.

Methods: After screening 256 potential studies in press since the last publication of three major systematic reviews and meta-analyses (April 2005), we identified 35 additional studies as appropriate for this analysis. Criteria included: pre-diabetes population, NCEP or WHO definitions of metabolic syndrome, and adjusted relative risk or odds ratio estimates for diabetes, coronary heart disease (CHD), cardiovascular disease (CVD), stroke, and all cause mortality. Both fixed and random effects meta-analyses were conducted.

Results: Summary relative risk (RR) estimates among subjects with metabolic syndrome versus those without for study endpoints were as

follows: for diabetes, RR 4.80 (4.17-5.52); for CHD, RR 1.60 (1.52-1.69)j for CVD, RR 1.66 (1.57-1.75);for all cause mortality, RR 1.29 (1.24-1.34); for stroke, RR 1.63 (1.50-1.78).All reported studies adjusted for age and gender at minimum. Results were consistent regardless of geographic study source and similar to the previously published meta-analyses.

Conclusions: Metabolic syndrome appears to be an independent predictor of new onset diabetes, CHD and CVD, stroke, and overall mortality. However, many of the reported studies failed to adjust for traditional cardiometabolic risk factors.

METABOLIC SYNDROME IN MEXICAN ADULTS. RESULTS FROM THE NATIONAL HEALTH AND NUTRITION SURVEY 2006

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Objectives: To examine the prevalence of Metabolic Syndrome (MS) and its associated factors in Mexican adults, using data derived from the National Health and Nutrition Survey (NHNS) 2006.

Methods: The NHNS 2006 was conducted between October, 2005 and May, 2006. Adult questionnaires were applied to 45,446 subjects aged 20 and more. Fasting blood specimens were provided by 30% of participants. We selected randomly a sub-sample of 6,613, and laboratory measurements were analyzed for glucose, insulin, triglycerides, total cholesterol and HDL-cholesterol; we included only results from eight or more hours of fasting samples (n=5,509). We used individual weighted factors in the statistical analysis and considered the survey's complex sampling design using SPSS 15.0.

Preliminary results: In accordance with definitions by AHA/NHLBI, and IDF, the prevalence of MS in Mexican adults aged 20 or more, was 31.2%, and 40.8%, respectively. Women were more affected than men, due to the higher prevalence of central obesity in that gender. Prevalence of MS increased with age, and was higher among populations living in metropolitan areas, in the west-central region, and those with lower education.

Discussion: A large proportion of Mexican adults have MS. MS can predict type 2 diabetes and cardiovascular disease, two of the main causes of death in this country. Due to its interrelation, the presence of one component of MS should alert the health professional to look for the remaining factors. Treatment of each component should be implemented properly to prevent or delay onset of type 2 diabetes and cardiovascular disease.

ASSOCIATION BETWEEN RAISED BLOOD PRESSURE AND DYSGLYCAEMIA IN HONG KONG CHINESE

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Objective: Hypertension and diabetes are closely related. We therefore investigated the association between raised blood pressure (SBP≥130mmHg or DBP≥85mmHg) and dysglycaemia (fasting plasma glucose≥5.6 mmol/L or OGTT 2-hour glucose≥7.8mmol/L) in the Hong Kong Cardiovascular Risk Factor Prevalence Study Cohort.

Methods: We studied the association between hypertension and diabetes in 1862 subjects in the cohort at baseline and the factors predicting their development after a period of 6 years in 1496 subjects who did not have either condition at baseline.

Results: At baseline, hypertension and diabetes were both related to age, obesity indices, blood pressure, glucose, HDL and triglycerides. Only 59.7% of subjects had normal blood pressure and glucose tolerance, 11.4% had raised blood pressure and dysglycaemia, 17.1% had raised blood pressure only and 11.8% had dysglycaemia only. 58% of people with diabetes had raised blood pressure while 56% of people with hypertension had dysglycaemia. At the 6-year follow-up, age, systolic blood pressure and triglycerides were independent predictors of new-onset hypertension while body mass index, fasting glucose and triglycerides were independent predictors of new-onset diabetes. Body mass index, systolic blood pressure and 2-hour glucose predicted the development of hypertension and diabetes together.

Conclusions: Hypertension and diabetes share common aetiological factors. There is a large overlap between raised blood pressure and dysglycaemia due to obesity and the metabolic syndrome. Patients with either hypertension or diabetes should be screened for elevated blood pressure and blood glucose.

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ADULT TREATMENT PANEL III METABOLIC SYNDROME CRITERIA MORE STRONGLY THAN INTERNATIONAL DIABETES FEDERATION CRITERIA PREDICT THE INCIDENCE OF TYPE 2 DIABETES IN ANGIOGRAPHIED CORONARY PATIENTS

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Aims: The incidence of type 2 diabetes (T2DM) in coronary patients is unknown. We therefore prospectively recorded incident T2DM in a large population of angiographied coronary patients. We further addressed the question whether the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) or the International Diabetes Federation (IDF) criteria of the metabolic syndrome (MetS) more strongly predict T2DM in these patients.

Methods: We recorded the incidence of T2DM over 6 years in a population of 503 non-diabetic patients undergoing coronary angiography for the evaluation of stable coronary artery disease.

Results: At baseline, 144 (28.6%) of our patients had the MetS according to NCEP-ATPIII criteria, and 204 (40.6%) had the MetS according to IDF criteria. During the follow-up period, T2DM was newly diagnosed in 86 (17.1%) patients. Both definitions of the MetS significantly predicted incident diabetes; however, the adjusted odds ratio was higher for the NCEP-ATPIII MetS (3.55 [2.16-5.86]; $p < 0.001$) than for the IDF MetS (2.13 [1.32-3.43]; $p = 0.002$). Among the 120 patients (23.9%) in whom the two definitions of the MetS led to discordant diagnoses, the incidence of T2DM was significantly higher in patients who fulfilled the NCEP-ATPIII MetS criteria, but not the IDF criteria than in those who conversely fulfilled the IDF but not the NCEP-ATPIII criteria (33.3% vs. 15.6%; $p = 0.035$).

Conclusions: Among angiographied coronary patients, the incidence of diabetes is high. The NCEP-ATPIII criteria of the MetS more strongly than the IDF MetS criteria predict the incidence of T2DM in these patients.

GENDER-SPECIFIC DIFFERENCES IN ASSOCIATIONS WITH THE METABOLIC SYNDROME IN REGIONAL AUSTRALIA

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Aims: To determine the prevalence of the metabolic syndrome (MetS) and its relationship to other cardiovascular disease (CVD) risk factors in participants from a regional risk-screening program in the state of Victoria, Australia.

Methods: CVD screening consisted of basic clinical assessments and questionnaires concerning diet, physical activity and other lifestyle factors, including mental health status. MetS was defined according to the 2005 International Diabetes Federation definition. Owing to the low number of fasting participants (6.7%), we defined MetS in the absence of dysglycaemia.

Results: From 1,606 participants (54.4% female, mean age 57 ± 15 years, 95.5% European/Caucasian ethnicity), the prevalence of MetS was 28.5% for males and 24.6% for females. In males, ex-smokers were at increased risk of having MetS (Odds Ratio [OR] = 1.67, 95% CI 1.2-2.4), compared to non-smokers. Multivariate logistic regression analyses was performed, adjusted for age and smoking, showed that in males, vigorous intensity exercise was associated with a reduced risk of having the MetS (OR = 0.64, 95% CI 0.42-0.96) when compared to those who did not exercise. In contrast, females who had potential depression) were at increased risk of having the MetS (OR= 1.7, 95% CI 1.2-2.6 for CES-D).

Conclusions: A high prevalence of the MetS in regional Victoria was observed, reinforcing the need for effective and sustainable CVD prevention clinics to support local healthcare services and facilities. Variables associated with the MetS differ according to gender.

TENDENCY TO DECLINE IN THE RATE OF METABOLIC SYNDROME FROM 2003 TO 2007 AMONG HONG KONG CHINESE ADOLESCENTS

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Aims: To assess the change of rates of Metabolic Syndrome (MES) among Hong Kong adolescents from 2003 to 2007.

Methods: We have conducted 2 cross-sectional, population-based studies on Hong Kong school children in 2003 (study 1) and 2007 (study 2). With cluster sampling method, adolescents were randomly selected from all secondary schools in Hong Kong. MES was defined by (1) the modified National Cholesterol Education Program (NCEP) criteria: ≥3 of the following: TG ≥1.24 mmol/L; HDL-C ≤1.03 mmol/L; waist ≥90%tile (for age and sex); BP ≥90%tile; fasting PG ≥6.1 mmol/L; or (2) the International Diabetes Federation (IDF) criteria: for adolescents aged 10-16 years: waist ≥90%tile or adult cutoff if lower plus ≥2 of the following: TG ≥1.7 mmol/L; HDL-C < 1.03 mmol/L; BP ≥130/85 mmHg; fasting PG ≥5.6 mmol/L (for adolescents aged ≥16 years, adopt adult criteria).

Results: There were 2116 (age: mean ± SD 15.6 ± 2.0 years, 45.4% boys) and 1317 (age: 15.5 ± 1.8, 38.6% boys) adolescents in study 1 and 2, respectively. The overall prevalence of MES was: boys - 1.77% vs. 1.57% (NCEP) and 1.25% vs. 1.18% (IDF); girls - 1.73% vs. 0.99% (NCEP) and 0.69% vs. 0.62% (IDF) (p: all NS).

Conclusions: In 2007, MES was found in 0.6-1.6% of Hong Kong Chinese school children. There is a tendency of decline in the rate of MES as compared to 4 years ago.

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PREVALENCE OF METABOLIC SYNDROME IN LOW AND MIDDLE URBAN WOMEN IN INDIA AND IMPACT OF POPULATION BASED STRATEGY ON INCREASING AWARENESS

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Background: Metabolic syndrome is increasing in Indian population especially in urban area; but efficacy of population based education module is unknown.

Objectives: To determine the prevalence and efficacy of population based education for a short duration on awareness of its risk factors and management.

Materials and methods: A door to door survey was done in four urban areas of Jaipur and 532 healthy women (aged 35-70 years) were selected for the study. After taking written consent background information was collected. Fasting venous blood samples (12 hour) were taken to analyze Hb, blood sugar, and lipid profile. Anthropometric data-weight, height, waist and hip circumference, were measured. Metabolic syndrome was defined by ATP-III guidelines. Knowledge regarding various NCDs and its risk factors was assessed at baseline. An educational module was developed to impart community education. Post intervention Knowledge was assessed using same tool after six months.

Results: Around 459 subjects participated in the study. Among metabolic syndrome risk factors 31.9% subjects had WC>88 cms, 22.9% TG≥150 mg/dl, 85.8% HDL-C < 50 mg/dl, 48.6% HTN and 8.4% BSF ≥110. Prevalence of metabolic syndrome was 29.6% (age adjusted prevalence 31.8%). Post intervention data showed significant change in knowledge; HTN (mean score 4.15±3.04 Vs 5.66±3.64, p=0.002); CVD (6.32±4.20 Vs 8.45±4.39, p=0.001); DM (4.62±4.89 vs. 7.21±5.57, p=0.000); obesity (4.80±2.86 vs 6.47±2.77, p= 0.000); stroke (0.78±1.43 vs. 1.72±1.83, p=0.000)

Conclusion: Lifestyle education through community based preventive strategy encourages and empowers people to take responsibility for their health and enable them to manage their condition themselves.

THE ASSOCIATION OF -308A ALLELE OF THE TNF- GENE WITH METABOLIC SYNDROME PROGRESSION: A 5-YEAR FOLLOW-UP STUDY

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Objectives: To investigate whether the promoter polymorphism of the TNF-α (G-308A) gene predict the metabolic syndrome progression in clinically healthy middle-aged patients.

Methods: The G-308A polymorphism of the TNF-α gene was screened in 42 men and 50 women. The frequencies of the genotypes were 63.0% G-308G, 34.7% G-308A, and 2.3% A-308A and they were in Hardy-Weinberg equilibrium. Their mean BMI was 26.3±1.1 kg/m^2 and age 42.1±1.3 years. There were no difference in clinical characteristics, fasting and 2-h levels of glucose and insulin in the oral glucose tolerance test (OGGT) and fasting serum lipids at baseline according to the G-308A promoter polymorphism.

Results: During the 5-year follow-up the triglycerides levels in the -308A allele group became significantly higher (more than 3 times) in

homozygous for G allele patients. The apolipoprotein index level higher than 1 was observes more often than twice in this group. In -308A allele group 14.7% patients developed FIG, 20.6% - IGT and 5.9% - type 2 diabetes vs. 6.9%, 8.6% and 1.7% with the G-308G genotype ($p< 0.05$). The presence of the -308A allele of the TNF-α gene was associated with more than twofold higher risk of pre-diabetes or type 2 diabetes incidence compared with the G-308G genotype in the Cox regression model as hazard ratio (HR=2.4), 95%CI: 1.28-4.56; $P = 0.008$).

Conclusion: The -308A allele of the TNF-α gene was associated with a significant higher risk for dyslipidemia, pre-diabetes and type 2 diabetes incidence during the 5-year follow-up in middle-aged patients.

DIURNAL VARIATION IN WAIST CIRCUMFERENCE - IMPLICATIONS FOR THE DIAGNOSIS OF THE METABOLIC SYNDROME

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Diagnostic criteria for the metabolic syndrome include measurement of waist circumference (WC) - a marker of central obesity. This criterion is expressed categorically, i.e. above or below a 'cut-point' based on gender and ethnic group. Little is known about the degree of variation of WC in individuals during the day. Such variation is likely due to person-specific factors such as food and fluid intake, activity levels, flatus production and elimination.

Following a pilot study, we identified two times (08.00 and 14.00) associated with the greatest diurnal variation in WC and performed measurements in 50 stable ambulant hospital inpatients (all Caucasian) receiving normal hospital diet; breakfast at 08.15 and lunch 12.30. Measurements were an average of three readings using WHO guidelines for the measurement of WC. We expressed results as percentage differences in individual mean WC between the two times.

WC was lowest at 08.00 for 48 patients. The greatest absolute difference was 5.8cm and greatest percentage change was 6.5%. A one-sample t-test showed percentage change between individual's readings is not by chance, mean = 2.23, SD = 1.62, with a significance of $p < 0.001$ ($t = 9.72$, $df = 49$, [95% CI; 1.77 to 2.69]).

These data show that patients exhibit variation in WC during the day with smaller measurements in the morning. Although the variation is small in percentage terms, the implication is that an individual might satisfy the criteria for a diagnosis of the metabolic syndrome in the afternoon but not in the morning.

PREVALENCE OF METABOLIC SYNDROME ACCORDING TO ATP III AND IDF CRITERIA : A POPULATION BASED STUDY

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Objective: The objective study was to examine the prevalence of metabolic syndrome (MeS) among adult Qatari population according to the revised criteria of NCEP ATP III and IDF, assess which component contributed to the increased risk of the metabolic syndrome and identify the characteristics of the subjects with MeS.

Design: A cross sectional study was carried at the PHC Clinics.

Subjects and metods: Of the 1496 subjects who were approached to participate in the study, 1204 (80.5%) gave their consent. Metabolic syndrome was defined using the National Cholesterol Education Program - Third Adult Treatment Panel (ATP III) as well as International Diabetes Federation (IDF).

Results: The overall prevalence of metabolic syndrome in studied subjects was 26.5% and 33.7% according to ATPIII and IDF. The prevalence of MeS according to IDF was higher than by ATP III. The prevalence of MeS by ATP III and IDF was associated significantly with age, gender, educational status and physical activity. According to ATP III and IDF, the prevalence of MeS and its components - obesity, hypertension and diabetes - increased with age. Among the components of MeS, central obesity was significantly higher in subjects. The There was a big difference in the prevalence of MeS in women above 60 years old according to IDF, when compared to ATP III. Multivariate logistics regression analysis showed that age and BMI were significant contributors for MeS.

Conclusion: The current study observed a significant increase in the risk of metabolic syndrome among Qataris.

PREVALENCE OF METABOLIC SYNDROME AND CARDIOVASCULAR COMPLICATION IN DIABETIC AND NON-DIABETIC POPULATION

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Aim: Aim of the study was to examine the prevalence of metabolic syndrome (MetS) and cardiovascular disease (CVD) in Type 2 diabetes mellitus (DM) patients and in non-diabetic subjects.

Patients and methods: Anthropometrical and biochemical measurements were performed in 288 randomly selected patients with Type 2 diabetes mellitus (DM) and in 293 non-diabetic subjects, 20-74 years old . The prevalence of MetS was measured and prevalent CVD was assessed by verified history.

Results: The prevalence of MetS in diabetic men (67.8%) was statistically significant lower than in diabetic women (82.1%; $p< 0.05$), but higher in non-diabetic men (39.6%) compared to non-diabetic women (17.4%). In diabetic group history of myocardial infarction (MI) was found in 13.4% of the patients with MetS and in 8.3% of patients without MetS. In 24.5% of the patients with MetS and in 16.7% of the patients without MetS angina was found. History of cerebro-vascular disease reported 4.6% of patients with MetS and 4.2% without MetS. There was not found statistically significant relationship between MetS and CVD in both diabetic and non-diabetic population ($p>0.05$). But when we compared the prevalence of CVD in diabetics and non-diabetics we found statistically significant relationship between CVD and DM ($p< 0.001$).

Conclusion: Our results show that despite the higher prevalence of cardiovascular risk factors in patients with MetS, the prevalence of CVD in this population was not differed compared to the subjects without MetS. This observation emphasized the role of Type 2 DM as an independent risk factor for cardiovascular complications.

PREVALENCE OF METABOLIC SYNDROME IN OVERWEIGHT - OBESE WORKERS

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Obesity can cause an important working disability; the presence of related pathologies such as metabolic syndrome (MS) type 2 diabetes and cardiovascular diseases increases the number of workers'sick days and also the number of limitations on fitness to work. Shift workers are at risk of

developing MS because of alterations of the circadian rhythms, diet and lifestyle.Aim of study was to evaluate in 369 consecutive overweight-obese workers (95M/274F, mean-age 45,2±12,3), examined in our "Obesity and work" Clinic, the prevalence of MS applying the AHA/NHLBI2005 criteria: waist circumference >88cm in females >102cm in males; triglycerides >150mg/dL and HDL cholesterol < 40mg/dL in males < 50mg/dL in females or therapy; fasting glycemia >100mg/dL and/or DT2 and/or therapy; arterial pressure >130/85 or therapy.The overall prevalence of MS was 37%, in particular 43/95 males (45%) and 93/274 females (34%) fulfilled the AHA/NHLBI 2005 criteria for MS diagnosis. In particular both male and female patients affected with MS were older and had a higher mean BMI, resulting, in this way, classified in a moderate obesity rank (BMI>35kg/m2).Waist circumference seemed to be the most frequent out of five criteria, followed by blood pressure, plasma glucose and lipids alterations. In conclusion our study showed a higher metabolic syndrome prevalence among our obese workers patients than the general population compared by age. We strongly suggest that, during periodic medical examinations, the occupational health physician should also measure waist circumference for a better identification of workers affected with metabolic syndrome and with elevated cardiovascular risk.

PREVALENCE OF METABOLIC SYNDROME IN A COMMUNITY OF THE ISLAND OF MAURITIUS

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Background: The metabolic syndrome is an important cluster of coronary heart disease risk factors with common insulin resistance. The extent to which the metabolic syndrome is associated with lifestyle factors in the Mauritian population is unknown.

Methods: Metabolic syndrome-associated factors and prevalence, as defined by WHO, are being evaluated a representative sample of adult Mauritians who participated in the national Non communicable Diseases survey carried out in 2004. This exercise is also extended to the cohort of persons attending a private health institution of a particular community

Results: First indications show that the metabolic syndrome is present in 35.7% and 28.9% of the community men and women, respectively (P = .88). Considering the four main ethnic groups in the population, the age-specific prevalence was highest in main ethnic group of both sexes. Ethnic differences persisted even after adjusting for age, body mass index, and socioeconomic status. The metabolic syndrome was present in 8.1%, 32.3%, and 81.1% of normal-weight, overweight, and obese adults, respectively. Older age, higher body mass index, high carbohydrate intake, and physical inactivity are associated with increased odds of the metabolic syndrome.

Conclusions: The metabolic syndrome is present in more than 30% of the adult population of the community and is associated with age, socioeconomic status, as well as with several potentially modifiable lifestyle factors. Identification and clinical management of this high-risk group is an important aspect and the role of the private health sector in the detection of metabolic syndrome in the population appears beneficial.

PREVALENCE OF METABOLIC SYNDROME IN POPULATION-BASED STUDY, VITÓRIA, ES - BRAZIL

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Metabolic Syndrome (MS) is a complex disorder including several factors predisposing to development of cardiovascular diseases and diabetes. Despite the importance of MS for the health system, the epidemiological characteristics of this condition in the Brazilian population are still scarce. The prevalence of MS as a function of gender, age and socioeconomic level was determined in a population-based study in Vitória/ES, Brazil by using the NCEP-ATPIII diagnosis criteria. Socioeconomic, biochemical, anthropometric and hemodynamic data were obtained in 1,663 individuals from a random sample of Vitória population (25-64 y). The estimated prevalence of MS was 29,8% (CI_{95} = 28-32%). No significant sex-related differences were observed. Prevalence increased from the youngest (26-34 y) to the oldest (55-64 y) group (15.8% and 48.3%, respectively). A progressive increase of MS frequency was observed in women from the higher to the lowest socioeconomic level**.** The most frequent trait of MS in males was high blood pressure, followed by hypertriglyceridemia, low HDL-c levels, hyperglycemia and central obesity. In females, hypertension was also the most frequent factor, followed by low HDL-c levels, abdominal obesity, hypertriglyceridemia and hyperglycemia. Our data show that prevalence of MS is high in the studied population, even in the youngest group. Moreover, high blood pressure gives a significant contribution to the diagnosis of this syndrome in both sexes. The precocious control of risk factors is necessary to reduce the impact of cardiovascular morbidity and mortality.

Keywords: Metabolic syndrome; Hypertension; Insulin resistance; Abdominal obesity.

PREVALENCE OF INSULIN RESISTANCE SYNDROME IN A PRIMARY HEALTH CENTRE IN KUWAIT

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Objectives and background: Insulin resistance syndrome (IRS) which represents a group of atherogenic risk factors has caused much concern over the past few years. People with IRS are at high risk of cardiovascular events. The aim of this study was to detect the prevalence of IRS in a primary health care centre in Kuwait.

Methods and subjects: The study was conducted in 2002; subjects were Kuwaiti individuals, ages 30-60 years. According to the National Cholesterol Education Program (NCEP) third report (ATP III) published in 2001; the diagnosis of IRS was based on the existence of three or more of the disorders that constitute the syndrome (insulin resistance, hypertension, low level of HDL-C, high levels of TG and central obesity). The screening included measurements of blood pressure, waist circumference, fasting plasma glucose, fasting triglycerides (TG) & high density lipoprotein cholesterol (HDL-C).

Results: Among 609 participants, 39.4% males and 60.6% females. The diabetic patients comprised 12% and the hypertensive patients 11.8%. Increased waist circumference was seen in 57.5%, IFG was detected in 13.6%, and high TG and low HDL-C were found in 46.5% and 56.0% respectively. The prevalence of IRS was 32.8%. Our results concluded that IRS was affected by the age group it was 26% in the ages 30-40 and 34.4% in the ages between 40 to 60.

Conclusion: IRS is highly prevalent among the Kuwaiti individuals attending our primary health centre in Kuwait. General practitioners need to have the skills necessary to properly identify and manage this high risk condition.

THE PREVALENCE OF METABOLIC SYNDROME AMONG EMPLOYEES

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Aims: To determine the prevalence of metabolic syndrome (MS) in employees of enterprises in Rostov-on-Don, Russia.

Methods: 2100 adults were involved in this study. Among these people there were 895 women (42,6 %) and 1205 men (57,4 %) with an average age of 49 years old (range 20 to 70). The diagnosis of MS was done according to International Diabetes Federation definitions.

Results: The general prevalence of MS was 49.8 % and 57,7% in men and 28,3% in women. The prevalence rose with age in both sexes, 4.8% among participants aged 20-29 years and 43% for participants over 60 years old (p for trend < 0.0001). There was a 14.7-fold increase in odds ratio for having MS in the age group > 70 years old in compassion with group of 20-29 years old (p < 0.0001). Hypertension (53%) and low high density lipoprotein and moderate hypertriglyceridaemia (38%) were the most common abnormalities in both sexes.

Conclusions: These results show that the MS is highly prevalent in employees and demonstrate the necessity to change lifestyle for preventing CVD.

GENDER CHARACTERISTICS OF INSULINEMIA IN THE DEVELOPMENT OF THE METABOLIC SYNDROME

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We studied 143 men and 83 women (average age 48,3±0,7 years old) with metabolic syndrome. Control groups include normotensive men and women without obesity and dislipidemia.

Groups of men and women were similar in a number of metabolic parameters (BMI, glycemia, hypercholesterolemia), however, they were different in the degree of abdominal obesity (waist circumference 99,86±1,28 and 88,96±2,07 respectively p< 0,001), triglyceride levels (2,21±0,17 and 1,56±0,10 mmol/l, p< 0,001) and α-cholesterol levels (1,29±0,04 and 1,54±0,08 mmol/l; p=0,022).

Men with metabolic syndrome had basal insulinemia levels (16,02±1,05 mked/ml) higher than in control group (9,88±0,34; p=0,026) for more than 3 σ (σ=1,7), that shows hyperinsulinemia. Comparing basal insulinemia in women with metabolic syndrome and group of control (9,62±1,90 and 6,20±0,87; p>0,05), showed only a tendency to hyperinsulinemia.

Basal insulinemia in men depended on BMI (r=0,34; p=0,047), waist circumference (r =0,66; p=0,004), and triglyceride levels (r=0,29; p=0,046). Basal insulinemia in women was correlated only with waist circumference: r=0,40 (p=0,02).

Revealed differences in the degrees and correlations of basal insulinemia with anthropometric and lipid parameters show different role of insulin in the development of the metabolic syndrome in men and women, and assign different methods of diagnostic hyperinsulinemia/insulin resistance. Basal insulinemia is a surrogate and acceptable marker of such in men. However, in women possibly it is necessary to measure insulinemia with loading tests, mathematical model or clamp-test. At the same time universality of basal insulinemia correlation with waist circumference shows the significance of such simple measurement in the diagnostic of the metabolic syndrome.

PREVALENCE OF THE METABOLIC SYNDROME AMONG ADULTS IN TUNISIA

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Objective: This study was aimed to determine the prevalence of metabolic syndrome (MS) and the association with socioeconomic level in the population of the Great Tunis.

Subjects and methods: This study included 2483 individuals; 958 male and 1525 females, aged 35 to 70 years dwelling the Great Tunis region, recruited between March 2004 and June 2005. The sample was weighted using the inverse of response rate according to governorate, district and sex. A metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III.

Results: The prevalence of MS 27.1% (33.2% vs 19.6%, p< 0.001) was significantly higher in women than men, abdominal obesity (69% vs 20%, p< 0.001), hypertension (50.3% vs 43.1%, p< 0.001) and low HDL-c (40.6% vs 33.6%, p< 0.001).Only a hyper triglyceridemia (31.2% vs 26%, p< 0.02) was higher in men. The prevalence of MS increased with age in both sex, but the increase was steeper in women In the age group 35-44 years, 13% of men and 20% of women had MS. In the age group 55 years and over, the prevalence were 28% and 51%, respectively. An inverse relationship was observed between level of education and prevalence of metabolic syndrome (p < 0.001).Prevalence was highest in illiterate people and lowest in people who graduated from universities. As education level increased, the prevalence of MS decreased.

Conclusion: The prevalence of MS is dramatically high in the population of the Great Tunis. These findings predict a future expansion of cardiovascular disease in this population.

COMPARISON OF METABOLIC SYNDROME PREVALENCE USING FIVE DIFFERENT DEFINITIONS IN A GROUP OF OBESE CHILDREN AND ADOLESCENTS

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As there is no unique definition of the metabolic syndrome (MS), the aim of this study was to analyse variations of the MS prevalence in obese youth, using five different definitions (IDF, Cook, de Ferranti, Cruz, Weiss). Prevalence of the MS according to proposed definitions was studied in 90 Croatian obese children and adolecents aged 10-18 years (mean age 13.1 years, 53 males, 37 females). Obesity was defined as WC >75th, ≥90th or BMI-Z score ≥2.0. Blood pressure, fasting triglycerides, HDL- cholesterol and glucose were determined in each subject, but different cut-offs were used as criteria for MS definition. OGTT was performed in order to detect impaired glucose tolerance. The prevalence of the MS varied significantly, being between 12% and 58% , depending on the definition used. Only 7 children fulfilled the criteria of the MS in all definitions. Since the prevalence of the MS varies widely in obese children and adolescents depending on the definition used, an internationally accepted definition of the syndrome is necessary to compare different populations and studies.

INSULIN RESISTANCE AND RISK FACTORS FOR CARDIOVASCULAR DISEASE IN YOUNG ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Aims: Determine the prevalence of insulin resistance and other risk factors for cardiovascular disease (CVD) in young adult survivors of childhood ALL.

Patients and methods: In this cross-sectional evaluation of 118 survivors of childhood ALL (median age, 23.0 years; range, 18-37), insulin resistance was estimated using the homeostasis model for assessment of insulin resistance (HOMA-IR). Gender-specific comparisons were made with a cohort of 30-37 year-old individuals from the same region participating in the Dallas Heart Study (DHS, N=782). ALL survivors were stratified by treatment with and without cranial radiotherapy (CRT).

Results: Female ALL survivors had a significantly higher HOMA-IR (CRT, mean 4.6, 95% confidence interval [95% CI] 3.6-5.7; no CRT, mean 3.3, 95% CI 2.8-3.8) in comparison with DHS women (mean 2.4, 95% CI 2.2-2.7). Eighty percent of women treated with CRT had at least three of six CVD risk factors and they were significantly more likely to have ≥ 3 risk factors compared with DHS women (odds ratio [OR] 5.96, 95% CI 2.15-16.47). Male ALL survivors had a significantly higher HOMA-IR (CRT, mean 4.0, 95% CI 2.8-5.6; no CRT, mean 3.4, 95% CI 2.9-3.9) in comparison with DHS men (mean 2.3, 95% CI 2.1-2.6), but were not more likely to have multiple CVD risk factors.

Conclusions: ALL survivors had an increased prevalence of insulin resistance in comparison with a cohort of older individuals from the same community. Importantly, women treated with CRT appear to have an increased prevalence of multiple CVD risk factors warranting close monitoring and risk-reducing strategies.

OPTIMAL WAIST CIRCUMFERENCE AND VISCERAL ADIPOSE TISSUE AREA FOR IDENTIFYING RISK FOR THE METABOLIC SYNDROME IN LARGE GENERAL POPULATION

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Background and aim: Central obesity is considered to play a key role in the metabolic syndrome (MS). It was not known about the optimal cut point values for central and visceral adiposity to identify Koreans at risk for the MS. We have investigated the appropriate visceral adipose tissue (VAT) cut-off values for predicting MS factors in the Korean general population.

Methods: Study subjects included 3,233 healthy subjects. The non-adipose variables of the MS were defined using NCEP-ATP-III, and the accuracy of identifying at least two of these by VAT area as measured by computed tomography and waist circumference was assessed using area under receiver operating characteristic (AUROC) curves.

Results: In men, the prevalence of MS was 26.5% and in women that was 22.3%. AUROC curve for VAT exceeded that for waist circumference (men 0.695 vs. 0.661; women 0.770 vs. 0.719). In men, AUROC for diagnosing MS decrease in the order of HOMA index (0.740), VAT, waist circumference, body mass index (0.639) and in women ,VAT, HOMA index (0.753), waist circumference, body mass index (0.504). For women, the optimal cut points for VAT and waist circumference were 84.5 cm^2 and 82.2 cm. For men, the optimal cut points for VAT and waist circumference were 138.5 cm^2 and 88.3 cm.

Conclusions: VAT cut-offs of 138 cm^2 in men and 85 cm^2 in women are useful for defining visceral obesity in Korean subjects. Appropriate waist circumference cut points are from 88.3 cm in men and 82.2 cm in women.

PARTICULARITIES OF METABOLIC SYNDROME AND CORONARY HEART DISEASE IN WOMEN PERI AND AFTER MENOPAUSE

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Purpose: This study assessed the metabolic syndrome within a selected female population, represented by women admitted to Medical ClinicIII, between 2004-2008 and the relation between coronary heart disease and the metabolic syndrome.

Material and method: We included in our study patients with chest pain, multiple cardiovascular risk factors, alteration of ECG and grouped them into two categories: 220 women before menopause averaging 49±3.2 and 240 women after menopause averaging 59±3.2 years of age. The metabolic syndrome was diagnosed according to the ATPIII and IDF criteria.

Results: From the women included in the study 36%(p=0.007), had metabolic syndrome in the group perimenopause and 54%(p=0.1) in the menopause group. Patients had a waste circumference 92±4cm in perimenopause and 98±6cm after. Metabolic syndrome components were present in the group before and after menopause as follows: hypertension 92% vs.94%, diabetes mellitus 28% vs.38%, low HDL cholesterol 87% vs.97% and high triglyceride 65% vs.91%.Coronary disease in patients with metabolic syndrome was encountered in 57% in perimenopause and 65% after menopause(p=0.0049). Angiography results in the groups before and after menopause were: single vessel disease 43.3% vs.48%, multiple artery disease 43% vs.44%.

Conclusion: The prevalence of the metabolic syndrome increases significantly after menopause(p=0.00008). In women with metabolic syndrome coronary disease was significantly higher after menopause, with coronary damage mainly explained by the increase of obesity and triglyceride values, due to the loss of the cardiovascular protection offered by estrogens. Women with metabolic syndrome present an increased cardiovascular risk, higher than the sum of its components.

CARDIO-METABOLIC RISK CLUSTERING IN AUSTRALIAN MEN: HOW IMPORTANT ARE ABDOMINAL FAT AND TESTOSTERONE?

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Objective: To examine cardio-metabolic risk factor clustering in Australian men and determine the contribution of abdominal fat and serum testosterone to clustering and HbA1c levels.

Design: Cross-sectional analysis using: Expectation Maximization clustering to define risk sub-populations; non-iterative partial least squares to determine the important contributors to clustering; and structural equation modeling to test abdominal fat, testosterone and HbA1c interactions.

Setting: Florey Adelaide Male Ageing Study (FAMAS) cohort; north and west suburbs of metropolitan Adelaide, South Australia.

Participants: Population-based sample of men aged 35 to 80 years at baseline. 1195 men (45.1% response rate) attended study clinics. Men taking medications influencing androgen levels (N=26) were excluded, leaving 1169 men for this analysis.

Methods: Resting blood pressure was measured after 5-minutes seated. Total testosterone, glucose, insulin, triglycerides, total cholesterol and HDL were measured in fasting morning serum and HbA1c in whole blood. HOMA-IR was calculated. Abdominal fat was assessed from whole body DEXA scans.

Results: Clustering revealed three populations of progressively increasing risk representing 36%, 53% and 11% of the population. Clustering was explained by HbA1c, HOMA-IR, SHBG, insulin, abdominal fat (component 1, $R^2Y=0.303$) and diastolic BP, HDL-c, testosterone, triglycerides, total cholesterol (component 2, $R^2Y=0.235$). Most plausibly, abdominal fat affects HbA1c levels indirectly through insulin. Reduced testosterone and SHBG are likely a result of increased HbA1c and abdominal fat respectively.

Conclusions: Low testosterone and SHBG are likely markers, but not drivers of poor glycaemic control. Population reduction in abdominal fat should be the major goal for diabetes risk reduction in men.

THE SIMETRIC SPANISH PROJECT (METABOLIC SYNDROME AS CARDIOVASCULAR RISK FACTOR). CLINICAL USEFULNESS OF DIFFERENT CALCULATION METHODS OF STROKE RISK IN PRIMARY CARE

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Cerebrovascular risk (CVR) has multiple methods of calculation. Nevertheless, their application is not uniform in primary care.

Objective: Esteeming what method predicts better the CVR in patients assisted in primary care.

Design and location: Cohorts study, with 10-year follow-up, in primary care, based in an urban randomized representative sample.

Measurements: CVR esteemed according to: Framingham score; algorithm of the ARIC study (Atherosclerosis Risk In Communities) and of the UKPDS (United Kingdom Prospective Study Diabetes). Of an aleatory sample formed in 1998 to study the Metabolic Syndrome (MS) (NCEP criteria (National Cholesterol Education Program); n=1489) we selected individuals between 54-85 years (applicable margin) without stroke, evaluating sociodemographic data, MS components and cardiovascular risk factors: systolic blood pressure, hypertension drug treatment, cardiovascular disease (angina, myocardial infarction, peripheral arteriopathy), atrial fibrilation, left ventricular hypertrophy, type 2 diabetes and smoking habit. Statistical analysis: comparison between scores and confirmed strokes of each method according to events, by means of ANOVA.

Results: 726 subjects (66.4±7.4 years) were analyzed, 409 (56.3%) women. From them, 175 were diabetics (24.1%), fulfilling 228 (31.4%) MS criteria. In the 10 years of current follow-up were registered 58 cases of cerebrovascular disease (31 men). The comparison of averages of the result of the CVR between the subgroup with stroke in front of the subgroup without it, was respectively: ARIC 5.1/2.9 ($p< 0.001$) (range:0.4-19.1); UKPDS 20.2/13.6 ($p=0.018$) (range:2.9-83.1) and Framingham 17.4/10.8 ($p< 0.001$) (range:1.0-79.0).

Conclusions: In Primary Care, Framingham and ARIC scores were those that predict better the CVR. UKPDS score also predicts it in diabetic population.

DOES METABOLIC SYNDROME ALSO MEAN PROBLEMS WITH MENTAL DISORDERS AND COGNITIVE IMPAIRMENT?

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Objectives: There has been some evidence about relationship between metabolic syndrome (MetS) and mental disorders or cognitive dysfunctions. The aim of our study was to examine prevalence of depression, other mental disorders, particularities of cognitive functions, and cross-sectional relationship between measured variables in patients with MetS.

Method: 55 type 2 diabetic patients (29 female, 26 male) with MetS aged 44-82 (M=65,63±9.84) from diabetic outpatients clinic were included in the study. Data were assessed using Hamilton Depression Inventory (HDI), Symptom Checklist-90-Revised (SCL-90-R), Repeatable Battery for the Assessment of Neuropsychological Status, Stroop Test, and Tower of London. Sociodemographic data were controlled.

Results: The prevalence of clinically relevant depression (HDI≥19) was relatively high: 14,5% of the sample. Scores of scl-90-R were significantly higher (t=5,637; $p< 0,05$) in our patients compared to the normative sample (healthy USA sample), and also in all its subscales.

There were significantly declines ($p< 0,05$) from the norms with respect to lower general cognitive functioning (t=-5,573), immediate (t=-6,187) and delayed (t=-3,741) memory, attention (t=-5,898), language (t=-4,057), speed of cognitive processing (t=-8,156) and executive functioning (t=--2,870). There was no association between mental disorders and cognitive functions.

The women had more expressed symptoms of mental disorders (t=1,978), and lower scores of executive functions (t=-2,674) and immediate verbal memory (t=-2,113).

Conclusions: Patient with MetS have a higher prevalence and intensity of symptoms of mental disorders, and somewhat lower cognitive abilities, but there is no special relationship between these variables. The study is limited due to the unavailability of national norms.

GLUCOCORTICOID RECEPTOR GENE VARIANTS AS POTENTIAL PREDICTORS OF METABOLIC SYNDROME IN HEALTHY POPULATION

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Introduction: Glucocorticoids (GCs) play important role in energy metabolism and they modulate a number of physiological systems. GCs effect is accomplished through binding to glucocorticoid receptor (GR). Level of GR expression is proportional to glucocorticoid response. Presence of some GR gene polymorphisms can modulate GCs effects.

Objective: In this study we investigated the possible relation between *Bcl*I, N363S, ER22/23EK and A3669G polymorphisms in GR gene in 221 healthy volunteer (143 men, 78 women; mean age 42.33 ± 10.23 and mean BMI 26.29 ± 3.91) recruited from the National Blood Bank Register, and their metabolic profile and body composition.

Materials and methods: DNA was extracted from peripheral blood leucocytes. Genetic testing was performed using PCR-RFLP, allele-specific PCR and DNA sequencing. Detail biochemical, anthropometric and endocrine testing were also performed.

Results: *Bcl*I polymorphism was detected in 53 (23.9 %) healthy volunteers, N363S in 8 (3.6 %), ER22/23EK in 2 (0.9 %) and A3669G in 19 (8.6 %). Only in subjects with *Bcl*I polymorphism some significant differences in body composition and metabolic parameters ($p< 0.001$ for all) were found. These individuals had significantly elevated cholesterol levels and higher waist circumference, comparing to non-carriers.

Conclusion: Presented findings suggest that, only *Bcl*I variant of GR gene can be associated with metabolic risk factors. In that way presence of *Bcl*I polymorphism in our study population, can be considered as potential predictor of metabolic syndrome.

ROLE OF PREHEPARIN LIPOPROTEIN LIPASE MASS AS A BIOMARKER IN KOREAN METABOLIC SYNDROME SUBJECTS

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Background: Metabolic syndrome, characterized by a cluster of symptoms including abdominal obesity, hypertension and dyslipidemia, is a common underlying condition for cardiovascular disease. Lipoprotein plays a central role in lipid metabolism and transport by catalyzing the hydrolysis of triglyceride-rich liporpteins.

Methods: To prove the relationship between the major symptoms of metabolic syndrome and preheparin LPL mass, we recruited 374 subjects from Seoul Medical Center. Measurements included anthropometrics, blood biochemistries, and the factors related reverse cholesterol transport(RCT) such as lecithin:cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein(CETP), lipoprotein lipase(LPL), apo C-II and apo E after screening by the modified criteria for Korean MetSyn.

Results: We observed an apparently higher preheparin LPL level in women than in men. The increase in number of symptoms tended to lower both the mean levels of LPL mass and plasma adiponectin. The correlation between LPL and adiponectin level was found to be strongly significant. LPL mass correlated positively with HDL, and negatively with body weight, waist circumference and TG. These results suggest that LPL mass might be a marker for insulin resistance, and lipid metabolism and the control of body weight and fat.

Conclusions: Among metabolic syndrome subjects, LPL mass may be a marker of metabolic syndrome and may indicate the severity of metabolic syndrome.

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RELATIONSHIP BETWEEN VITAMIN D STATUS AND METABOLIC SYNDROME (METSYN)

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Aim: MetSyn has been associated with vitamin D status. We evaluated whether the vitamin D status, and vitamin D and calcium intakes are related to MetSyn in adult population in Sao Paulo, Brazil.

Methods: 339 people (68% women) was included. An overnight blood sample, and anthropometric measurements (weight, height, waist circumference) were obtained. Nutrient intakes were evaluated by 24h dietary record and analyzed at Nutrition Data System software. The MetSyn was defined by NCEP-ATP III criteria. Serum levels of 25(OH)D was measured by HPLC, iPTH and serum calcium by standard methods. Vitamin D insufficiency was defined as £ 75nmol/L. The results are presented as mean (SD), and significance level was $p < 0.05$. Student t test and chi-square test were used.

Results: MetSyn was found in 50% of the sample. Calcium and vitamin D intakes were similar in both groups. Calcium 589(330) vs 600(377)mg/day; vitamin D 2.9(2.1) vs. 2.8(1.8)µg/day, with and without Metsyn respectively. Comparing individuals without and with MetSyn, a significant higher age 48(16) *vs.* 56(13) years, BMI 27(6) *vs.* 32(6)kg/m^2 and waist circumference 93(14) *vs.* 104(13)cm, iPTH 42(18) vs. 49(23)pg/ml and serum calcium 9.3(0.6) vs. 9.4(0.5)mg/dl was observed in individual with MetSyn. Vitamin D insufficiency was present in 89% of the participants, and was more prevalent in patients without MetSyn (53%) than with MetSyn (47%) (X^2=11.2, $p< 0.01$).

Conclusion: The analysis demonstrates a positive association between MetSyn and vitamin D status, which is different from previous studies. The heterogeneity of our sample, in part could explain this finding.

PROXIMAL TUBULAR DYSFUNCTION IN INDIVIDUALS WITH RENAL HYPOURICEMIA

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Background: Increasing evidence suggests that uric acid may play a role in the metabolic syndrome. Primary renal hypouricemia refers to a rare condition of low serum urate levels and increased renal urate clearance. ^{1}H NMR spectroscopy of urine provides overall profiles of low molecular weight metabolites that are significantly altered in situations where renal damage is present.

Methods: The study group consisted of 36 unrelated asymptomatic subjects with primary renal hypouricemia, defined as serum uric acid levels (sUA) < 2.5 mg/dL and fractional excretion of uric acid (FEUA) >10%, after exclusion of diseases and drugs that may affect urate homeostasis. We also studied 39 sex- and age-matched healthy individuals with normal sUA levels (>4.0 mmol/L) and FEUA< 10%.

Results: Individuals with primary hypouricemia presented with similar biochemical profiles to those observed in the control group without significant differences with regard to FE of electrolytes and renal threshold for phosphate excretion. Individuals with primary hypouricemia were differentiated from healthy individuals in the Orthogonal Signal Correction Partial Least-Squares-Discriminant Analysis (OSC/PLS-DA) models of the NMR data. The components contributing to this separation were the lower levels of hippurate, creatinine and trimethylaminoxide, and the higher levels of phenylalanine, alanine, glycine, glutamate, acetate and of an unidentified metabolite (3.3 ppm) observed in hypouricemic subjects compared with control group.

Conclusions: Our study showed that primary renal hypouricemia is often associated with a more generalized proximal tubular disorder mimicking a partial Fanconi syndrome.

PREMETABOLIC SYNDROME: CAN THE DEVELOPMENT OF THE METABOLIC SYNDROME BE PREDICTED?

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Aims: Identifying parameters that could lead to the development of the Metabolic Syndrome (MetS) in a low risk population, would allow for the innovation of new strategies that could prevent the MetS. This study was undertaken to indentify factors that lead to MetS and so categorise a higher-risk group with a premetabolic syndrome.

Methods: In this study 204 subjects were screened prior to 2004 and identified as not having MetS. Over the next four years those who developed the MetS were obsevered and data was analysed comparing differences between the two groups on information collected prior to 2004.

Results: In the group (males 80 (39.2%), mean age 67.4 yrs (SD ±10.4, range 36.2-91.2)), 59 (28.9%) developed the metabolic syndrome. There

were no significant differences in age, BMI and blood pressure in the two groups. There was a significant difference in HDL (negative MetS 1.66 mmol/L (SD±0.37, range 1.04-3.07) vs developed MetS 1.42 mmol/L (SD±0.27, range 0.88-2.13, $p< 0.05$), and also for triglycerides ($p< 0.05$) and waist circumference (WC) ($p< 0.05$). When the sexes were analysed separately the significance was not maintained for WC in males or triglycerides in females.

Conclusions: MetS appears to be driven by the development of central obesity in females and dyslipidaemia in males. Targeting interventions at these will have the greatest impact in reducing the progression to the MetS. However screening negative for the MetS does not necessarily identify a population at low risk of developing cardiovascular complications or progressing to diabetes.

RELATIONSHIPS OF PLASMA ALDOSTERONE WITH LEFT VENTRICULAR MASS IN HYPERTENSIVE PATIENTS WITH THE METABOLIC SYNDROME

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The aim of our study was to evaluate the relationships of plasma aldosterone to metabolic syndrome and left ventricular mass in nondiabetic Caucasian patients with essential hypertension.

Measurements were obtained with patients off antihypertensive medications and included 24-hour blood pressure monitoring, plasma renin activity and aldosterone, and an echocardiogram.

Compared with subjects without the metabolic syndrome (n = 249), those with the metabolic syndrome (n = 201) had higher levels of age-adjusted plasma aldosterone (101.9 ± 58 vs 116.1 ± 59 pg/ml; $p = 0.01$) and greater left ventricular mass indexed for body surface area (97 ± 31 vs 106 ± 34 g/m^2; $p = 0.006$). The difference regarding plasma aldosterone between the two groups was independent from plasma renin activity and was chiefly explained by obesity. In patients with and in those without the metabolic syndrome, left ventricular mass correlated significantly with plasma aldosterone ($p < 0.005$). In the group with the metabolic syndrome, this association remained statistically significant ($\beta= 0.24$; $p = 0.001$), after adjustment for various potential confounders, including body mass index and blood pressures, in multiple regression analyses. In the group without the MetS, the same relationship became of borderline statistical significance.

Our results suggest that the elevated levels of aldosterone may help to explain the increased left ventricular mass observed in the subjects with the metabolic syndrome and, in this way, may contribute to enhance the cardiovascular risk associated with the metabolic syndrome.

COMPARISON OF METABOLIC SYNDROME WITH GLUCOSE MEASUREMENT FOR PREDICTION OF TYPE 2 DIABETES: THE ISFAHAN DIABETES PREVENTION STUDY

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Objective: Both metabolic syndrome (MetS) and impaired glucose regulation identifies high risk individuals for diabetes. Therefore, the aim of this study was to compare the ability of the MetS and impaired glucose regulation to predict progression to diabetes in non-diabetic first-degree relatives (FDR) of patients with type 2 diabetes.

Research design and methods: A total of 706 non-diabetic FDR 20-70 years old in 2003 to 2005 were followed through 2008 for the occurrence of type 2 diabetes mellitus. At baseline and through follow-ups, FDR were underwent a standard 75 g 2-h oral glucose tolerance test. MetS was defined by NCEP ATPIII.

Results: The fasting and 2-h glucose values were better predictors of progression to diabetes than MetS. Compared to FDR without MetS, the age-adjusted relative risk (RRs) of diabetes was similar for FDR with metabolic syndrome (1.09 (95% CI 0.92, 1.29)). The age adjusted relative risk of diabetes among those with impaired glucose tolerance and MetS was 1.89 (95% CI 1.47, 2.42) and among those without MetS was 1.59 (95% CI 1.32, 1.91). Areas under the receiver-operating characteristic curves were 0.789 for fasting plasma glucose and 0.760 for 2-h glucose vs. 0.595 for number of metabolic abnormalities ($P< 0.001$).

Conclusions: These data indicate that a single fasting glucose measurement or impaired glucose regulation may be more effective and efficient than MetS in predicting progression to diabetes.

NEONATES FROM THE MÉRIDA COHORT WITH HIGH INSULIN LEVELS ARE CANDIDATE FOR FUTURE INSULIN RESISTANCE AND METABOLIC SYNDROME

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Background: Insulin sensitivity is usually described as the ability of insulin to lower plasma glucose levels while insulin resistance describes an impaired biological response to insulin. Low birth weight has being related to insulin resistance but to the best of our knowledge insulin resistance/sensitivity in normoweight neonates has not been tested yet.

Aim: To study how high insulin levels at birth can affect the insulin sensitivity and insulin resistance in normoweight neonates.

Methods: Quantitative Insulin Sensitivity Check Index (QUICKI) and some Homeostatic Model Assessment (HOMA)-related equations, proposed as indicators of insulin sensitivity (HOMA-S), insulin resistance (HOMA-R), insulin secretion (HOMA-B) and glucose availability (HOMA-D) were evaluated in 197 singleton, normoweight, without foetal distress Spanish Caucasian neonates of the Mérida (Spain) Birth Cohort. References for neonatal markers were used (1).

Results: Neonates having high insulin (> P75, 6.0 μUI/mL) were compared with neonates with low insulin levels (< P25, 1.8 μUI/mL). Birthweight, BMI, Glucose, IGF-I, the insulin/cortisol ratio, HOMA-R and HOMA-D were significantly higher while GH, QUICKI, the glucose/insulin ratio and HOMA-S appeared significantly lower in newborns with high insulin levels. 45% of these neonates presented insulin levels higher than 15 μUI/mL while 43% presented HOMA-R higher than the P75 (4.09) of neonatal reference values.

Conclusion: A large percentage of the neonates with high insulinemia, despite being full term and normoweight infants, are likely candidates to develop insulin resistance and, thus, metabolic syndrome later in life.

ROSUVASTATIN IS ASSOCIATED WITH FEW IMPROVEMENTS IN COMPONENTS OF THE METABOLIC SYNDROME, WITH NO CHANGE IN INSULIN RESISTANCE, IN RENAL TRANSPLANT RECIPIENTS

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Aims: Insulin resistance and the constellation of cardiovascular disease risk factors that constitute the metabolic syndrome (MS) are common post-transplantation. The lipid-lowering and pleiotropic benefit of statins may influence insulin sensitivity and directly and/or indirectly modify these risk factors. We conducted a randomized controlled trial to assess the value of rosuvastatin treatment in renal transplant recipients.

Methods: 20 renal transplant recipients were recruited into this randomized, double blind, placebo controlled crossover study. Patients received rosuvastatin 10mg or placebo daily for 12 weeks after which clinical/biochemical profiles and insulin sensitivity was determined, the latter by minimal model analysis of an intravenous glucose tolerance test. After washout, patients crossed over to the opposite arm and investigations repeated after 12 weeks. MS was defined by ATP III criteria.

Results: Rosuvastatin led to significant decreases in triglycerides (-19%, $p = 0.013$). No other significant changes were noted: systolic BP (+1%, p = NS), diastolic BP (+1%, p = NS), HDL cholesterol (+8%, p = NS), waist circumference (no change, p = NS) and fasting glucose (no change, p = NS). No significant change in insulin sensitivity was noted (-8%, p = NS), despite significant decreases in lipid levels (total cholesterol: -30%, $p < 0.001$, LDL cholesterol: -44%, $p < 0.001$ and triglycerides) and non-significant decrease in anti-inflammatory markers (CRP: -31%, $p = 0.097$).

Conclusions: Rosuvastatin failed to make an impact on many components of the MS or insulin resistance. Further work and clarification is required into the utility of MS diagnosis and treatment post-transplantation.

POOR CORRELATION BETWEEN INSULIN RESISTANCE INDEXES AND INSULIN SENSITIVITY IN NON-DIABETIC RENAL TRANSPLANT RECIPIENTS MAINTAINED ON TACROLIMUS TREATMENT

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Aims: Insulin resistance is common post-transplantation and combines with declining insulin secretion to cause new-onset diabetes after transplantation. Various insulin resistance indexes have been validated in non-diabetic renal transplant recipients on cyclosporine treatment. Similar validation has not been obtained in transplant recipients on tacrolimus, which is more diabetogenic. This study aimed to validate various insulin resistance indexes against insulin sensitivity in non-diabetic renal transplant recipients on tacrolimus treatment.

Methods: Fasting insulin, fasting glucose:insulin ratio, homeostatic model assessment (HOMA), quantitative insulin sensitivity check index (QUICKI) and McAuley's index were assessed for correlation against insulin sensitivity as derived by mathematical minimal model analysis from an IVGTT. Pearson or Spearman's correlation was used for parametric and non-parametric analysis respectively. A p value < 0.05 was considered statistically significant.

Results: All insulin resistance indexes analysed in this study failed to correlate significantly with insulin sensitivity as derived from the IVGTT: fasting insulin ($r = -0.033$, p = NS), fasting glucose:insulin ratio ($r = 0.018$, p = NS), HOMA ($r = -0.065$, p = NS), QUICKI ($r = 0.057$, p = NS) and McAuleys index ($r = 0.009$, p = NS). All indexes correlated significantly with each other index (all $p < 0.001$).

Conclusions: We have demonstrated poor correlation between various surrogate estimates of insulin resistance, previously validated in non-diabetic cyclosporine treated renal transplant recipients, in non-diabetic renal transplant recipients maintained on tacrolimus as a primary immunosuppressant. Further work is required to find a validated simple tool to estimate insulin resistance in these patients.

CO-ADMINISTRATION OF SARTANS WITH DIFFERENT DEGREE OF PPARΓ ACTIVATING CAPACITY PLUS ROSUVASTATIN IN PATIENTS WITH MULTIPLE METABOLIC RISK FACTORS

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Aims: Sartans differ with regard to their peroxisome proliferator-activated receptor γ (PPARγ) activating capacity. We sought to evaluate whether this property is clinically relevant when co-administrating a sartan with a statin.

Methods: 45 patients with mild hypertension, impaired fasting plasma glucose (FPG), elevated triglyceride (>150 mg/dl) and low density lipoprotein cholesterol levels (>160 mg/dl) were given dietary intervention and rosuvastatin (10 mg/day). Patients were randomized to:

1) a sartan which partially activates PPARγ (telmisartan 80 mg/day),

2) a sartan with low efficacy in activating PPARγ (irbesartan 300 mg/day) and

3) a sartan with no efficacy in activating PPARγ (olmesartan 20 mg/day).

Patients were re-evaluated 3 months after treatment onset.

Results: All measured parameters had similar baseline values between groups. Systolic and diastolic blood pressure was similarly reduced in all 3 groups. FPG and glycated hemoglobin (HbA1c) levels were not significantly altered in any group. However, homeostasis model assessment (HOMA) index (i.e. a marker of insulin resistance) significantly decreased by 19% ($p < 0.05$) in the telmisartan group, but showed a non-significant trend to increase in the irbesartan (19%) and olmesartan (24%) groups ($p < 0.05$ for the comparison between telmisartan vs the other 2 groups). No significant changes in lipid parameters were observed in the 3 groups.

Conclusions: Co-administrating rosuvastatin with different sartans regarding their PPARγ activating capacity was not associated with differential changes in blood pressure, FPG, HbA1c or lipid parameters. However, only the rosuvastatin-telmisartan combination was associated with a decrease in HOMA index.

OSTEOPROTEGERIN AND LEPTIN CONCENTRATION ARE INCREASED IN MIDDLE-AGED WOMEN WITH A METABOLIC SYNDROME

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Osteoprotegerin (OPG) is a humoral osteoclast activation inhibitory factor. Leptin is thought to be involved in bone metabolism too, acting as an inhibitor of bone formation.

The aim of the present study was to establish relationships of these two parameters and varaibles characterizing the diabetic facette of the MetS. Among middle - aged women (40-65 years) of the PSYRECA arm of the DRECAN_2005 survey the prevalence of the MetS was 20% . 43% of them were diabetics (known / treated or f-P-glucose >7.2 mmol/L) or prediabetics (f-P-glucose >5.6 mmol/L), 42% were insulin resistant (HOMA-IR>2,5).

OPG concentration but not leptin concentration was age dependent. Concentration of OPG and leptin were not correlated. Both variables were significantly higher among women with a MetS: OPG 5,27±1,73 vs. 4,35± 1,48 pmol/L ($p < 0,01$); leptin 24,82±12,31 vs. 15,65±9,47 ng/ml ($p < 0,05$). In contrast to leptin (23,52±13,16 ng/ml vs. 15,54±8,59 ng/ml ($p < 0,001$) there was no significant difference in serum OPG concentration among women with low fasting P-glucose and women with impaired fasting glucose (5,6-7,1 mmol/L): 4,41±1,59 pmol/L vs. 4,85±1,52 pmol/L).

Both OPG and leptin were correlated with f-P-glucose (r=0,183 / 0,360; p < 0, 05 / 0,001), f-Insulin (r =0,264 / 0,513, P< 0,001) and HOMA-IR (r=0,283 / 0,536; p< 0,001).

The presence of a Mets among middle aged women of the DRECAN study was associated independently with higher serum concentration of OPG (κ=0, 15*, 33%) and leptin (κ=0,179**; 49%). Both were significantly correlated with HOMA-IR (κ=0,235**; 48% / κ=0,243***; 52%).

NUMBER OF CHILDREN AND RISK OF METABOLIC SYNDROME IN IRANIAN WOMEN

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Introduction: More than one third of Iranian adult women have the metabolic syndrome. We conducted this study to assess the effect of parity on the prevalence of metabolic syndrome in analyses controlling for sociodemographic and reproductive variables as well as behavioral risk factors.

Methods: We evaluated the relationship between number of children and metabolic syndrome in 6331 adult non-pregnant women >20 years of age. The data source for this study was Isfahan Helthy Heart Program (IHHP). Metabolic syndrome was defined according to Adult Treatment Panel (ATP) III.

Results: Overall, 34.2% of women met the criteria for metabolic syndrome. The number of childbearing in women with metabolic syndrome was significantly higher than others (5.2±3.1 vs. 3.5±2.6, p< 0.0001). In logistic regression analyses, the odds of metabolic syndrome increased 24% (95% CI 22%-26%) with each additional child, but after adjustment for sociodemographic, reproductive and behavioral characteristics, the odds of metabolic syndrome was attenuated (OR 1.03, 95% CI 1.00-1.06). Further adjustment for BMI yielded similar results (OR 1.02, 95% CI 0.98-1.05).

Conclusion: A combination of lifestyle risk factors and/or biological changes associated with childbearing may explain the positive association between parity and increased risk of metabolic syndrome.

Keywords: Metabolic syndrome, parity, women, age, BMI.

STUDY ON THE IMPROVEMENT OF METABOLIC SYNDROME FACTORS AND PREVENTION OF REBOUND WEIGHT GAIN AFTER WEIGHT REDUCTION USING FORMULA DIET (MICRO-S)

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Background: No study has focused on th management of rebound weight gain after successful use of formula diet. This study examined rebound weight gain after weight reduction using MICRO-S formula diet and considered ways to prevent it.

Method: The subjects consumed MICRO-S in place of a meal every day for 12 weeks. The subjects who achieved 5% weight resumed 3 normal meals and were monitored for the subsequent 24 weeks. Those who gained 3% or more above the body weight attained through weight reduction were subjected to another 12-week randomized controlled test, divided into the normal meal group and the MICRO-S group.

Results: The results for the 29 subjects after the 12-week weight reduction period showed significant decreases in body weight from 73.8±10.1 to 68.3±9.6 kg (p< 0.001), BMI from 28.8±3.4 to 26.6±3.1 kg/m^2 (p< 0.001), waist circumference from 93.2±9.9 to 87.2±8.9 cm (p< 0.001), and body fat percentage from 73.8±10.1 to 68.3±9.6% (p< 0.001). Systolic and diastolic blood pressures also decreased significantly. AST, ALT, FBS and TG showed significant decreases. As a result, the occurrence of metabolic syndrome factors significantly decreased (p< 0.05), and the number of patients having metabolic syndrome dropped from 5 to 2. The results of the eating behavior questionnaire showed significant decreases in substitute eating, eating rhythm abnormalities and total score.

Conclusion: Significant weight reduction was achieved using formula diet through behavior modification, improved glucose and lipid metabolism and hypertension, and reduced metabolic syndrome factors. We are continuing further studies on minimizing rebound weight gain.

CT-SCAN DERIVED MUSCLE FAT INFILTRATION INDICES IN RELATION TO THE METABOLIC SYNDROME AND INSULIN SENSITIVITY IN POSTMENOPAUSAL WOMEN

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This study explored the relationship between muscle fat infiltration derived from midthigh ct-scan, regional fat distribution and metabolic measures in postmenopausal women.

Using mid-thigh CT scans, the surface of muscle with low attenuation (0-34 HU) represented the specific component of fat-rich muscle. Insulin sensitivity (M/I) was evaluated by an euglycemic-hyperinsulinemic clamp. Multiple metabolic measures were also obtained.

A group of 103 women aged 57.0 ± 4.4 yrs (BMI: 28.0 ± 4.6 kg/m^2) was studied. The metabolic syndrome (MS) was found in 39 women who presented, as expected, higher levels of waist circumference, total, subcutaneous abdominal and visceral AT (VAT) (P < 0.005). They also had significantly higher levels of low attenuation muscle surface (LAMS) compared to those without the MS (27.7 ± 1.1 vs 22.6 ± 0.9 cm^2, P < 0.001). Moreover, women with the MS displayed significantly lower insulin sensitivity (M/I) but a similar insulin secretion. To further study the impact of muscle fat infiltration on metabolic parameters, we divided the whole group based on the median of LAMS and VAT. The worst metabolic profile was found in the High-LAMS/High-VAT group and the best in the Low-LAMS/Low-VAT group. Women with Low-LAMS/High-VAT were more insulin resistant, presented higher FFA levels, glycemia and c-peptide values compared to the High-LAMS/low-VAT group.

Although increased muscle fat infiltration was related to a deteriorated metabolic profile, visceral adipose tissue appears as a more important contributor to alterations in glucose-insulin homeostasis in postmenopausal women.

VITAMIN D SUPPLEMENTATION REDUCES INSULIN RESISTANCE IN WOMEN WHO ARE INSULIN RESISTANT AND VITAMIN D DEFICIENT

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Background: Low serum 25(OH)D_3 has been shown to correlate with increased risk of type 2 diabetes. Small, observational studies suggest an action for vitamin D in improving insulin sensitivity and/or insulin secretion.

Objective: To investigate the effect of improved vitamin D status on insulin resistance.

Study design: Randomised controlled double-blind intervention administering 4000 IU 25(OH)D_3 (n=42) or placebo (n=39) daily for 6 months to South Asian women, aged >20 years, living in Auckland, New Zealand. Subjects were insulin resistant (HOMA-IR >1.93) and had serum 25(OH)D_3 concentration < 50 nmol/L. Exclusion criteria included diabetes medication and vitamin D supplementation > 1000 IU/day. The HOMA2-IR computer model was used to calculate insulin resistance, secretion and sensitivity.

Results: A significant improvement was seen in insulin sensitivity and insulin resistance (P = 0.003, P = 0.02 respectively), and insulin secretion decreased (P = 0.04) from baseline to end with supplementation compared to placebo. Insulin resistance was most improved when endpoint serum 25(OH)D_3 ≥80 nmol/L. Median (25^{th}, 75^{th} percentile) serum 25(OH)D_3 increased significantly from 21 (11, 40) to 75 (55,84) nmol/L with supplementation and also in the placebo group from 22 (15, 32) to 32 (24, 36) nmol/L probably due to seasonal variation.

Conclusion: Increasing serum vitamin D levels in insulin resistant (but not diabetic) women resulted in decreased insulin resistance, improved insulin sensitivity and subsequently reduced demand for insulin secretion. Optimal vitamin D concentrations for protection against insulin resistance were shown to be ≥80 nmol/L, providing further evidence for increasing the minimum adequate levels.

THERAPEUTIC POTENTIAL OF PARTIAL A_1 ADENOSINE RECEPTOR AGONISTS IN INSULIN RESISTANCE

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Elevated levels of circulating free fatty acids (FFA) play an important role in the pathogenesis of insulin resistance and diabetes. Lowering FFA levels by reduction of lipolysis in adipocytes may be of potential benefit in treatments of dyslipidemia and type II diabetes. A_1 adenosine receptor (A_1AdoR) agonists are potent anti-lipolytic agents that inhibit adipose tissue lipolysis and lower circulating FFA levels. We have discovered a novel partial agonist (CVT-3619) of the A_1AdoR that inhibits adipose tissue lipolysis and lowers circulating FFA levels. CVT-3619 is 10-30-fold selective for the A_1AdoR vs. other adenosine receptors. CVT-3619 inhibits lipolysis in rat adipocytes with IC_{50} values of 6 and 44 nM, respectively. In in-vivo studies, CVT-3619 decreases both FFA and triglyceride (TG) levels (15-57%) in a dose-dependent manner in awake rats. The anti-lipolytic effect of CVT-3619 is not associated with a rebound increase in FFA levels as seen with Nicotinic acid. CVT-3619 increases the potency of insulin to decrease lipolysis by 3-fold. CVT-3619 also lowered FFA and TG levels in rats with impaired insulin sensitivity caused by 2 weeks of high fat diet feeding. An oral glucose tolerance test (OGTT) in high fat diet fed rats treated with CVT-3619 for 2 weeks showed improved insulin sensitivity as compared to untreated control rats. In conclusion, CVT-3619 is an orally bioavailable A_1AdoR partial agonist that lowers circulating FFA levels resulting in improved insulin sensitivity. Thus, CVT-3619 may be particularly useful for the treatment of diabetes as it targets the underlying cause of insulin resistance.

METABOLIC SYNDROME IN WOMEN OR WOMEN'S SHAPE

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Metabolic Syndrome (MS) incidence increases with age and becomes predominant in women after menopause. Changes in body fat distribution, with deposits around the waist, along with insulin resistance, are observed. Estrogens play a fundamental role in body fat distribution.

Increased waist circumference has a higher predictive value for SM in women than in man, particularly in subjects with normal BMI.

The European Prospective Investigation of Cancer (EPIC) study, following 350,000 adults, 65 percent of them women, for ten years, has shown that abdominal adiposity is correlated independently to death risk, especially when the BMI is normal.

Overall cancer incidence is related to obesity, but, in addition, male-pattern adiposity is particularly correlated with colorectal and breast cancer risks. Breast cancer incidence increases with the number of MS features.

In summary, when a woman complains of her shape and her waistline, it is important to take into account the MS and the associated risks: diabetes, CVD, cancer and thrombosis.

$P66^{SHC}$ IS A GENETIC DETERMINANT OF METABOLIC SYNDROME

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$P66^{Shc}$ was the first gene identified whose mutation prolongs life span without defects in mammals [(1)].

Several evidences, reported in the last years, have demonstrated that $p66^{Shc}$ is involved in damage response, including diabetic and cardiovascular stresses, and in the regulation of intracellular redox balance. Finally, $p66^{Shc}$ has been found to catalyze the formation of hydrogen peroxide by mitochondrial respiration through a redox reaction with cytochrome c [(2)].

More recently we have found that $p66^{Shc}$ plays an important role in the control of fat development both *in vitro* and *in vivo* [(3)]. Indeed, primary adipocytes isolated from white or brown fat tissue of $p66^{Shc}$ null mice show impaired adipogenesis *in vitro*. Furthermore fat tissue and overall body weight are significantly reduced in $p66^{Shc}$ null mice and strikingly, $p66^{Shc}$ null mice are resistant to high fat diet induced obesity[(3)].

Here we report that $p66^{Shc}$ promotes adipokines secretion and decreases systemic insulin sensitivity. Thus, $p66^{Shc}$ appears to be a genetic determinant of the metabolic syndrome.

[(1)] *Nature* (1999) 402: 309-13.

[(2)] *Cell* (2005) 122: 221-33.

[(3)] *J Biol Chem* (2008) in press.

NORMAL WEIGHT OBESE (NWO) WOMEN: AN EARLY INDICATOR OF METABOLIC SYNDROME

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Background and aims: Central obesity and excessive gain in abdominal fat, correlate with hyperinsulinaemia, insulin resistance, type 2 diabetes and coronary heart disease in both obese and metabolically obese individuals. Recently the Normal Weight Obese (NWO) syndrome has been described (body mass index BMI < 25 Kg/m2), but high fat mass percentage (FM%>30). We determined the relationship among body fat distribution, inflammatory parameters and muscular efficiency to distinguish NOW.

Methods and results: 150 clinically healthy Caucasian Italian women were analysed. Significant differences in cytokines plasma concentrations were observed. Significant differences were observed in the CVD risk indexes between NWO and normal weight (NW); no difference was observed

between NWO and OB group. NWO individuals showed significant ($p< 0.01$) reductions of lean leg mass and lean left leg mass compared to NW, while no significant difference was observed comparing NWO with OB. A comparison of physical performance capacity between the groups was assessed by isometric and isotonic muscular efficiency analysis of advanced and inferior districts. Three different muscular efficiency indexes were calculated. Significant difference was observed between NW and NWO. Moreover, no significant difference between NWO and OB were obtained.

Conclusions: The pro-inflammatory cytokines represent significant prognostic indicators for obesity, CVD and metabolic syndrome risks in NWO women.

We believe that the leg indexes derived from body composition analysis, combined with blood parameters and muscular efficiency evaluations are promising clinical tools for diagnosing the new subset of Normal Weight Obese syndrome and for predicting, years in advance metabolic syndrome and obesity-related diseases.

DEVELOPMENT OF METABOLIC SYNDROME AFFECTS HEALTH-RELATED QUALITY OF LIFE

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Aim: To evaluate the relationship between development of metabolic syndrome and health-related quality of life (HRQOL).

Methods: The North West Adelaide Health Study (NWAHS) is a randomly selected, representative cohort of people aged 18 years and over living in north west Adelaide. Longitudinal data from the NWAHS were used to examine the relationship between developing metabolic syndrome between Stage 1 (2000-2003) and Stage 2 (2004-2006) and HRQOL. Of the original cohort at Stage 1 (n=4060), 94.3% were contacted at Stage 2 with metabolic syndrome status obtained at follow-up for 78.9% (n=3206) of original participants. Metabolic syndrome was defined using the IDF consensus definition as waist circumference ≥94cm for men and ≥80cm for women plus any two of triglyceride >1.7mmol/L, HDL cholesterol < 0.9mmol/L for men and < 1.1mmol/L for women, blood pressure ≥130/85mmHg or FPG ≥5.6mmol/L. HRQOL was measured using the eight subscales of the Short Form 36 (SF-36). A multi-level repeated measures model was used to compare changes in SF-36 scores among those who developed metabolic syndrome with those who did not develop metabolic syndrome.

Results: At Stage 2, participants who developed metabolic syndrome had lower HRQOL scores than those without metabolic syndrome. The decrease in HRQOL scores from Stage 1 to Stage 2 was statistically significantly greater for participants who developed metabolic syndrome than those who did not develop metabolic syndrome on the Vitality dimension of the SF-36, even after adjusting for the effect of age.

Conclusions: These findings demonstrate that HRQOL is reduced as metabolic syndrome develops.

WHICH DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME IS BETTER FOR THE PREDICTION OF MICROALBUMINURIA IN T2DM PATIENTS?

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Background: The aim of this study is to compare the clinical usefulness of each metabolic syndrome(MS) defined by different diagnostic criteria for prediction of microalbuminuria in T2DM patients.

Methods: The cross sectional study with 250 T2DM patients (M=125 ,F=125) who were registered at Diabetes Unit, Medical Center of Dong-A University were performed. We compared the prevalence of MS, which was defined by ATP III and IDF criteria. We also evaluated prevalence of microalbuminuria and the relationship between microalbuminuria and MS with multiple regression analysis.

Results: The prevalence of MS defined by IDF and ATP diagnostic criteria was 58.4% and 72.4%. The gap(the prevalence of MS who was positive by ATP III but negative by IDF criteria) was 14%. MS by ATP III was more strongly associated with microalbuminuria than MS by IDF criteria {adjusted odds ratio (OR) 2.672 versus 1.935}.Hypertension was independent predictor for microalbuninuria{OR=1.945(p=0.020)}. The OR of microalbuninuria for subjects was significantly increased as added on by the number(n) of component of MS{n=3, 2.427(P=0.043), n=4, 3.618(P=0.028), n=5, 4.394(P=0.015)}.

Conclusion: Total number of metabolic component is more important than the combination pattern of each component for prediction of microalbuminuria in T2DM patients. In addition, metabolic syndrome defined by ATP III criteria is better than by IDF criteria.

GLYCEMIC HOMEOSTASIS IN THE METABOLIC SYNDROME EXPLORED BY A CONTINUOUS GLUCOSE MONITORING SYSTEM AFTER OGTT

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Aim: The minimal model has been applied for a novel study of glucose homeostasis in patients with MS.

Methods: 18 MS patients and 6 controls underwent to OGTT while submitted to a 6 hrs Glucoday ® tecnique (Menarini, Italy) as a continuous glucose monitoring system. The minimal model is based on the equation ($dG/dt = -b_1[G(t) - G_b] - X(t)G(t) + R_a(t)/V$; $dX/dt = -b_2X(t) + b_3[I(t) - Ib]$): plasma glucose concentration at time t(G(t)), basal glucose concentration(G_b), insulin activated action at time t(X(t)), plasma insulin concentration at time t(It), basal insulin concentration(I_b), rate of glucose plasmatic appearance($R_a(t)$), glucose distribution volume(V=1.7dl/Kg), b_1=insulin independent glucose diffusion rate (glucose effectiveness); b_3=size of the insulin activated action proportional to the difference between plasma insulin concentration I(t) and the basal insulin I_b; b_2=rate of disappearance of insulin action on interstitial fluid. The ratio $S_I=b_3/b_2$ (insulin sensitivity) measures the amount of the insulin action on plasmatic glucose.

Results: After OGTT, 11 patients had IGT, 3 diabetes and 4 no glycemic alterations. Time to reach maximum insulin peak (min): normal controls =75,0±21.2, MS patients without diabetes or IGT =82.5±15,0, MS patients with IGT=126,0±30,9, MS diabetic patients=140,0±17.3 ($p< 0.05$). No difference in the HOMA test was found. Slope to maximum glucose (mg/dl/min): MS patients=3.6±7.5, controls=1.05±0.2 ($p< 0.05$). Minimal model (in 10 pts and 2 controls): in MS pts, insulin sensitivity=$6.6x10^{-4}$ml/uU/min and glucose effectiveness=1.4x10-2 min^{-1}, values consistent with previous published reports.

Conclusion: The minimal model describes accurately the glucose kinetics and may have implications in the study of MS patients.

DETERMINATION OF BODY COMPOSITION IN PATIENTS WITH METABOLIC SYNDROME, BY BIO-IMPEDANCE METHOD USING DIFFERENT DEVICES

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Introduction: The study of body composition by bio-impedance is a used method with different devices. The results may influence the therapeutic choice.

Method: 51 patients (22m/29w) with metabolic syndrome (IDF2005), admitted in the "N.Paulescu" Institute, were included in this study. Their mean age was 55.17±10.98years. Their body composition was examined, using next devices: In Body 3.0, Omron BF 500, BCM-Fresenius Medical Care. Weight, BMI, fat-tissue, intra- and extracellular liquid volumes were determined. Data were statistically processed using SPSS 15.0 (T-Student test).

Results: As reference the results of In Body3.0 were used, where total body water(TBW) was 42.12±8.38L, distributed as following: 28.21±5.52L intracellular body water(IBW) and 13.89±2.98L extracellular body water(EBW). Results of BCM-Fresenius: TBW=37.47±7.76L, IBW=20.4±4.23L and EBW=17.4±3.26L (p=0.204 for TBW, p=0.441 for IBW, and p=0.59 for EBW). Results for BMI(kg/m²) were similar: 30.41±4.55(In Body) and 30.48±4.55(Omron,p=0.086). Determined weight: 84.2±14.54 kg(In Body) and 84.42±14.56 kg(Omron) (p=0.098). The percentage of fat tissue was 31.99±7.67%(In Body), 35.14±10.03%(Omron,p=0.0906), 38.29±8.05%(Fresenius,p=0.199), with a higher value for women than men: 35.31±6.46%(In Body), 40.82±7.48%(Omron,p=0.271) and 41.6±6.64% (Fresenius,p=0.283, for women), 27.34±6.69%(In Body), 27.28±7.12%(Omron,p=0.003) and 33.85±7.83% (Fresenius,p=0.297 for men). Resting Metabolism Rate(kcal/day):1452.94±211.25(In Body) and 1653.52±241.82(Omron,p=0.304).

Conclusions: Under water weighting and DEXA (dual-energy-x-ray absorptiometry) are considered to be "gold standard" procedures for determining body composition, but they are inaccessible and expensive. As the differences in the results are statistically significant, bio-impedance stands yet approachable alternative in clinical practice, but data could be limited helpful in determining body composition in patients with MS. The device could influence the behavior in clinical practice.

DO METABOLIC FACTORS GOVERN THE RISK FOR BREAST CANCER-ASSOCIATED LYMPHEDEMA (BC-L)?

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Among the systemic factors associated with lymphedema risk following axillary lymph node dissection (ALND), hypertension and obesity have been consistently identified. Since insulin resistance (IR) is also associated with breast cancer-associated lymphedema (BC-L), we studied insulin sensitivity in 23 breast cancer survivors with and without BC-L. Ratios of limb volume were calculated with the truncated cone approximation. The presence of LE was defined as a ratio>1.1 and was confirmed by measuring the bioimpedance ratios (BR) in each patient. 13 patients were BC-L + and 10 were BC-L -. The groups were matched for age, BMI and elapsed time since ALND. Insulin sensitivity was assessed by quantitation of steady state plasma glucose (SSPG) during octreotide infusion and further confirmed with oral glucose tolerance test (OGTT). Average SSPG values were not significantly different in BC-L + (129±58) *vs.* BC-L- (168±67) but abnormal values >180 were statistically much more frequent in the BCL- group (Chi square=7.333, P< 0.007). Plasma glucose (PG) values were signficantly higher in BC-L- patients at T=30 and 60 mins, respectively (P< 0.02). There was a strongly positive correlation between the BR and the 60 min PG (r=0.7), indicating an inverse relationship between prevailing PG and the presence of edema. Therefore, paradoxically, the risk of BC-L appears to be inversely related to the patients' measured insulin sensitivity. The results are nevertheless strikingly significant, suggesting that further investigation of these phenomena will shed insight into the mechanisms of risk.

MONOCYTE CHEMOATTRACTANT PROTEIN-1 (MCP-1) IS ELEVATED IN THE METABOLIC SYNDROME

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Aim: To evaluate the effect of atorvastatin on serum MCP-1 in people with the metabolic syndrome (MS).

Methods: 43 subjects with MS (IDF criteria), mean age 49.8 ±7 years (67% male), were compared to 23 lean controls, mean age 46.3 ±7.1 years (57% male). Exclusions included: diabetes, statin treatment, and C-reactive protein (CRP) >10 mg/L. MS subjects were randomised to atorvastatin (10 mg/day) or placebo for six weeks. Fasting blood was collected for lipid profiles, glucose, hsCRP and serum MCP-1 (High Sensitivity Cytokine Array I biochip; Randox Laboratories).

Results: The metabolic syndrome subjects differed significantly from the lean subjects in the following respects: mean BMI (32.2 vs 23.7 kg/m^2, p< 0.001); LDL (3.4 vs 3 mmol/L, p< 0.05); HDL (1.3 vs 1.9 mmol/L, p< 0.001); triglycerides (2.1 vs 0.8 mmol/L, p< 0.001); and glucose (5.7 vs 5 mmol/L, p< 0.001). They also differed in median pre-treatment CRP (2.2 vs 1.0 mg/L, p< 0.001) and MCP-1 (265.8 pg/mL vs 183.9 pg/mL, p< 0.01). Spearman's rank correlation coefficient showed significant correlations between BMI and CRP (p< 0.001), as well as BMI and MCP-1 (p = 0.01), but not between CRP and MCP-1. Neither CRP nor MCP-1 correlated with age. Atorvastatin treatment had no significant effect on either CRP or MCP-1. There was a small but significant rise in both CRP and MCP-1 in the placebo group, which was probably a chance finding.

Conclusion: This study confirms that MCP-1 is elevated alongside CRP in obese subjects with the metabolic syndrome.

METABOLIC SYNDROME IS ASSOCIATED WITH SILENT BRAIN INFARCTION IN NONDIABETIC ADULTS

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Aims: Metabolic syndrome (MetS) is associated with an increased risk of the subsequent development of cardiovascular disease or stroke even among persons without diabetes. MetS was found to be significantly associated with silent brain infarction (SBI) in neurologically healthy people. However, information is scant regarding its relationship of MetS to the SBI in nondiabetic adults. Therefore, we conducted a cross-sectional study.

Methods: We studied 1,029 healthy consecutive elderly subjects aged ≥65 who underwent MRI of the brain as part of their routine health check. Exclusion criteria were as follows: history of a stroke or TIA, history of diabetes, or taking antidiabetic medications. We examined associations between full syndrome (at least 3 of the 5 conditions) as well as its components and SBI by controlling possible confounders.

Results: One hundred fifty subjects (14.6%) were found to have one or more SBI on MRI. Age was found to be significantly related to SBI prevalence (OR, 1.09; 95% CI, 1.05-1.13). MetS was significantly associated with SBI (OR, 2.02; 95% CI, 1.36-2.99). The components model of MetS showed a strong significance between high blood pressure (OR,

1.83; 95% CI, 1.13-2.98) and SBI. An increasing number of MetS components showed more prevalent SBI and multiple SBIs ($P < .001$).

Conclusions: MetS was found to be significantly associated with SBI in nondiabetic adults. Though only elevated BP was found significant component, subjects with a greater number of MetS components showed more prevalent SBI.

METABOLIC SYNDROME AND SURGERY - A SOLUTION?

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Introduction: The therapeutic of metabolic syndrome is essentially based in control of all the factors involved, with new options emerging in the past recent years. Surgery in the metabolic syndrome has been an option with growing use in some countries and with good recent results. In Portugal (in this hospital) there is a pioneer surgical technique which is the subject of this study.

Objectives: Evaluate the progress of patients with metabolic syndrome before and after partial gastrectomy and ileal interposition.

Materials and methods: A retrospective study of patients submitted to these surgical techniques from July 2007 until July 2008. The evaluated parameters were: age, gender, medications, micro and macrovascular complications, blood pressure, waist circumference, bioelectrical impedance and complications after surgery. We have studied the following analytical parameters: evolution of blood glucose, cholesterol, albumin, transferrin, retinol, glycated hemoglobin, leptin, adiponectin, grelin, resistin, among others.

Results: We evaluated 40 patients, 30 females and 10 males. There was a progressive weight loss with decreasing abdominal circumference and bioelectrical impedance values, with tendency to normalization of the evaluated analytical parameters.

Conclusions: Despite being a relatively new therapeutic option in our country, the results makes us believe that it will be a viable solution for the therapeutic approach of the metabolic syndrome. Comparing to the experience of other countries, the results are so far promising, with a very favourable evolution of metabolic control in blood glucose, in dislypidemia, in blood pressure, and in obesity.

THE METABOLIC SYNDROME IS NOT ASSOCIATED WITH HOMOCYSTEINEMIA: THE PERSIAN GULF HEALTHY HEART STUDY

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Background: It is uncertain whether homocysteine and the metabolic syndrome or its components are related in the general population and studies investigating the association between homocysteine levels and insulin resistance have shown conflicting results.

Methods: In an ancillary study to the Persian Gulf Healthy Heart Study, a cohort study of Iranian men and women aged ≥ 25 years, a random sample of 1754 subjects were evaluated for the association of plasma homocysteine levels and the metabolic syndrome using National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP)-III criteria. Total homocysteine levels and high sensitivity C-reactive protein (CRP) were determined by enzyme-linked immunosorbent assays.

Results: Subjects with lower HDL-C and higher blood pressure showed significantly higher homocysteine levels ($p< 0.001$ and $p< 0.0001$; respectively). There was no significant difference in serum levels of homocysteine between subjects with and without the metabolic syndrome. In multiple logistic regression analysis, the metabolic syndrome did not show a significant association with serum homocysteine levels after adjusting for sex, age, smoking, fruit and vegetable intake pattern, body mass index and physical inactivity. Concurrent elevated CRP levels and the metabolic syndrome (inflammatory metabolic syndrome) did not also show a significant association with serum homocysteine levels after adjusting for sex, age and lifestyle cardiovascular risk factors.

Conclusion: There was no association between the metabolic syndrome using NCEP-ATPIII criteria and homocysteinemia in this study. These data refute the hypothesis that homocysteine levels are influenced by the metabolic syndrome, at least in general healthy population.

THE ASSOCIATION OF VIRAL AND BACTERIAL INFECTIOUS BURDEN AND THE METABOLIC SYNDROME

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Background: The number of infectious pathogens to which an individual has been exposed (infectious burden) independently contributes to the progression of carotid atherosclerosis and the long-term prognosis in patients with documented coronary artery disease. The infectious aspects of the metabolic syndrome including the relationship between pathogen burden and the metabolic syndrome have not been investigated.

Methods: In a cross-sectional, population-based study, we used National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP)-III criteria in 1642 subjects, aged 25 years and over, selected by cluster random sampling in three Iranian ports in the northern Persian Gulf. Sera were analyzed for IgG antibodies to Chlamydia pneumoniae, HSV-1, Helicobacter pylori (H. pylori) and CMV using ELISA.

Results: There was an increased trend of prevalence of the metabolic syndrome with increasing number of pathogen (4.0%, 22.6%, 43.4% and 29.7% for 1, 2, 3, and 4 pathogens, respectively; p for trend < 0.0001). Infectious burden, divided into 2, 3 and 4 seropositivities, was significantly associated with the metabolic syndrome, with odds ratios of 1.46 (95% CI, 1.22-1.75; $p< 0.0001$) for 2, 1.60 (95% CI, 1.38-1.86, $p< 0.0001$) for 3 and 3.12 (95% CI, 1.96-4.96; $p< 0.0001$) for 4 compared with 0 to 1 seropositivities after adjustment for age and sex.

Conclusion: Our results support the hypothesis that the number of infectious pathogens to which an individual has been exposed independently associated with the metabolic syndrome. The mechanism(s) underlying the association remain to be elucidated further.

PIOGLITAZONE DECREASES PLASMA ANGIOTENSIN II CONCENTRATION IN TYPE 2 DIABETES

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Aims: Adipocytes express all components of the renin-angiotensin system (RAS) and the RAS inhibits adipogenic differentiation and regulates adipocyte metabolism. We have verified that plasma Ang II is associated

with body fat accumulation and insulin resistance. The aim of this study is to investigate the effect of insulin sensitizer, pioglitazone, on plasma angiotensin II (Ang II) in type 2 diabetes (T2D).

Methods: Fifty Japanese subjects with T2D were eligible for enrollment (BMI: 23.8 ± 3.1 kg/m^2, HbA1c: 7.91 ± 0.90%). The patients were randomly divided into two groups. One group was administered pioglitazone 30 mg/day (pioglitazone group, n = 25) and the other group was not administered (control group, n = 25) for 16 weeks. Plasma Ang II was measured by radioimmunoassay. Lipoprotein lipase mass in preheparin serum (LPL mass) was measured as an adipocyte-derived factor and a marker of insulin sensitivity.

Results: The mean Ang II at baseline was 10.75 ± 5.41 pg/dl. In pioglitazone group, the mean BMI increased by 2.5% ($p < 0.0001$), HbA1c decreased by 13.3% ($p < 0.0001$), LPL mass increased by 16.6% ($p < 0.0001$) and plasma Ang II decreased by 20.8% ($p = 0.0007$), whereas these parameters were unchanged in control group. The change in plasma Ang II correlated negatively with the change in LPL mass ($r = -0.312$, $p = 0.0389$) in pioglitazone group.

Conclusions: Pioglitazone decreases plasma Ang II in T2D. The insulin-sensitizing effect of pioglitazone may be involved in suppressing the RAS in adipocytes.

CIRCULATING ANGIOTENSIN II IN OBESE PATIENTS WITH TYPE 2 DIABETES

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Aims: Adipocytes express all components of the renin-angiotensin system (RAS) and the RAS is involved in obesity and insulin resistance. Circulating angiotensin II (Ang II) is detectable in blood, but its significance in obesity remains unknown. The aim of this study is to investigate plasma Ang II in obese patients with type 2 diabetes (T2D).

Methods: Fifty Japanese obese subjects with T2D [body weight: 75.0±14.1 kg, BMI: 29.1±3.7 kg/m^2, visceral fat area (VFA): 169.3±54.3 cm^2, HbA1c: 7.6±1.5%] were enrolled. The subjects were prescribed a diet of daily caloric intake of 20 kcal/kg for 24 weeks. Plasma Ang II was measured by radioimmunoassay. Leptin, adiponectin and lipoprotein lipase mass in preheparin serum (LPL mass) were also measured as adipocyte-derived factors.

Results: After 24 weeks of weight reduction diet, the mean body weight, VFA and HbA1c decreased significantly by 2.3 %, 7.0 % and 8.3 %, respectively. The mean plasma Ang II decreased by 24% ($p< 0.0001$) and correlated with body weight both at baseline ($r=0.425$, $p=0.0018$) and at 24 weeks ($r=0.332$, $p=0.0181$). The change in Ang II correlated with changes of body weight ($r=0.335$, $p=0.0167$) and VFA ($r=0.329$, $p=0.0191$). The change in Ang II also correlated positively with change in leptin ($r = 0.348$, $p = 0.0127$) and tended to correlate negatively with change in LPL mass ($r=-0.260$, $p=0.0683$), which is a marker of insulin sensitivity.

Conclusions: Plasma Ang II is high in obesity, decreases during weight loss, and is associated with insulin resistance in obese subjects with T2D.

THE CLINICAL SIGNIFICANCE OF MEASUREMENT OF CAVI IN SUBJECTS WHO HAD A HEALTH EXAMINATION, AND THE EFFECT OF METABOLIC SYNDROME ON CAVI

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Recently, a novel arterial stiffness parameter called cardio-ankle vascular index (CAVI) has been developed in Japan, which essentially reflects the stiffness of the aorta. The characteristic of this method is to be independent of blood pressure. In this study, using CAVI in subjects who had a health examination, the usefulness of CAVI as a diagnostic method of atherosclerosis and the effect of metabolic syndrome (MetS) on it were studied. 14782 subjects who had a health examination were enrolled in this study. Body mass index, blood pressure, fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), triglycerides, HDL-cholesterol, LDL-cholesterol and CAVI were measured. CAVI was positively correlated with age significantly ($p< 0.0001$), and showed high levels significantly, according to increases of complicated numbers of atherosclerotic risk factors. Furthermore, CAVI of MetS was higher significantly than that of non-metabolic syndrome. A stepwise multiple regression analysis using risk factors of atherosclerosis as independent variables identified systolic blood pressure and HbA1c as positively related to the severity of CAVI. From these findings, CAVI may be useful for discriminating the probability of atherosclerosis, and MetS may be one of important factors aggravating CAVI.

CLINICAL SIGNIFICANCE OF SERUM APO-B48 LEVELS FOR DIAGNOSIS OF METABOLIC SYNDROME (MET S)

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Objective: A diagnostic criteria of Met S was established by 8 Societies including Japanese Society of Hypertension in 2005. We reported ApoB48 levels are higher in males with Met S at 2nd International congress on PREDIABETS and the METABOLIC SYNDROME. However, a relationship of ApoB48 levels with Met S in females was not clear. At this time, we increased the number of female cases to clarify a clinical significance of ApoB48 levels in diagnosis of Met S in females.

Design and methods: Fasting serum ApoB48, triglyceride, total-cholesterol, HDL-cholesterol, LDL-cholesterol, plasma glucose, HbA1c, abdominal circumference, body weight, body mass index and blood pressure were determined in 216 outpatients in our clinic.

Results: LogApoB48 levels were significantly higher in males(0.55±0.39 (Mean±SD) vs 0.32±0.36, $P=0.008$) and females(0.53±0.38 vs 0.34±0.36, $P=0.017$) with Met S in comparison to those without Met S. LogApoB48 levels positively correlated with serum TG levels in males($r=0.53$, $P< 0.0001$) and females($r=0.61$, $P< 0.0001$). Stepwise regression analysis revealed that logApoB48 levels, but not serum TG and HDL-cholesterol levels, were selected as a significant independent variable for the Met S, in addition to gender, HbA1c, systolic blood pressure, and abdominal circumference. This contribution rate was 56%.

Conclusions: LogApoB48 levels were significantly higher in males and females with Met S. These results suggest that determination of serum ApoB48 levels may be useful to diagnose Met S, especially in relation to abdominal obesity since serum levels of ApoB48 might reflect the exogenous fatty acid intake.

METABOLIC SYNDROME IS ASSOCIATED WITH SILENT MICROBLEEDS IN PATIENTS WITH ISCHEMIC STROKE

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Purpose: Metabolic syndrome (MetS) is associated with an increased risk of the subsequent development of cardiovascular disease or stroke. Cerebral microbleeds are representative of bleeding-prone microangiopathy and closely associated with hemorrhagic stroke. In this study, we investigated whether MetS is associated with the presence of microbleeds.

Methods: A total of 809 patients with ischemic stroke, who were consecutively admitted to our hospital, were included in this study. We collected demographic, clinical and laboratory findings including MetS, and examined the presence and the number of microbleeds using T2*-weighted gradient-echo MRI.

Results: There were 241 patients with microbleeds (29.8%). Age, hypertension, systolic blood pressure at admission, and presence of MetS were found to be significantly related to the presence of microbleeds. Patients with MetS were more likely to have microbleeds. After controlling for possible confounders including vascular risk factors, the presence of MetS remained significant [adjusted odds ratio (OR), 1.66; 95% confidence interval (CI), 1.20-2.31]. The association was significant in men (OR 1.63; 95% CI, 1.08-2.46), but not in women.

Conclusions: Our results indicate that MetS is an independent risk factor for the presence of microbleeds, although the effects might be different between genders.

PREVALENCE OF THE METABOLIC SYNDROME AMONG HYPERTENSIVE PATIENTS IN A COMMUNITY PRACTICE IN ISRAEL

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Background: The metabolic syndrome (MS) is a risk factor for cardiovascular disease and DM. Appropriate treatment can reduce cardiovascular morbidity and mortality. However, family physicians in Israel may not routinely diagnosis the MS.

Purpose: To measure the prevalence of the MS among hypertensive patients in a community clinic,to identify the characteristics of this population.

Method: A sample of hypertensive patients were invited by mail to an appointment in which they filled out a questionnaire, underwent a physical exam, and appropriate lab tests. Additional information was obtained from the patient files.

Results: 200 patients were invited to the clinic, of which 82% participated .The age range of the participants was 28-95 years,48% were men,10% were smokers. 47% reported that they followed a diet and 48% reported doing physical activity.

Only 4 patients had been diagnosed with metabolic syndrome before the study. 110 additional hypertensives were found to meet the criteria for the syndrome.

Significant correlation was found between metabolic syndrome and life style. Patients on a diet had a lower prevalence of MS (58 Patients - $p< 0.008$). Hypertensives without MS smoked less (35 Patients- $p=0.024$).

Conclusions: In this sample, 69% of hypertensives suffer from MS but only 2.4% had this diagnosis recorded in their medical file before this intervention. Keeping to good diet is associated with less MS.

Interventions should be planned to increase the awareness of family physicians in Israel to diagnose and treat the MS.

ASSOCIATION OF PHOSPHATIDYLETHANOLAMINE N-METHYLTRANSFERASE GENE POLYMORPHISM AND METABOLIC SYNDROME IN KOREAN

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Aims: Phosphatidylethanolamine N-methyltransferase (PEMT) is related to the synthesis of phosphatidylcholine which regulates lipoprotein metabolism. We investigated the association of PEMT polymorphism and metabolic syndrome (MS) in Korean.

Methods: A cross sectional study was conducted on 542 Korean adults. MS was defined according to the modified National Cholesterol Education Program/Adult Panel III. PEMT -V175M polymorphism was studied to elucidate the possible roles to MS.

Results: G/G genotype was 294 (54.2%), G/A genotype was 207 (38.2%), and A/A genotype was 41 (7.6%). BMI, waist circumference, systolic and diastolic blood pressure (BP), fasting blood glucose and lipids were not significantly different among the genotype groups. In G/G and G/A genotype, systolic and diastolic BP, blood glucose and lipids were different between abdominal obesity (AO) and non-AO group. However, in A/A genotype, no differences were showed except for systolic BP.

With controls for age, sex, and alcohol intake, the binary logistic regression analyses of G/G and G/A genotype showed higher Odds Ratios for high BP, hyperglycemia, hypertriglyceridemia, low HDL-cholesterol, and MS (≥2 of 4 components) in AO group. AA genotype showed no significant differences between AO and non-AO group.

Conclusion: These results suggest that PEMT -V175M variant significantly associated with MS in Korean.

INTIMA-MEDIA THICKNESS AND CARDIOVASCULAR RISK IN YOUNG SUBJECTS WITH THE METABOLIC SYNDROME

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The metabolic syndrome is a constellation of increased abdominal obesity associated with dyslipidemia, impaired glucose tolerance and hypertension, being also a recognized risk factor for atherosclerosis.

Aim: To assess carotid artery intimal-medial thickness (IMT) and cardiovascular risk in a population-based cohort of young policemen, screened for emerging clinical and lipid risk factors.

Methods: Eighty consecutive subjects were enrolled into the study (**75M, 5F;** mean age 41 years) and subsequently split into two groups who either had the **metabolic syndrome** (n=30) or not (n=50), as per the definition proposed by International Diabetes Federation. Cardiovascular risk was prospectively evaluated through Framingham risk score, whereas carotid IMT was measured in all subjects.

Results: The respective groups differed in: age (39.5±5.40 year vs. 44.0±5.20 year; $p< 0.0001$), BMI (28.55±3.86 kg/m^2 vs. 33.16±3.87 kg/m^2; $p< 0.0001$), plasma concentration of uric acid (337.50±77.30 µmol/L vs. 401.34±76.30 µmol/L; $p=0.0005$) for those without, as compared to the subjects with the metabolic syndrome. Mean IMT (0.65±0.13 mm vs. 0.54±0.08 mm; $p< 0.0001$) and calculated Framingham risk score (10.11±5.69% vs. 3.74 ±2.83%; $p < 0.0001$) were also higher in the subjects with the syndrome. There was a positive correlation between IMT and Framingham risk score ($r=0.49$, $p< 0.0001$) for all subjects.

Conclusions: Carotid artery IMT facilitates non-invasive diagnosis of atherosclerosis, being a surrogate marker of early cardiovascular risk. Since in young adults exposed to multiple cardiovascular risk factors endothelial dysfunction is an early feature of atherosclerosis, its measurement may serve as an effective clinical screening method.

INSULINE RESISTANCE ASSOCIATED WITH LOW SUSTAINED VIROLOGIC RESPONSE IN CHRONIC HEPATITIS C

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Aims: Several host factors, such as body mass index, visceral adiposity, and insuline resistance, have been associated with the development of steatosis (metabolic steatosis) in chronic hepatitis C (CHC). Irrespective of virus genotype, metabolic syndrome was also associated with lower virologic response to treatment. The aim of this study was to assesss the influence of insuline resistance on the anti-viral treatment.

Methods: We studied 43 naive patients with CHC, treated with peginterferon and ribavirin. There were 17 men and 26 women with mean age 48.79 years (29-64). Fourteen patients were previously diagnosed with type 2 diabetes mellitus (DM) or with lower glucose tolerance (LGT).

Results: Steatosis was present in 11 liver biopsy from patients without DM/LGT and in 2 with DM. Virologic response was estimated at weeks 12, 24 and 48 of treatment and week 24 posttreatment. Sustained virologic response (SVR) was present in 22 patients (51.16%), but only in 7 patients with steatosis (31.8%) and 4 with DM/LGT (18.2%). Non-responders or incomplete responders were 21 patients, 4 with steatosis and 10 with DM/LGT. This patients represented 36% from those with steatosis and 71.4% from those with DM/LGT.

Conclusions: Insuline resistance is a major negative predictor of SVR in naive patients with CHC treated with peginterferon alfa and ribavirin.

MULTIVARIATE ANALYSIS OF THE ASSOCIATED RISK FACTORS ABOUT METABOLIC SYNDROME IN BEIJING AND NANJING

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Objective: To explore the associated risk factors of metabolic syndrome in Beijing and Nanjing.

Methods: Using identical protocol and questionnaire, an epidemiological study was carried out in a population of 6123 adults in Beijing and Nanjing. IDF(2005)was used as the diagnostic criteria of metabolic syndrome. Univariate and multivariate logistic regression model were used to identify associated risk factors.

Results: The age-standardized prevalence of metabolic syndrome in males and females were 19.5% and 33.6%, respectively. The results of multivariate logistic regression analyses displayed that female (OR=1.49;95%CI(1.40, 1.59)), age increasing (OR=1.23;95%CI(1.16, 1.31)), low physical activity (OR=1.76;95%CI(1.13, 2.76)), with diabetes family history (OR=1.33;95%CI(1.11, 1.60)), with hypertension family history (OR=1.46;95%CI(1.29, 1.65)), the interaction of age and gender (OR=1.29;95%CI(1.21, 1.40)), live in Urban (OR=1.09;95%CI(1.02, 1.18)) could significantly increase the risk of disease development. On the other hand, live in Nanjing (OR=076;95%CI(0.71, 0.81)) can perform the protective effect.

Conclusions: Metabolic syndrome was the common results of a variety of risk factors. Female, with chronic disease family history and low physical activity are important risk factors.

Keywords: Metabolic syndrome; multivariate analysis; logistic regression method; epidemiology.

SERUM VASPIN LEVELS ARE POSITIVELY ASSOCIATED WITH METABOLIC SYNDROME AND SUBCLINICAL ATHEROSCLEROSIS IN A GENERAL POPULATION WHERE OBESITY IS RARE

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Objective: Recently, visceral adipose tissue-derived serine protease inhibitor (vaspin) has been identified as a novel adipocytokine with potentially insulin-sensitizing properties. Several studies demonstrated that adipokines secreted from adipocytes modulates insulin sensitivity, vascular sclerotic processes and inflammation, and vaspin is considered to have some relationships with atherosclerosis. In humans, elevated vaspin levels are associated with obesity and insulin resistance. But, so far, epidemiologic studies about vaspin in a general population are very few. Therefore, we investigated the relationships between serum vaspin levels and cardiometabolic risks in population where obesity and diabetes are rare.

Methods: We investigated serum vaspin levels by ELISA in 226 subjects (86 men and 140 women) of a general Japanese population (mean BMI< 24kg/m^2). Uni- and multivariate analyses were performed to evaluate correlation of vaspin with components of metabolic syndrome (METs) and intima-media thickness (IMT).

Results: Mean vaspin levels were 0.78±0.02 ng/ml. Age- and sex- adjusted vaspin levels were positively associated with HOMA-IR, eGFR ($p< 0.01$), BMI, insulin, triglycerides, uric acid ($p< 0.05$, respectively), and IMT ($P< 0.05$). HOMA-IR and IMT stratified by tertiles of serum vaspin levels showed a positive significant trend ($p< 0.01$) after adjustments for age and sex.

Conclusions: This study is the first report demonstrating that serum levels of vaspin are strongly associated with components of METs and subclinical atherosclerosis in a general population where obesity is rare.

INSULIN RESISTANCE AND BLOOD PRESSURE VARIABILITY

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Objective: Insulin resistance is associated with multiple risk factors for atherosclerosis, including increased blood pressure. The purpose of our study was to assess the association of variability of insulin stimulated glucose disposal rate (M value) during the hyperinsulinaemic euglycaemic clamp with blood pressure variability in hypertensive patients with type 2 diabetes.

Methods: In 71 patients, included in the DEMAND (delapril and manidipine for nephroprotection in diabetes) study, the coefficient of variation (CV) of the M value between the 5-minute intervals during the 120 minute clamp was calculated as mean/standard deviation of the M value. Similarly, the CV of 24 hour blood pressure was calculated as mean/standard deviation of blood pressure, measured by a portable automatic blood pressure monitor.

Results: In patients (35 males; age 61 ± 9 years; BMI 30.5 ± 5.2 kg/m2; systolic and diastolic blood pressure 134 ± 11 and 79 ± 8 mmHg, respectively; HbA1c 8.3 ± 1.3%; M index 4.7 ± 2.6 mg/kg/min) CV of the

M value was positively associated with CV of the systolic blood pressure during the night (r=0.257, P<0.05).

Conclusions: Variability of systolic night blood pressure is positively associated with variability of M value during the clamp in hypertensive patients with type 2 diabetes. These results imply that possibly both, insulin resistance and arterial hypertension, are related to disbalance in authonomic nerve system.

Acknowledgements: The authors are grateful to Dr. Giuseppe Remuzzi and Piero Ruggenenti for organising the DEMAND study.

TRP64ARG POLYMORPHISM OF THE ADRB3 GENE PREDICTS THE HYPERURICEMIA RISK IN A POPULATION FROM SOUTHERN SPAIN (PIZARRA STUDY)

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Introduction: The inclusion of plasma levels of uric acid as diagnostic criteria to define the metabolic syndrome is under discussion. Responsible genes for insulin resistance could contribute to develop hyperuricemia. Previous cross sectional studies, have proposed the ADRB3 gene as a possible candidate gene in the development of hyperuricemia and insulin resistance.

Objective: To study the role of the Trp64Arg polymorphism of ADRB3 on the risk of developing hyperuricemia in a population of 1051 subjects with a follow up to 6 years

Methods: Prospective population-based cohort study. A total of 1051 persons from the town of Pizarra (Spain) were studied in 1997-98 and reassessed six years later. Metabolic phenotype was done at baseline and second follow-up. Insulin resistance was measured by homeostasis model assessment (HOMA-IR). The Trp64Arg polymorphism of ADRB3 was detected by real time PCR. Subjects were considered normouricemic if their serum uric acid levels were less or equal than 7mg/dl for men and less or equal than 6 mg/dl for women.

Results: Normouricemics subjects in baseline study carriers Arg64 allele had more risk of developing hyperuricemia six years later (OR =1.9; IC =1.025-3.842). Logistic regression analysis showed that the OR of having hyperuricemia six years later was significantly associated with the Arg64 allele, after adjusting for age, weight gain, and baseline levels of triglycerides and serum uric acid (OR= 2.4; IC = 1.12-5.12).

Conclusions: The Trp64Arg polymorphism of the ADRB3 gene predicts the risk of developing hyperuricemia in adult population of southern Spain.

PREVALENCE OF METABOLIC SYNDROME AND ASSOCIATED RISK FACTORS IN TYPE 2 DIABETIC PATIENTS

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Aim of our study was to estimate the prevalence and risk factors of metabolic syndrome (MS) in people with type 2 diabetes mellitus (T2DM) using routinely collected data from diabetic patients treated at Clinic of endocrinology, diabetes and metabolic disorders in Skopje, Macedonia.

Methods: Consecutive diabetic patients (350 total, 168 male and 182 female) have been examined. The mean age of participants was 57.0±8.6 years, duration of diabetes was 8.5±4.3 years at initial registration. A Treatment Panel (ATP) III definition was used for the definition of MS.

Results: The prevalence of MS was 62.0%, with higher rate in females than males and it was bigger with older age. The age-adjusted prevalence rate of MS was associated with female gender, duration of diabetes, fasting blood glucose, systolic blood pressure, body mass index (BMI), sedentary lifestyle, smoking, triglyceride, HDL cholesterol, hypertension. Using a stepwise binary logistic regression model, age, gender, fasting blood glucose, systolic blood pressure, BMI, sedentary lifestyle, triglyceride, and HDL cholesterol were significant predictors of MS for T2DM patients.

Conclusions: These findings suggest that MS in our population of type 2 diabetic patients is common, and with an estimated prevalence of 62.0%, MS is evidently important risk and health threat to diabetic patients. Increasing physical activity and healthy diet in T2DM subjects are needed to stop the progress of chronic vascular complications in T2DM.

THE CUTOFF VALUES OF WAIST CIRCUMFERENCE FOR IDENTIFYING SUBJECTS AT RISK FOR CAROTID ATHEROSCLEROSIS IN KOREAN ADULTS: THE KOREAN HEALTH AND GENOME STUDY

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In Korea, the recommended cutoff level for abdominal obesity has been suggested based on the associations between components of metabolic syndrome and waist circumference (WC), not on those of WC and atherosclerosis. We estimated the cutoff point of waist circumference (WC), waist/hip ratio (WHR), and body mass index (BMI) for detection of increased carotid intima-media thickness (CIMT), which represents subclinical atherosclerosis, in Korean population.

A total of 3465 (1825 men, 1640 women) adults (mean age, 48.7±7.5; BMI, 24.5±2.8 mg/kg2) who did not have previous history of cardiovascular disease were chosen in this cross-sectional study from an ongoing, prospective, population-based study. CIMT was measured by high-resolution ultrasound system at the common carotid arteries. The accuracy of identifying ≥0.9 mm of mean CIMT by WC, WHR, and BMI was assessed using the receiver operating characteristic (ROC) curve analysis.

Four hundreds ninety three of 1825 men and 259 of 1640 women had ≥ 0.9mm of mean CIMT. The area under the ROC curve (AUC) for WC showed greater AUC values than BMI (men: 0.614, 0.606, 0.572; women: 0.663, 0.662, 0.609; AUC for WC, WHR and BMI, respectively). The optimal cut points for WC, WHR and BMI in identifying ≥0.9 mm of mean CIMT were 83.8cm, 0.91 and 24.9kg/m^2 for men and 79.4cm, 0.86 and 24.4kg/m^2 for women.

These results suggest that subjects with ≥83.8cm of WC in men and ≥79.4cm of WC in women have higher risk of atherosclerosis in Korean middle-aged population.

METABOLIC SYNDROME AND CARDIORENAL ALTERATION IN UNTREATED AND TREATED HYPERTENSIVE PATIENTS: KOREAN MULTICENTER REGISTRY

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The metabolic syndrome (MS) is associated with increased cardiorenal events in hypertension. We analyzed the prevalence and the relationship between MS and cardiorenal alteration in a large population of Korean hypertensive patients.

377 untreated and 677 treated patients were enrolled. None had cardiovascular disease, alleged diabetes, and current medication for dyslipidemia. MS was defined according to the ATP III and central obesity criteria for Koreans. Albuminuria was measured as spot urine albumin to creatinine ratio. Left ventricular hypertrophy (LVH) was assessed by ECG.

The prevalence of MS was higher in treated patients than in untreated patients (60.0 vs 50.4%, p=0.003). Treated patients had higher number of MS components except hypertension than untreated patients (1.8±1.1 vs 1.6±1.2, p=0.001). In untreated patients, the prevalence of increased serum creatinine (s-Cr) or low eGFR was similar in those with and without MS (2.6 vs 5.4%, p=NS). The prevalence of microalbuminuria (MA) was also similar (21.6 vs 16.4%, p=NS). In treated patients, however, those with MS showed higher prevalence of increased s-Cr or low eGFR (11.9 vs 4.8%, p< 0.01) and MA (19.5 vs 9.0%, p< 0.001) than those without MS. The prevalence of LVH was increased when MS was present in untreated patients (6.1 vs 1.7%, p< 0.05), while it was similar in treated patients with and without MS (3.0 vs 2.6%, p=NS).

The impact of MS on renal alteration is pronounced in treated patients. This may suggest that current practice of antihypertensive treatment is suboptimal for renoprotection in Korean hypertensive patients with MS.

"HYPERTRIGLYCERIDEMIC WAIST" AND NEWLY-DIAGNOSED DIABETES IN A LARGE POPULATION SAMPLE OF REMOTE-DWELLING INDIGENOUS AUSTRALIANS

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Aims: To assess the utility of "hypertriglyceridemic waist" and also, separately, high waist girth or triglyceride concentration in predicting, independent of body mass index (BMI), the likelihood of newly-diagnosed diabetes in Indigenous Australians at elevated risk of metabolic disease.

Methods: Remote-dwelling Indigenous men and women ≥15 years (n=2,631), not known to have diabetes, from six regions across Australia, provided fasting blood samples from which [glucose] and [triglyceride] (T) were assayed. Diabetes was classified as fasting glucose ≥7.0 mmol/L. Waist girth (WG), weight and height were obtained; BMI was calculated. Waist girth was defined as high (HWG) (≥102cm (men) or ≥88cm (women)) or, otherwise, "normal" (NWG). [T] was defined as hypertriglyceridemia (HT) ([T]>=1.7 mmol/L) or, otherwise, "normal" (NT). Sex-specific associations of WG and/or [T] combinations with diabetes were analysed by multivariate logistic regression with covariates including region, age, and BMI.

Results: The prevalence of newly-diagnosed diabetes was 10.0% for men (n=1,194) (mean age [SD], 35.2 [17.5]), and 12.0% for women (n=1,437) (35.8 [16.1]). In multivariate analyses adjusting for all covariates, the odds (95% CI) of diabetes were, for men and women, respectively: 4.7 (1.8-12.2) and 5.9 (2.5-13.7) for HWG+HT (frank "hypertriglyceridemic waist"); 3.2 (1.6-6.4) and 3.3 (1.4-7.9) for NWG+HT; and 2.2 (0.7-6.6) and 2.7 (1.2-6.5) for HWG+NT. Multivariate analyses not including BMI yielded odds of diabetes nearly twice as high.

Conclusions: "Hypertriglyceridemic waist" (HWG+HT) is strongly associated, whereas high waist girth (HWG) and triglyceride concentration (HT) are, alone, moderately associated, with newly-diagnosed diabetes in high-risk Indigenous Australians, independent of BMI.

THE EFFECTS OF A BEHAVIORAL INTERVENTION IN A COHORT OF JAPANESE-BRAZILIANS AT HIGH CARDIOMETABOLIC RISK

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Aim: Type 2 diabetes and other cardiovascular risk factors are common in the Japanese-Brazilian population. We conducted a community health promotion program for Japanese-Brazilians and assessed its effect on cardiometabolic risk.

Methods: 653 participants in a cross-sectional study of the prevalence of diabetes conducted in 2000 were enrolled in 2005 in 1-year intervention program based on healthy diet and physical activity orientations. 466 completed the program and follow-up measurements. Change in blood pressure, anthropometric and metabolic parameters between 2005 and 2006 were compared with annual change in the same variables between 2000 and 2005.

Results: After the intervention, greater annual decreases in waist circumference (-0.5±3.8 vs. 1.2±1.2 cm per year, p< 0.001), systolic blood pressure (-4.6±17.9 vs. 1.8±4.3 mmHg per year, p< 0.001), 2-hr plasma glucose (-1.2±2.1 vs. -0.2±0.6 mmol/L per year, p< 0.001), LDL-cholesterol (-0.3±0.9 vs. -0.1±0.2 mmol/L per year, p< 0.001) and Framingham risk (-0.25±3.03 vs. 0.11±0.66 per year, p = 0.02) but not triglycerides (0.2±1.6 vs. 0.1±0.42 mmol/l per year, p< 0.001) or fasting insulin (1.2±5.8 vs. -0.7±2.2 IU/ml per year, p< 0.001) were observed compared with pre-intervention period. Compared with individuals with normal glucose tolerance, individuals with glucose intolerance in 2005 showed greater decreases (p< 0.05) in plasma glucose during the intervention.

Conclusion: The frequency of individuals with disturbances of glucose metabolism dropped after one-year intervention. A one year community-based health promotion program was associated with a reversal of the increase in cardiometabolic risk observed over the preceding five years in this high risk population.

HEPATITIS C VIRUS INFECTION INCREASES THE RISK OF METABOLIC SYNDROME - A COMMUNITY-BASED STUDY IN AN ENDEMIC AREA

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Background/ aim: Metabolic syndrome (MS) is a complicated disorder encompassing clinical features of obesity, hyperglycemia, hypertension, dyslipidemia and insulin resistance. MS carries a high risk for future development of micro- and macrovascular complications. The extent, severity, and characteristics of MS in hepatitis C virus (HCV)-infected patients have rarely been investigated in a community-based setting. The study aimed to determine the difference regarding to the prevalence and the distribution of MS components between HCV-infected patients and healthy controls.

Methods: A multi-purpose mass screening was conducted for adults living in an HCV-endemic area of southern Taiwan. Clinical data of MS as well as viral hepatitis markers were assessed.

Results: Two hundreds and thirty-seven adults (M:F=94:143, mean age= 55.5 ± 10.8 years) were recruited. The prevalence of anti-HCV and HBsAg seropositivity were 39.2% (93/237), and 17.3% (41/237), respectively. Those 93 HCV-infected subjects had a higher prevalence rate (24.7%, 23/93) of MS than those 144 sex- and age-matched controls (13.2%, 19/144, P=0.02). In terms of MS components, HCV-infected subjects carried a higher prevalence of high waist circumference (51.6% vs 25.7%, P< 0.001) and hypertension (58.1% vs 36.8%, P=0.001) than controls.

Conclusion: HCV infection carried a higher prevalence of MS. High waist circumference and hypertension were the common features of MS in patients with HCV infection.

ASSOCIATION BETWEEN TYPE D PERSONALITY AND THE METABOLIC SYNDROME

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Background: Type D personality is a type of personality which is characterized by two global personality traits: negative affectivity and social inhibition. To date, there is no evidence for potential associations of this type of personality with traditional cardiovascular risk factors.

Aim of the study: To test the hypothesis whether there is a higher prevalence of type D personality among subjects with the metabolic syndrome (MetSyn) as compared to healthy controls.

Materials and methods: In this cross-sectional study 100 subjects with the MetSyn as well as 100 age- and sex-matched subjects who did not fulfill the diagnostic criteria for the MetSyn (controls) participated. The MetSyn was defined according to the National Cholesterol Educational Program Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria. The Denollet's scale (DS14) was used for the definition of type D personality.

Results: The prevalence of type D personality was higher among subjects with the MetSyn as compared to controls (48% versus 13% respectively, p< 0.01). Further analysis indicated that the presence of type D personality was associated with the number of the MetSyn components (r=0.21, p< 0.01). Logistic regression analysis showed a strong association of type D personality with the presence of the MetSyn, after adjustment age, sex and the presence of anxiety or depressive disorders [odds ratio 4.3 (95% confidence intervals 1.5 - 12.11, p=0.006)]).

Conclusion: Type D personality is independently associated with the metabolic syndrome as well as with the number of its components.

PREVALENCE OF SLEEP APNEA SYNDROME IN PATIENTS WITH METABOLIC SYNDROME (MS): THE IMPACT OF AGE, GENDER AND EACH MS COMPONENT

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Aims: To determine the frequency of SAS in patients with MS and to investigate the impact of age, gender and each MS component on its prevalence.

Methods: Berlin Questionnaire was distributed to 260 consecutive patients hospitalized in our Departments. We received valid answers from 203 patients (45,7% men; age=67±11,4 years; BMI=30,1±6,4Kg/m^2).

Results: 62% of total population had MS, according to NCEP ATP III criteria. The percentage of MS patients at a high risk for SAS was significantly superior to the one of patients without MS (64,3% vs.47,4%; p=0,019).

	MS patients					
	High risk for SAS			Low risk for SAS		
	Men	Premenopausal women	Postmenopausal women	Men	Premenopausal women	Postmenopausal women
BMI	31,34±4,03	36,69±10,99	32,58±7,64	30,41±5,31	30,8±1,13	29,04±3,77
Obese	96,6%	100%	93%	100%	100%	88,9%
Hypertensives	86,7%	83,3%	97,7%	79,2%	100%	72,2%
Diabetics	90%	66,7%	93%	95,8%	100%	94,4%
Dyslipidemic	76,7%	83,3%	76,7%	50%	100%	61,1%

High risk men were dyslipidemic at a higher percentage compared to those at low risk (76,7% vs.50%, p=0,041), whereas high risk postmenopausal women were hypertensive at a higher proportion compared to those at low risk (97,7% vs. 72,2%, p=0,002). On the contrary, high risk premenopausal women did not differ significantly from low risk ones concerning MS components.

Conclusion: Patients with MS were more prone to develop SAS compared to those without. In these patients, according to their age and gender, either dyslipidemia or hypertension significantly affected the risk for SAS.

EXPERIMENTAL STUDIES OF RHEIN ON METABOLIC SYNDROME

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Objective: To investigate the treatment of Rhein on metabolic syndrome in high-fat diet-induced insulin resistant fatty (HFD) mice.

Methods: The HFD models were induced by high-fat diet in male C57BL/6J mice, and treated with 30, 60, 120 mg/kg/day Rhein for 24 days. The age-matched mice were used as normal control (Con). The concentration of glucose, TG, TC, and the activity of Glutamine: fructose 6-phosphate amidotransferase (GFAT) were determined by enzymology assays, respectively. The serum insulin concentration was measured by radioimmunoassay kit. The insulin resistance was evaluated by serum insulin levels, HOMA-IR index, OGTT, and insulin tolerance test (ITT). The expression of protein and mRNA was estimated by Western blot and RT-PCR, respectively.

Results: After Rhein treatment, compared with HFD mice, the values of bodyweight, serum TC and ectopic fat accumulation in liver and skeletal muscle were reduced significantly, respectively, in Rhein-treated mice; the glucose tolerance and insulin tolerance were improved; the levels of insulin and HOMA-IR were decreased. Meanwhile, in liver, the expressions of some signal factors involved in insulin signaling transduction and lipid metabolism system were regulated by Rhein in HFD mice. Furthermore, the activity of GFAT was inhibited by Rhein with IC50 value of 60.8 μM.

Conclusions: Rhein showed treatments of metabolic syndromes by improving lipid metabolic disorders and insulin resistance. Its major mechanism maybe associated with the inhibition on GFAT activity and the effects on the insulin signaling transduction and the lipid metabolic system.

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METABOLIC CHANGES AFTER RADICAL TREATMENT OF PRIMARY HYPERPARATHYROIDISM

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Objective: It was previously shown that patients with primary hyperparathyroidism (PHPT) are insulin resitant and have atherogenic dyslipidaemia. The aim of our study was to evaluate the effect of surgical treatment on insulin sensitivity (SI) and lipid levels in patients with PHPT.

Material and methods: In 26 patients with PHPT (age: 57.15±9.54 years, BMI 26.00 ± 4.55 kg/m2, PTH 276.61±64.83 ng/l, Calcium 2.95±0.19 mmol/l) insulin sensitivity and lipid status (total cholesterol (TC), HDL-C, LDL-C, triglyceride (TG), ApoA1, ApoB, and Lp(a) levels were determinated before and 4 months after surgical treatment. Insulin sensitivity was measured using euglycaemic hyperinsulinaemic clamp.

Results: After operation PTH (51.47±8.57 ng/l) and serum calcium (2.33±0.12 mmol/l) were normalized, there was no change in BMI index before and after operation (26.00±4.55 vs. 26.36±4.31 kg/m2, $p>0.05$). There was significant improvement in insulin sensitivity (M index: 3.91±2.01 vs 6.08±4.88, $p< 0.05$) after surgical treatment. There was no change in TC (6.02±1.33 vs. 6.00±1.11 mmol/l, $p>0.05$), HDL-C (1.26±0.32 vs. 1.28±0.30, $p>0.05$), LDL-C (3.84±1.07 vs. 3.94±1.01, $p>0.05$), TG (1.78±0.76 vs. 2.04±0.97, $p>0.05$), Apo A1 (1.637±0.305 vs. 1.627±0.302, $p>0.05$), Apo B (1.165±0.276 vs. 1.145±0.325), and Lp(a) (0.19±0.05 vs. 0.16±0.04, $p>0.05$) after operation. There was significant correlation between PTH and Lp(a) levels ($r=0.534$, $p< 0.05$), as well between SI and TC ($r= -0.489$, $p< 0.05$) and ApoB ($r= -0.573$, $p< 0.05$).

Conclusion: Four months after radical treatment insulin sensitivity was significantly improved while there was no improvement in dyslipidemia in our group of patients with PHPT.

INSULIN RESISTANCE AND RESPONSE TO COMBINATION THERAPY IN PATIENTS WITH GENOTYPE 1 HEPATITIS C VIRUS INFECTION

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Background/aims: Insulin resistance (IR) might be associated with hepatitis C virus (HCV) infection. The present study aimed to elucidate impacts of IR on the response to combination therapy with peginterferon-alpha (PEGIFN)/ribavirin in chronic hepatitis C (CHC) patients with HCV genotype 1 infection.

Methods: 150 Taiwanese patients who were without overt diabetes were enrolled and treated with PEGIFN/ribavirin for 24 weeks. Serum HCV RNA was deteced using a qualitative RT-PCR assay with the detection limit of 50 IU/mL. HCV genotypes were determined by using genotype-specific primers. Pretreatment HCV RNA levels were determined using a branched DNA assay with the quantification limit of 615 IU/ml. The IR was evaluated by homeostasis model assessment of IR (HOMA-IR) before treatment.

Results: Patients with sustained virologic response (SVR) were significantly younger ($P=0.036$), had a significantly lower pretreatment HCV RNA level ($P=0.001$), a significantly lower frequency of high HOMA-IR (>2.5) ($P=0.015$) and a lower mean HOMA-IR ($P=0.069$) than nonresponders. Multivariate logistic regression analyses showed that HCV RNA level, pretreatment HOMA-IR and age were independent factors associated with SVR. In 76 patients with high baseline viral loads (≥400,000 IU/ml), patients with high HOMA-IR (>2.5) had a significantly lower SVR rate than those with low HOMA-IR (≤ 2.5) ($P=0.002$).

Conclusions: IR was associated with SVR to PEGIFN/ribavirin combination therapy for CHC patients with HCV genotype 1 infection. These findings suggested clinical application of pretreatment HOMA-IR to predict treatment outcome and determine treatment regimens.

HOMOCYSTEINE LEVEL IS CORRELATED WITH METABOLIC SYNDROME BUT NOT WITH PREDIABETES STATE IN OBESE PATIENTS

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Background: Metabolic syndrome and prediabetes state (IFG, IGT) are more prevalent in obese patients. Parameters of these conditions are some of the risk factors for cardiovascular diseases. Homocysteine, a new untraditional risk factor for cardiovascular diseases, is associated with a proinflamatory state witch is more prevalent in obese patients.

The aim of this study was to evaluate prevalence of prediabetes and metabolic syndrome in a group of obese patients (previously not knew with diabetes) and to assess levels of homocysteine associated to these conditions.

Material and method: The study was conducted in a group of 162 patients (mean age 40.5±11.4 years; 109F/53M) with obesity (BMI≥30kg/m^2). We assessed anthropometric parameters (BMI, waist), blood pressure, and laboratory parameters (fasting plasma glucose, 2 hours plasma glucose in OGTT, HDL cholesterol, triglycerides, level of homocysteine). In order to establish the presence of metabolic syndrome we used NCEP/ATP III definition.

Results: Among 162 obese patients, 94 (58%) had normal glucose tolerance (NGT), 45 (27.8%) had prediabetes (22 patients IFG (13.6%), 23 (14.2%)

IGT) and 23 (14.2%) had diabetes. Metabolic syndrome was present in 91 patients (56%). According glucose tolerance, level of homocysteine (μmol/l) was 7.26±2.64 in NGT versus 7.77±3.06 in prediabetes states (p=NS). Patients with metabolic syndrome had level of homocysteine (μmol/l) 8.28±2.94 versus 6.55±2.37 in patients without metabolic syndrome (p=0.01).

Conclusion: Homocysteine level significantly correlates with presence of metabolic syndrome in a group of young obese patients. All the same it level is higher in prediabetes states but not statistically significant.

RELATIONSHIP BETWEEN HOMEOSTASIS MODEL ASSESSMENT OF INSULIN RESISTANCE AND ATHEROSCLEROSIS MARKERS IN CIGARETTE SMOKING

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Background: Smoking and insulin resistance have known as risk factors for initiating cardiovascular dysfunction. Cigarette smoking could promote atherosclerosis, by its effects on lipid profile, increase inflammatory activation and prothrombotic factors. We examined the relationship between homeostasis model assessment of insulin resistance (HOMA-IR) levels and atherosclerosis markers in cigarette smoking.

Methods: The study was observed with a cross sectional design. We included 19 male smokers and 20 male non-smokers, 19 to 42 years of age with normal blood pressure, normal blood glucose levels and body mass index below 25. Serum total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, apo B, hs-CRP, adiponectin, and fibrinogen levels were compared in smokers and non-smokers. The relationship between HOMA-IR and risk markers for atherosclerosis was determined in smokers and non-smokers.

Results: There were not significantly different in serum total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, Apo B, hs-CRP, adiponectin, and fibrinogen levels in all healthy smokers and non-smokers subjects. In smokers with HOMA-IR ≤1 showed HDL-cholesterol lower than its levels in non-smokers (p>0.05), while triglyceride, hs-CRP and fibrinogen levels were higher in smokers (p>0.05). Whereas serum adiponectin levels was significantly lower in smokers than in non-smokers with HOMA-IR ≤1 (4.26 mg/mL vs 5.48 mg/mL; p = 0.04). We also found a significantly correlation between time exposure of cigarette smoking and hs-CRP levels (r = 0.40; p=0.043) and LDL-cholesterol levels (r = 0.48; p=0.040).

Conclusions: These findings suggest that cigarette smoking with HOMA-IR levels may have important risks in promoting atherosclerosis.

EVALUATION OF ENDOTHELIN-1 PLASMA CONCENTRATION IN YOUNG HYPERTENSIVE SUBJECTS DURING ACE-INHIBITOR THERAPY

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Some clinical studies indicated that in young hypertensive patients plasma endothelin-1 (ET-1) concentration is elevated at the early stage of hypertension. It was proved that some antihypertensive drugs can effectively reduce blood pressure (BP) values as well as ET-1 concentrations. The aim of this study was to evaluate the relationships between plasma ET-1 concentrations and BP values after short-term (6 weeks) and long-term (6 months) trandolapril therapy in young hypertensive subjects.

Methods: 19 patients aged 17.6 ± 1.4 years with mild-to-moderate hypertension were enrolled. Patients with secondary arterial hypertension were excluded. Lipid profile, ET-1 plasma concentrations and BP were measured three times: before enrolling, after 6 weeks and finally after 6 months of trandolapril monotherapy (2 mg per day).

Results: After 6 weeks of trandolapril therapy we observed a significant reduction of systolic BP (from 142.6 ± 9.7 to 129.3 ± 8.4 mmHg, p< 0.0003) and diastolic BP (from 85.7 ± 6.9 to 79.8 ± 8.6 mmHg, p< 0.01). The reduction of average plasma ET-1 concentration was statistically non-significant. After 6 months of trandolapril therapy BP reduction was on the similar level, but there was a significant reduction of plasma ET-1 concentration (from 9.33 ± 1.9 to 7.49 ± 2.7 fmol/ml, p< 0.05). There was no influence of trandolapril on lipid profile during the study.

Conclusions:

1. Both short-time and long-time trandolapril therapy gave a significant blood pressure reduction.
2. The long-time therapy caused a significant plasma ET-1 concentration reduction.
3. The influence of trandolapril on lipid profile was neutral.

GLUCOSE STATUS AND CARDIOVASCULAR RISK FACTORS IN PERSONS WITH TYPE 2 DIABETES AND METABOLIC SYNDROME EVALUATED BY CONTINUOUS GLUCOSE MONITORING SYSTEM

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Aims: Glucose variability augments cardiovascular risk and longterm evolution in diabetes and metabolic syndrome (MetS). The aim of this study is to assess the relation between cardiovascular risk factors of MetS (abdominal obesity, lipid parameters, blood pressure), weight, body mass index (BMI), and glucose variability (mean amplitude of glucose excursions - MAGE) or glycated haemoglobin A1c (A1C), in persons with type 2 diabetes (T2D) and MetS monitored by continuous glucose monitoring system (CGMS, Medtronic, MiniMed).

Methods: 30 persons with T2D and MetS (8 women, 22 men, insulin-treatment-14, oral-treatment-16), assessed by CGMS. Mean diabetes duration-11.43(0-30)years, mean age-56.59(39-80)years, mean insulin-therapy duration 5.71(0-16)years. We assessed A1C, MAGE (based on glucose data from CGMS data, with the method of Monnier et al(2006)), total cholesterol(T-chol), HDL-cholesterol(HDLc), triglycerides(TG) and calculated LDL-cholesterol(LDLc). We used IDF 2005 criteria for diagnosing MetS.

Results: Mean weight-86.91±11.01(SD)kg, mean BMI-30.10±4.00 kg/m^2, mean waist circumference 107.17±10.44cm, mean systolic and diastolic blood pressure (mmHg) (SBP-139.17±16.63,DBP-82.92±8.65 respectively). Mean A1C-8.27% (6.1-12.0 %), Mean MAGE-89.59±34.61mg/dl.

Glucose variability increased with A1c category (p=0.015).

MAGE was higher in women (p=0.035).

Weight was inversely related with glucose variability(MAGE) (p=0.021).

SBP increased with diabetes duration and insulin-therapy duration.

T-chol improved with age(p=0.034), HDLc decreased with age(p=0.022), and LDLc decreased with increasing insulin-therapy duration (p=0.014).

Conclusions: Glucose variability was significantly inversely related to weight, but non-significantly correlated with other cardiovascular risk factors in persons with T2D and MetS.

ASSOCIATION OF THYROID-STIMULATING HORMONE WITH INSULIN RESISTANCE AND ANDROGEN PARAMETERS IN WOMEN WITH PCOS

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Backgrounds and aims: There is a relationship between thyroid function and insulin sensitivity and alterations in lipids and metabolic parameters. Little information is available regarding this relationship in women with polycystic ovary syndrome (PCOS). However all those pathologies are also described to often affect women with PCOS. The aim of our study was to study the comparison between the the patients with thyroid-stimulating hormone < 2.5 mIU/L and ≥ 2.5 mIU/L and evaluate their association with insulin resistance and endocrine parameters in 103 women with polycystic ovary syndrome.

Materials and metods: Clinical, metabolic, and endocrine parameters were obtained and an oral glucose tolerance test was performed with calculation of insulin resistance indices . Body Mass Index (BMI) was calculated.

Results: Women with thyroid-stimulating hormone ≥ 2.5 mIU/L had a significantly higher BMI, higher fasting insulin levels, and altered insulin resistance indices, higher total testosterone and free androgen indices, and decreased sex hormone-binding globulin levels in comparison with women where thyroid-stimulating hormone < 2.5 mIU/L. Generally, all of these parameters correlated significantly with thyroid-stimulating hormone only in women with thyroid-stimulating hormone ≥ 2.5 mIU/L.

Conclusion: Women with polycystic ovary syndrome and with thyroid-stimulating hormone ≥ 2.5 mIU/L had significantly altered endocrine and metabolic changes.

In women with PCOS and Subclinical Hypothyreosis, where the TSH value was ≥ 2.5 mIU/L (SCH), treatment with thyroxine in order to restore the endocrine metabolism might be a therapeutic option.

Therefore the relation of thyroid function and PCOS needs to be investigated further.

THE RELATIONSHIP BETWEEN INSULIN RESISTANCE AND COMPONENTS OF THE METABOLIC SYNDROME

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Aims: Insulin resistance has been suggested as the principal aetiological factor for the metabolic syndrome (MS). The aim of this study was to investigate the relationship between insulin resistance and the individual components of the metabolic syndrome.

Methods: Metabolic syndrome was diagnosed using the IDF criteria in 425 randomly selected subjects. The cohort was divided into octiles based on level of insulin resistance using the HOMA method. Logistic regression was used to determine the risk of MS and individual components of MS in each HOMA octile.

Results: The odds ratio (OR) [95% confidence intervals] for MS in each HOMA octile were as follows (from octile 2 to octile 8 relative to octile 1): 1.66 [0.29-9.39], 1.94 [0.36-10.42], 2.17 [0.40-11.72], 2.85 [0.55-14.73], 2.56 [0.49-13.40], 7.43 [1.48-37.20], 7.13 [1.41-35.95]. Only the ORs of octile 7 and 8 were significantly different from those of octile 1 ($p < 0.05$ for both). This trend of ORs increasing abruptly and significantly at octile 7 was also observed for risk of high triglyceride and risk for low HDL serum levels.

Conclusions: This study clearly demonstrates that the relationship between insulin resistance and risk for development of MS is not linear with the OR increasing abruptly at a HOMA value of 3.10. A HOMA value of >3.1 may therefore be a useful indicator for increased risk of MS. However, this cut-off value must be used with extreme caution since HOMA is reliant on accurate insulin measurement and no standardised, reference method for insulin determination is currently available.

PSYCHOLOGICAL DISTRESS IS ASSOCIATED WITH THE INSULIN RESISTANCE MEDIATED CLUSTERING OF CARDIO-METABOLIC FACTORS IN AFRO-CARIBBEAN IMMIGRANTS

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Aims: The high rate of cardio-metabolic abnormalities experienced by ethnic groups who migrate to more economically developed environments is usually atributed to the adoption of unhealthy lifestyle practices but not psychosocial distress. This study assessed the relationship of the psychosocial distress associated with immigration to the clustering of cardio-metabolic abnormalities in Afro-Caribbean immigrants to the U.S. Virgin Islands.

Methods: A population-based sample of 405 Afro-Caribbean immigrants age ≥20 was studied. Roger's Life Attitude Inventory questionnaire was used to assess psychosocial distress as feelings of social disconnection and dispair. Anthropometric and blood pressure measurements, together with serum glucose, insulin and lipids were measured for all subjects. The metabolic syndrome (Met-S) was determined by IDF criteria. Insulin resistance was estimated by the HOMA-IR method.

Results: In univariate analyses waist circumference, fasting glucose and fasting insulin were significantly correlated with psychosocial distress among those who lived in the USVI more than 15 years. In multiple logistic regression analyses adjusting for demographic and anthropometric measurements the Met-S (Odds Ratio = 1.48 (1.03 - 2.13)), but not any of its individual components, was significantly associated with psychosocial distress. The significant relationship of psychosocial distress to the Met-S was attenuated (Odds Ratio=1.32 (0.91 - 1.93)) only after adjustment for HOMA-IR.

Conclusions: High rates of insulin resistance and insulin resistance-mediated clustering of metabolic abnormalities among Afro-Caribbean immigrants may be related to the long-term effects of feelings of social disconnection and dispair.

VALIDITY OF INDICATORS OF CENTRAL OBESITY IN THE PREDICTION OF DIA BETES AND HYPERTENSION

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Through a home-based survey, 810 subjects aged 60 years and over in Abha City, Saudi Arabia, and 1800 subjects aged 18 years and over in 4 Egyptian

governorates were subjected to standardized waist and hip measurements, and central obesity was determined based on the waist circumference (WC) and waist-to-hip ratio (WHR) indicators. Then, 10th, 25th, 50th, 75th and 90th percentiles of WC and WHR were calculated.

The age-adjusted prevalence of central obesity based on the WC and WHR indicators was 32.4% and 43.5% respectively for Saudis and 24.1% and 28.7% for Egyptians. WC was significantly associated with both diabetes and hypertension in Saudis(OR=4.5& 2.4) and in Egyptians(OR=5.4& 6.6), while WHR was significantly associated with only diabetes among Saudis (OR=2.8), but not among Egyptians. After adjustment for sex and other confounding factors, WC was significantly associated with the risk of diabetes ($P < 0.02$ for both Saudis and Egyptians) and hypertension ($P = 0.0009$, $P=0.0007$ for Saudis and Egyptians respectively), while WHR was significantly associated with the risk of diabetes only among Saudis($P = 0.003$). No significant association was seen between BMI and diabetes or hypertension.

These findings suggest that high prevalence of central obesity should be avoided to decrease the risk of diabetes and hypertension. WC is a powerful independent predictor of mainly hypertension risk, while WHR may be a good predictor of only diabetes risk. BMI per se is not a significant predictor of diabetes or hypertension.

EFFECT OF SMOKING HABITS ON COMPONENETS OF METABOLIC SYNDROME IN NON DIABETIC MEN: THE ISFAHAN HEALTHY HEART PROGRAMME

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Introduction: There is limited evidence about the association between smoking and metabolic syndrome (MS). The aim of this study was to assess the association of smoking with the MS components.

Materials & methods: As part of the baseline survey of a community-based study, we studied 5573 non-diabetic men. All participants were interviewed and underwent physical examinations and blood collection.

Results: The study participants comprised of 1625 smokers and 3948 non-smokers, with a mean age of 38.07±14.85 years. Serum LDL-cholesterol and triglycerides (TG) were higher in smokers than in non-smokers (LDL-C: 115.34±39.03 vs.112.65±40.94 mg/dl, respectively, $P = 0.015$ and TG: 175.13±102.05 vs. 172.32 ±116.83 mg/dl ,respectively, $P = 0.005$). Body mass index, waist circumference and waist-hip ratio were lower in smokers than in non-smokers. The percentage of individuals with 2 MS components was higher in smokers than in non-smokers (39.64% vs. 33.00%, respectively, $P = 0.000$). However, the percentage of non-smokers with 3 MS components was higher than in smokers (49.62 % vs. 43.82%, respectively, $P = 0.000$).

Conclusions: Our findings support the hypothesis that lifestyle factors such as smoking can adversely affect MS components; however, we should acknowledge that these differences may have resulted from large sample sizes studied and may not be clinically significant. The lower prevalence of some MS components in smokers than in non-smokers might be because of their lower anthropometric measures.

Keywords: Anthropometric indexes, Biochemical factors, Metabolic syndrome, Smoking.

THE EFFECT OF BODY WEIGHT ON THE INCIDENCE AND PREVALENCE OF HYPERTENSION IN CAMEROON

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Aims: The prevalence of obesity and its related complications are on the increase in the industrialized as well as developing countries. This study assesses the relationship between obesity and hypertension in Cameroon.

Methods: The study was descriptive, cross-sectional and retrospective, involving 1919 participants (61.6% females mean age 33.7 ± 10.3 years old and 38.4% males; mean age 33.0 ± 11.5 years old), recruited during a screening of hypertension and cardiovascular diseases organized by the Laboratory of Nutrition and Nutritional Biochemistry of university of Yaounde, Cameroon. Anthropometric classification was done according to WHO criteria as $19 < BMI \leq 24.9$ (normal); $25 \leq BMI \leq 29.9$ (overweight) and $BMI \geq 30$ (obese); while hypertension was defined using both the National Cholesterol Education Program (ATP III) and World Health Organisation criteria.

Results: Of the 1919 participants - Diastolic hypertension was observed in 43% and 32.4% of participants using the NCEP and WHO criteria respectively with a higher incidence noticed in females. The prevalence of diastolic hypertension although the same between normal and overweight participants (9.1%); was however higher in obese participants (14.6%) with females highly exposed (10.9%) than males (3.7%).

Conclusions: This study revealed the strong association of BMI with hypertension and showed high prevalence of high blood pressure in general population, obese participants being the most exposed. The present result is consistent with the national emphasis on prevention and control of overweight and obesity and indicates that blood pressure measurements and control are especially important for overweight and obese people.

ARTERIAL STIFFNESS AND NOCTURNAL BLOOD PRESSURE CHANGE IN NORMOTENSIVES WITH METABOLIC SYNDROME

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Background: Metabolic syndrome (MS)is associated with an increased risk for cardiovascular events. Artery stiffness is an important predictor of cardiovascular morbidity and mortality. Disruptions of circadian rhythm of blood pressure(BP)such as excessive morning surge and excessive nocturnal dipping or blunted nocturnal dipping, have been shown to be associated with target organ damage. This study is to investigate the relationship between arterial stiffness and parameters of ambulatory blood pressure monitoring in normotensive individuals with metabolic syndrome.

Methods: We recruited subjects with metabolic syndrome whose blood pressure were within normal range without anti-hypertensive agents. Arterial stiffness was determined by cardio-ankle vascular index (CAVI) and internal common carotid artery intimal thickness using extracranial carotid Doppler ultrasound. Continuing 48 hours ambulatory blood pressure monitoring (ABPM) was measured with an ambulatory BP monitor.

Results: A 77 participants were included for data analysis. There was no significant correction between CAVI and internal common carotid intimal thickness ($r =-0.29$, $p =0.17$). MS score significantly corrected to CAVI ($r = 0.3$, $p = 0.009$). CAVI significantly correlated to dipping status ($r = 0.3$, $p = 0.009$). Significantly correlation was noted between the CAVI value and the morning BP surge ($F =4.72$, $p = 0.011$; $F =6.73$, $p = 0.002$). The extreme dippers group (>20% systolic blood pressure reduction in night time) had

significantly higher levels of CAVI compared to the non-dippers group (p = 0.012, p = 0.002).

Conclusion: Extreme dipping may attribute to arterial stiffness in normotenisve individuals with MS.

OBESITY AND METABOLIC SYNDROME: ASSOCIATION WITH ESTROGEN AND PROGESTERONE RECEPTOR STATUS

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Aims: Obesity is a known risk factor for breast cancer (BC). Obese postmenopausal women have an increased production of estrogens, increasing the risk of breast cancer. Recently, metabolic syndrome (MS) has also been identified as a risk factor for BC. Hyperinsulinemia interacts with estrogen to synergistically induce mitogenic responses in breast epithelium. It is not clear whether the positive association between obesity, MS and BC differs across estrogen receptor (ER) and progesterone receptor (PR) status of breast tumors.

Methods: In 42 non-diabetic breast cancer patients aged 40 years or more before any treatment, body mass index and waist circumference, blood pressure, lipid profile, ER and PR status were assessed.

Results: Mean age was 58.9(±11.7) years, mean body mass index (BMI) was 28.0(±4.6) kg/m^2 and mean waist circumference, 91.8(±10.8) cm. Overweight was present in 38.0%, obesity in 19.0% and MS in 50.0%; ER were positive in 85,3% and RP in 70.6% of the cases. Women with BMI of over 25 had more PR positive breast cancer (p=0.03), without statistically significant differences in this case between overweight and obesity. BMI did not show a statiscally significant relationship with ER status. MS and waist circumference did not show statiscally significant relationship with ER and PR status.

Conclusions: Our results suggest that obesity and overweight are associated with PR positive breast cancer. No association was found between overweight or obesity with ER status, neither between MS or central obesity with PR and ER status. These results were conditioned by the small sample size.

QUALITY OF SLEEP AMONG HYPERTENSIVE PATIENTS IN A SEMI-URBAN NIGERIAN COMMUNITY: A PROSPECTIVE STUDY

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Background: The prevalence of "poor sleep" in patients with chronic hypertension is unknown in Nigeria.

Objective: The study aimed to measure the prevalence of "poor sleep" in hypertensives and to examine the association between quality of sleep and severity of hypertension.

Methods: Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI) in chronic hypertensives in Nigeria.

Results: The mean age of the hypertensives did not differ from the controls at 58.15 ± 9.65 years (range, 19-76 years). A total of 80 (60.6%) were females with a mean age of 58.3 ± 12.2 years while 52 (39.4%) were males with a mean age of 58.8 ± 11.7 years. The mean body mass index (BMI) was 26.42 ± 4.13 kg/m^2 (range, 18.9-36.4 kg/m^2), with 63.1% being either overweight or obese. The mean SBP was 167.4 ±21.8 mmHg (range, 100-210 mmHg) while the mean DBP was 96.7±14.9 mmHg (range, 60-130 mmHg). Fifty-six (42.4%) hypertensive subjects were "poor sleepers" (global PSQI > 5), with a global mean PSQI of 5.03 ± 3.28. This was significantly more than 17.3% of control subjects, with a mean global PSQI of 3.10 ± 0.83. Among the hypertensives, there was no statistically significant relationship between the global PSQI and the age (P = 0.653), sex (P = 0.710), BMI (P = 0.253), systolic (P = 0.145), and DBP (P = 0.827).

Conclusions: Poor sleep is common in hypertensives and may be associated with lower health-related quality of life.

SUCCESSFUL LIFESTYLE INTERVENTION FOR METABOLIC SYNDROME PATIENTS

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Aims: This study was designed to measure the impact of an educational program involving a diet therapy and physical exercises on metabolic syndrome patients.

Methods: A number of 69 patients, 37 male and 32 female, mean age 62.14±7 years, with metabolic syndrome (diagnosed using ATP III criteria) were included into educational program. All patients completed at baseline, 1 month and 2 month a food frequency questionnaire and they were educated to keep a diary food weekly for 2 months. Body weight, blood pressure, lipid profile, proinflammatory state and prothrombotic state were measured at all visits. Each recording was analyzed in an individual meeting and they received professional advice.

Results: An average weight loss of 4.3±1.6 kg of the initial weight was recorded parallel with decreased in calories consumption (p< 0.05). Triglycerides decreased from 267±62 mg/dl to 143±71 mg/dl (p< 0.05), total cholesterol dropped from 244 ± 34 mg/dl to 207±68 mg/dl (p< 0.05), and HDL-cholesterol increased from 35±4 mg/dl to 37±15 mg/dl (p< 0.05), after 2 months. Systolic BP dropped from 145±30 to 130±20 mm Hg (p< 0.05). Diastolic BP decreased from 95±15 mm Hg to 85±15 mmHg (p< 0.05). Fibrinogen, plasminogen activator inhibitor, C-reactive protein decreased but we didn´t found significant statistically differences. This reduction is explained by the decrease of the amount of glucose and fats; quantity of proteins was similar.

Conclusions: The present study establishes the positive impact of an educational program in management of patients with metabolic syndrome.

THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH DIAGNOSED TYPE 2 DIABETES

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Aims: The aim of our study was to determine the prevalence of the Metabolic Syndrome (MS), as the NCEP/ATP III criteria in a selected population of type 2 diabetes and its relation with the degree of metabolic control.

Methods: 321 patients randomly selected from UHC "Mother Theresa" and regional hospitals in Shkodra and Pogradec. All the patients had completed anthropometric measures and lipid profile after an 8-hour fast. The patients having two or more criteria (diabetes present) were defined as having MS.

Results: 321 patients. Males 158 (49.2%), mean age 59.7±9.3 yrs, mean diabetes duration 9.1±5.8 yrs. The prevalence of the MS was 80.1%, Males 64.6% and Females 95.1%. Diabetes duration was slightly longer in patients with MS than without (M: 9.3±5.9 vs 8.9±5.7; F: 9.1±4.8 vs 8.8±4.7 yrs) (p>0.05). The number of components of the MS was related to the age

(ANOVA p< 0.05) but not to diabetes duration. Central obesity was present in 25.3% of Males, Females 77.9%, HTA 52.5 and 56.4%, low HDL 45 and 91.4%, high triglycerides 65.1 and 62.6% respectively. HbA1c was higher in persons with MS (8.6±2.7 vs 7.9±1.8%, p< 0.05).

Conclusion: The results show that MS is very frequent in type 2 diabetes and especially some of the most prominent cardiovascular risk factors. It urged immediate efforts directed at controlling the components of MS (mainly improved metabolic control, lipid profile, HTA and obesity).

METABOLIC SYNDROME IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Systemic Lupus Erythematosus (SLE) is an inflammatory rheumatic disease with risk factors for accelerated atherosclerosis including metabolic syndrome (MS).

Aims: Identifying MS prevalence in patients with SLE and evaluating cardiac risk factors and lupus activity in patients with and without MS.

Patients and methods: The study population consisted of 62 patients (59 women), aged 16 to 72 years, diagnosed with SLE in accordance with the criteria of the ACR followed at the Department of Internal Medicine. We compared patients with G1 and without G2 MS.

Results: Thirty patients (48%) had MS (29 women). G1 presented a significantly higher mean age (37.6 *vs* 32.7 years) and had longer duration (4.3 *vs* 2 years) of SLE. Presence of vasculitis, renal or central nervous system involvement is more frequent in G1 (64.3% *vs* 35.5%). Proteinuria (2.8 *vs* 4.4 gr/ 24h), C-reactive protein (5.6 *vs* 13.8 mg/l) and total cholesterol levels (5.1 *vs* 7.2 mmol/l) were higher in G1. C-HDL levels were lower in G1 (0.86 *vs* 1.01 mmol/l,). All patients with MS had high fasting glucose > 6 mmol/l, android obesity and hypertriglyceridemia > 2 mmol/l, but only 18 patients had hypertension. The use of corticosteroid was observed in all patients with MS *vs* 69% of the G2. The mean SLEDAI Score was higher in the G1 (10.8 vs 5.4).

Conclusion: Lupus and or its treatment confer additional metabolic risk of cardiovascular diseases. It is en enormous challenge to develop an effective prevention program for this group.

METABOLIC SYNDROME AND TOTAL CARDIOVASCULAR RISK: SYNERGISM AND CONTROVERSIES

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Objective: To evaluate the advantages and restrictions of cardiovascular risk estimation using SCORE in persons with metabolic syndrome (MS).

Methods: The study included 288 men and women aged 40-59 with hypertension I-II. All participants filled the questionnaire and were measured blood pressure, heart rate, waits circumference, height, weight, plasma lipids, fasting glucose and glucose tolerance test. MS was defined according to the NCEP ATP III criteria. Cardiovascular risk was estimated on SCORE.

Results: High cardiovascular risk was in 30,8% of participants with hypertension I-II. MS revealed in 32% of participants. Among the participants with high cardiovascular risk 6% had only hypertension without other risk factors, 21% had 2 risk factors (hypertension and obesity or hyperlipidemia), 30% had 3 risk factors (hypertension and obesity and hyperlipidemia) and 43% had MS.

Only every second person with different variants of MS had high cardiovascular risk. High and very high cardiovascular risk was estimated in 46,2% patients with central obesity, dislipidemia and glucose intolerance, in 32,2% persons with hypertension, central obesity and glucose intolerance. From the other side on the period of screening 60% of patients with MS had the history of cardiovascular events.

Conclusion: SCORE, based on the 5 major cardiovascular risk factors, estimates high cardiovascular risk only in 45% of patients with MS. In patients with MS strategy of cardiovascular prevention has to include not only total cardiovascular risk estimation, but also consider other components (central obesity, glucose intolerance and other) which can predict cardiovascular diseases.

PREVALENCE OF THE METABOLIC SYNDROME USING THREE PROPOSED DEFINITIONS IN A BRAZILIAN JAPANESE COMMUNITY

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Metabolic Syndrome (MS) is associated with increased risk of morbi-mortality, thus the characterization of the population magnitude of this syndrome is critical for allocating health care . However, prevalence estimates of MS in the same population could differ depending on the definition used. Therefore, we compared the prevalence of the MS using definitions proposed by: National Cholesterol Education Panel (NCEP), revised (NCEP-R) and International Diabetes Federation (IDF) in a brazilian japanese community (131 individuals, age 57±16 years, 1st and 2nd generation). Clinical and laboratorial evaluations were performed by trained professionals with adequate equipment. The prevalence of MS was 23.6%, 25.4% and 31.3% under the NCEP, NCEP-R and IDF definitions, respectively. All individuals identified under the NCEP definitions were also identified under the NCEP-R. IDF definition classified 19(14.5%) individuals with MS that were not classified under the other definitions and NCEP/NCEP-R definitions identified 13(9.9%) participants not identified under the IDF definition. Among all participants, 21(16.0%) individuals were similarly classified under the three definitions. We observed, in this group, higher waist circumference (p< 0.01) compared to all other individuals classified with MS, more severe lipid disorders, higher triglycerides and lower HDL serum levels (p< 0.01) compared to individuals identified only under the IDF definitions and lower fasting blood glucose levels (p=0.03) compared to those classified under the NCEP/NCEP-R definitions. Therefore, in this brazilian japanese community, waist circumference, a simple tool to evaluate insulin resistance, was a strong risk factor for MS, identifying those at higher cardiovascular risk .

RELATIONSHIP BETWEEN THYROID FUNCTION AND THE COMPONENTS OF THE METABOLIC SYNDROME IN EUTHYROID SUBJECTS

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Introduction: Thyroid disease and the metabolic syndrome (MS) are both associated with cardiovascular disease.

Objective: The aim of this study was to explore the hypothesis that thyroid function, in euthyroid subjects, is associated with components of the metabolic syndrome and insulin resistance.

Methods: 155 women were evaluated in their first morbid obesity appointment regarding anthropometric variables (weight, height, waist circumference (WC)), blood pressure, fasting plasma glucose (FPG) levels, LDL-cholesterol, HDL-cholesterol, triglycerides, FT3, FT4 and TSH concentrations. MS was defined using IDF-2005 criteria. TSH values between 0.35 and 4.94 ng/dL were considered as euthyroidism. Subjects who were not euthyroid and subjects taking thyroid medication were excluded. Homeostasis model assessment for insulin-resistance (HOMA-IR) was calculated. Results were expressed as a mean ± SD and in relative frequency. Pearson's correlation coefficients were obtained for FT3, FT4 and THS and BMI, MS components and HOMA-IR.

Results: The mean age of the analysed sample was 40.10±11.17 years, having a mean body mass index (BMI) of 43.28±7.05 Kg/m2 and a mean WC of 119.67±14.49 cm. The prevalence of MS in the analysed sample was 41.29%. TSH and FT4 were both positively correlated with BMI (r=0.18, p=0.03 and r=0.21, p=0.008, respectively). No correlations were found between FT3 and BMI, FT3, FT4, TSH and the components of MS and BMI, FT3, FT4, TSH and HOMA-IR.

Discussion: This study provides evidence for an association between thyroid status and BMI and no evidence for an association with the components of MS or insulin resistance.

THE INFLUENCE OF THE ATHEROSCLEROSIS RISK FACTORS ON RENAL FUNCTION IN PATIENTS WITH METABOLIC SYNDROME AND DIABETES COMPARING TO CONTROLLERS

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Objectives: To assess the influence of some atherosclerosis risk factors on renal function in patients with metabolic syndrome or diabetes versus controllers.

Methods: Evaluation of medical records of 535 patients, divided in: group A- 148 pts. with metabolic syndrome, group B - 98 pts. with diabetes mellitus and controllers group C -289 pts. (no diabetes, no metabolic syndrome). Patients with history or evidence of renal disease were excluded. We have correlated the blood pressure values, the components of lipid profile and blood glucose with creatinine clearance level as a marker of renal function. Impaired renal function was considered when creatinine clearance was lower than 90 ml/min.

Results: Impaired (vs. normal) renal function in group C, correlates with higher blood pressure values (mean SBP 137,16mmHg vs. 128,4mm Hg; p< 0,0001, mean DBP 75,36 mmHg vs. 70,7 mmHg; p=0,001) and greater levels of total cholesterol and LDL - cholesterol, (mean level 225,14 mg/dl vs. 214,13 mg/dl, p=0,03 and 145,5 mg/dl vs. 132,19 mg/dl, p=0,009 respectively).In group B, impaired renal function was significantly influenced only by SBP (mean value 146,79 mmHg vs. 141,11mmHg p=0,03) and DBP (mean value 84,17 mmHg vs. 76,96 mmHg, p=0,001), while in patients with diabetes (group A), there was no significant difference regarding BP values and lipid levels between patients with impaired renal function and patients with normal renal function.

Conclusion: Hypertension and dyslipidemia, may lead to renal dysfunction and may contribute to progression of renal impairment, but the influence of this factors decreases with progression of the metabolic changes.

THE EFFECT OF CELL SPECIFIC INSULIN RESISTANCE ON 3T3L1 CELLS VIABILITY AND GLUCOSE UPTAKE

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Insulin plays a key role in the stimulation of glucose uptake in tissue, such as muscle and adipocytes, as well as in the maintenance of glucose homeostsis. Impairment of insulin's ability to stimulate glucose uptake in the tissue is a major factor responsible for insulin resistance associated with type 2 diabetes. This study try to establish 3T3L1 specific insulin resistance model to assessed the effect of constant high glucose and high insulin concentrations. To achieve this purpose, we used 3T3L1 cell to characterize the insulin resistance system, and MTT, glucose uptake assay, GLUT1 and GLUT4 expression assay were used to determine the cell viability and whether GLUT1 and GLUT4 are related to glucose uptake under insulin resistance situation. The result found that while increase insulin and glucose concentration in the medium could increase 3T3L1cell viability. In the other hand, glucose utilization rate does not decrease significantly in the culture medium, however, in DMEM with different insulin concentrations (5ug/ml, and 50ug/ ml). The expression of GLUT1 and GLUT4 transporters did not show any significantly difference between the groups. In conclusion, our results indicate that constant high glucose and high insulin concentrations might change 3T3L1 cell insulin sensitivity, which similar to those observed in poorly controlled diabetic patients, may contribute this specific cell model to the study of development of metabolism syndrome.

CLUSTERING OF THE COMPONENTS OF METABOLIC SYNDROME IN TYPE 2 DIABETES PATIENTS: A STUDY AMONG THE BANGLADESHIES

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Aims: While we once saw type 2 diabetes, hypertension, obesity and dyslipidemia as separate conditions, we now have a much clearer understanding of the way in which they are linked. In many instances, they are simply different facets of the same disorder. These conditions tend to cluster with each other. In this study we assessed how frequent the other components of metabolic syndrome cluster with type 2 diabetes in Bangladeshi diabetes patients.

Methods: Two hundred and thirty type 2 diabetes patients who registered at a specialized diabetes care center in Chittagong, the port city of Bangladesh were included in the study. The prevalence of metabolic syndrome among type 2 diabetes was determined using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria with the modified waist circumference for the Asian-Indian ethnicity.

Results: The prevalence of metabolic syndrome was 75% among Bangladeshi type 2 diabetes patients. It was more common in female.(M vs F=54.6% vs 93.4%, P< 0.001). The highest prevalence of metabolic syndrome was 78% among the age group of 51-60 years. In addition to diabetes, 20%, 33%, 29.6%, and 12.6% patient had one, two, three, and four more components of metabolic syndrome respectively. Only 4.8% had no component of metabolic syndrome other than diabetes.

Conclusions: The prevalence of metabolic syndrome was quite high among Bangladeshi type 2 diabetes patients like other population. The vast majority of type 2 diabetes patients had one, two, three or four more components of metabolic syndrome.

THE CORRELATION BETWEEN HYPERTENSIVE WAIST AND VISCERAL ADIPOSE TISSUE

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Background and aims: A large body of evidences showed that abdominal visceral adipose tissue has been linked with cardiometabolic risk. Our previous studies demonstrated that hypertensive waist (HTW) have a high sensitivity and specificity for the prediction of the metabolic syndrome and for high cardiovascular risk. The aim of this study was to investigate the relationship between hypertensive waist and visceral adipose tissue.

Methods: A total of 207 women and men, randomly selected from general population, aged ³18 years were included in this study. HTW was defined as the presence of a systolic blood pressure ≥130mmHg and/or a diastolic blood pressure ≥85mmHg or history of treated hypertension plus a waist circumference ≥80cm for women and ≥94 for men. Visceral adipose tissue (VAT) was assessed by bioimpedance using InBody 720- Body Composition Analysis.

Results: In this group of patients, the mean waist circumference was 112.3cm in men (min.68 cm, max. 150cm) and 103.9cm in women (min.62cm, max.162 cm). The prevalence of hypertensive waist was 60.9%. 172 patients (83%) had a visceral fat area over 100cm ^{2}. Among both men and women, VAT was correlated with the presence of HTW ($r=0.532$, $p< 0.001$). General loglinear analysis showed that HTW was an independent predictor of a VAT >100cm^2 (PR 1.7 [95% CI 1.4-2.0], $p< 0.001$).

Conclusions: Hypertensive waist is an independent predictor of VAT, a condition associated with high cardiometabolic risk, therefore this simple clinical tool could be use to screen for the presence of increased visceral fat accumulation.

SERUM RETINOL BINDING PROTEIN-4 LEVELS AS INFLUENCED BY COMPONENTS OF METABOLIC SYNDROME IN A DIABETIC SAUDI COHORT

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Objective: Several studies have confirmed the association of retinol binding protein-4 (RBP4) to indices of glucose metabolism, but its link to insulin resistance and metabolic syndrome still remains clouded. We studied the association between RBP4 and various components of metabolic syndrome in Saudi population.

Subjects and methods: 81 patients, age and BMI matched with type 2 diabetes were screened for metabolic syndrome based on the definition of WHO. Anthropometrics were measured, fasting blood glucose and lipid profile were determined. Serum RBP4 levels were determined using ELISA.

Results: In this cross-sectional study, 67.9% (55) of patients had metabolic syndrome. RBP4 levels were higher compared to those without (28.16 ± 9.82 versus 24.59 ± 10.83), but didn´t achieve significance. Consequently, there was an increasing trend in RBP4 levels as components of metabolic syndrome increase (see table 1).

	With MS (N = 55)	Without MS (N = 26)	P-Value
Age	51.66 ± 10.1	49.72 ± 8.8	0.38
BMI	31.56 ± 4.40	30.32 ± 6.11	0.20
RBP4	28.16 ± 9.82	24.59 ± 10.83	0.14

	1 (N = 11)	2 (N = 15)	≥ 3 (N = 55)
RBP4	23.68 ± 10.7 (3.67-40.2)	26.19 ± 11.04 (8.89-45.4)	28.71 ± 9.60 (4.8-50.4)

Table 2: Serum RBP 4 levels in relation to presence of metabolic syndrome factors

Conclusion: Although RBP4 levels show an increasing trend as components of metabolic syndrome increase, further studies are still needed to confirm its association to metabolic syndrome since no significance was achieved.

THE EMERGING LINK BETWEEN METABOLIC SYNDROME & DIABETES IN GWALIOR-CHAMBAL REGION OF CENTRAL INDIA ON THE BASIS OF THE CLINICAL IMPLICATIONS

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The metabolic syndrome (Met S) is comprised of various medical conditions that confer increased risk of diabetes and cardiovascular disease. The pathophysiological components of MS include glucose abnormality, obesity or increased waist circumference, blood pressure, and hyperlipidemia.

Methods: We studied the prevalence of the metabolic syndrome (MetS) in Gwalior- Chambal region of Central India, according to two definitions (NCEP- ATPIII and IDF); and we also examined these issues upon link between metabolic syndrome and diabetes. We conducted an examination survey on a sample representative of the general population aged 30-70 years, attended by 385 participants in which 275 males and 110 females.

Conclusions: The prevalence of MetS increased markedly with age. According to the NCEP-ATPIII and IDF definitions, the prevalence of MetS was, 41.29% and 47.0% respectively. Approximately 65.15% of participants with diabetes also had MetS and the prevalence of MetS was approximately 7.79%, upon exclusion of diabetic individuals. High blood pressure, elevated triglycerides and waist circumference were the criteria found most frequently among MetS holders with diabetes. We identified a high prevalence of MetS in this population in epidemiological transition. The prevalence rate according to different definitions differs, because of limited agreement between the MetS definitions. Early identification and greater insight in to the mechanism behind the syndrome may improve our understanding of how to prevent and best manage this complex condition in precipitating into other health risks.

EFFECTS OF TELMISARTAN IN HIV POSITIVE PATIENTS WITH HYPERTENSION AND METABOLIC ALTERATIONS

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Aims: In HIV+ patients the choice of anti-hypertensive therapy must be made carefully and at present guidelines are lacking. Telmisartan, an angiotensin II receptor blocker (ARB) approved for treatment of hypertension, is also a partial agonist of PPAR-γ To value the role of telmisartan in HIV+ patients with hypertension and metabolic alterations.

Methods: Preliminary data of a study that enrolled HIV+ HAART treated patients with hypertension and hypertriglyceridemia are presented. The first 10 patients treated with telmisartan 80 mg daily were analysed. The

following parameters were measured at baseline (T0), one (T1), three (T3) and six (T6) months of therapy: systolic and diastolic blood pressure (SBP, DBP), BMI, TCh, LDL-C, TGs, creatinine, transaminases, CPK, CD4 and CD8 cell counts, HIV-RNA.

Results: Data showed that telmisartan significant decreased SBP and DBP at T1, T3 and further at T6 (p=0,001). Moreover it statistically reduced TG levels at T3 and T6 versus T0 (p< 0,05). TCh and LDL-C showed a trend of reduction whereas HDL-C levels increased. No alterations of BMI, CPK, creatinine and transaminases were shown. Finally at T6 versus T0 microalbuminuria showed significant decrease (p< 0,04).

Conclusions: It has been reported that telmisartan has more favorable effects on glucose or lipid parameters than other ARBs with no PPAR-γ agonist in hypertensives with diabetes. In our study telmisartan has been well tolerated and effective for control of hypertension and to improve lipid metabolism. Telmisartan may thus be the anti-hypertensive drug of first choice in HIV+ subjects on HAART affected with metabolic disorders.

IS THERE A LINK BETWEEN VITAMIN D STATUS AND BLOOD PRESSURE IN A SUNNY COUNTRY?

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Several studies demonstrate a relationship between essential hypertension (EH) and low vitamin D status.

Aim: To evaluate whether vitamin D status are related to blood pressure in adults living in a tropical country.

Methods: A total of 151 individuals (66% women) living in Sao Paulo, Brazil, participated in this study, conducted during all the seasons. Anthropometric measurements, blood pressure and a fasting blood sample were obtained. Serum levels of $25(OH)D_3$ was measured by HPLC, intact PTH by eletroquimioluminescence. Vitamin D insufficiency was defined by $25(OH)D_3 \leq 75$ nmol/l and high blood pressure (HBP) by levels ≥140/90mmHg, without a pharmacological treatment. The results are presented as mean (SD). Chi-square test was used to compare frequencies; significance level was p< 0.05.

Results: Mean age 47(15) years, BMI 29(6) kg/m², waist circumference 95(14) cm and PTH 44(20)pg/ml. Individuals with HBP were older and had significantly higher anthropometric measures and PTH levels. HBP was observed in 36% of participants [mean 147/90 (13/9)mmHg]. Mean vitamin D of the whole sample was 53nmol/L, being similar in individuals with HBP 51(18)nmol/l and normal blood pressure (NBP) 57(19)nmol/l. Vitamin D insufficiency was present in 86% of all participants, and the proportions didn't differ between HBP (82%) and NBP (89%). However, no significant association was observed between HBP and vitamin D insufficiency.

Conclusion: The absence of relationship between vitamin D and HBP in our sample. Didn't favor the hypothesis that vitamin D may be implicated in the physiopathology of EH.

THE EFFECT OF MENOPAUSE OF THE METABOLIC SYNDROME AMONG TUNISIAN WOMEN

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Introduction: Women with the metabolic syndrome are known to be at especially high risk cardiovascular disease. This study examined the effect of menopausal status on the risk of the metabolic syndrome (MS) in Tunisian women.

Methods: Data were obtained from the Tunis Atherosclerosis Risk Factors Study (2004 - 2005). A total of 1438 women who did not receive oral contraceptive pills or hormone replacement therapy, with 856 pre menopausal women (pre-M) and 582 post-menopausal (post-M) women were included. MS was defined according to the National Cholesterol Education Program Adult Treatment Panel III.

Results: post-M women had significantly higher mean waist circumference, systolic blood pressure, pulse pressure, total cholesterol, LDL cholesterol and triglyceride levels than pre-M women after adjusting for age (p< 0.001, p< 0.001, p=0.060, p< 0.001, p< 0.001, p< 0.001 respectively). Among post-M women, the age adjusted odds ratio was 1.030 (95%Cl 0.729-1.456) for abdominal obesity, 1.434 (95%Cl 1.042-1.975) for high elevated blood pressure, 1.271 (95%Cl 0.923-1.749) for low HDL cholesterol, 0.918 (95%Cl 0.923-1.304) for high triglycerides and 1.067 (95%Cl 0.695-1.639) for high fasting glucose compared with pre-M women. The prevalence of MS was significantly higher in post-M women [46.7% vs. 26.7%; Odds 2.29 (95% CI 1.52-3.47); p< 0.001].

Conclusion: post-M status is associated with an increased risk of the metabolic syndrome independent of normal aging in Tunisian women.

PREDICTION AND PREVALENCE OF METABOLIC SYNDROME IN OVERWEIGHT AND OBESE SUBJECTS IN CAMEROON

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Metabolic syndrome (MS) has reached pandemic proportion and has an impact on the incidence and severity of cardiovascular pathologies. The present study evaluates the prevalence of MS, and determines the appropriate definition for the evaluation of MS in overweight and obese subjects in Cameroon. The study is cross sectional, involving 1519 subjects (18-70 years), and body mass index (BMI) (25.01 to 62.50 Kg/m²). Physiological and anthropometrical measures were taken at the first visit of the subject. Glucose and lipid parameters were analysed from the plasma of fasting subjects. NCEP-ATPIII, AHA/NHLBI, and IDF criteria were used to evaluate MS. Receiver-operating characteristic curve analysis was used to evaluate the ability of the 5 definitions to predict the prevalence of MS in Cameroon. It was observed that the prevalence of MS and its individual component's prevalence among participants vary widely across definitions. The use of the IDF definition of the metabolic syndrome leads to a higher prevalence of the metabolic syndrome than other definitions. The IDF criteria were adopted as the appropriate definition of MS in Cameroon with a prevalence of 19.80 and an ROC area of 0.79.

Keywords: Anthropometry, cardiovascular diseases, hypertension, lipid profile, physiology.

Abbreviations: AHA, American heart association; **BMI**, body mass index; **BW**, body weight; **CD**, cardiovascular diseases; **EGIR**, European group for study of insulin resistance; **IDF**, international diabetes federation; **MS**, metabolic syndrome; **NCEP**, National Cholesterol Education Program; **NHLBI**, National health lung and blood institute.

METABOLIC SYNDROME AND CARDIOVASCULAR RISK IN THE PROVINCE OF SEGOVIA (SPAIN)

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Background: MS has been found to contribute to the cardiovascular risk in humans, although some studies have been dissapointed. Our aim in this study was to describe the predicted cardiovascular risk in a healthy representative population from Segovia Spanish province and to investigate the association of MS defined by AHA/NHLBI and IDF with a predicted

risk of coronary heart disease (CHD) ≥ 10% with the Framingham function and predicted risk of cardiovascular mortality (CVM) ≥ 3% with the SCORE.

Method: Cross-sectional design. 888 individuals aged 35-74 years, residents in the Province of Segovia. Period: January 2000 to January 2003. Waist circumference, SBP, DBP, fasting glucose, lipid profile of patients were obtained.

Results: Using the AHA/NHLBI and IDF definitions respectively, the age/sex standardized prevalence of the MS was 17% and 24,3%. The median 10-year predicted risk of CHD was 5% and the median 10 year predicted risk of CVM was 0,89%. OR of predicted risk of CHD ≥ 10% for participants with MS defined by AHA/NHLBI and IDF were 11,8 (95% CI, 6,6-20,8) and 10,7 (95% CI, 6,3-18,3) respectively. OR of predicted risk of CVM ≥ 3% for subjects with MS defined by AHA/NHBLI and IDF were 5,5 (95% CI, 2,3-12,9) and 4,1 (95% CI, 1,9 -8,8) respectively.

Conclusions:

1. The estimated CHD and CVM in Segovia are the lowest of Spanish provinces.
2. Both definitions of the MS were associated with high estimated CHD and CVM.

THE IMPACT OF THE TWO MORE RECENT DEFINITIONS OF THE METABOLIC SYNDROME ON THE PREVALENCE IN THE PROVINCE OF SEGOVIA (SPAIN)

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Background: The estimated prevalence of Metabolic Syndrome (MS) is higher with the AHA/NHLBI and the IDF definitions except for Asiatic cohorts. Our aim in this study was to investigate the prevalence of MS defined by Adult Treatment Pannel III (ATPIII), AHA/NHLBI and IDF in the Province of Segovia (Spain), the prevalence in rural and urban areas, and if these two recent definitions have positive correlation.

Method: Cross-sectional design. 888 individuals, aged 35-74 years. Residents in urban and rural areas of the Province of Segovia. Period: 2000 to 2003. Waist circumference, SBP, DBP, fasting glucose, lipid profile of patients were obtained.

Results: The standardized prevalence of the MS was: ATPIII 15,7%; AHA/NHLBI 17%; IDF 24,3%. No significant differences in MS prevalence between rural and urban areas were found: AHA/NHLBI 15,5% urban, 20,3% rural; 13,7% urban and 17,9% rural in males (p = 0,34); 16,7% urban and 22,6% rural in females (p = 0,16). IDF 25,8% urban, 24,8% rural; 27,0% urban and 26,8% rural in males (p = 0,28); 24,3% urban and 30,0% rural in females (p = 0,55). A high association was found between AHA/NHLBI and IDF (Kappa 0,846).

Conclusions:

1. A higher estimated prevalence of MS with IDF definition in Segovia with no differences between rural and urban areas.
2. A positive correlation, was found between AHA/NHLBI and IDF definitions.

ASSOCIATION BETWEEN METABOLIC SYNDROME AND PERIODONTAL DISEASE

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Introduction: Previous studies have been found association between periodontal disease (PD) to diabetes mellitus, obesity, hypertension and hyperlipidemia (1-3).In 2007 Shimazaki et al. found relationship of metabolic syndrome (MeS) to PD in Japanese Women (1).

Objective: Determine the association between periodontal disease to metabolic syndrome in Mexican adults.

Material and methods: We realize a case and control study. 99 MeS patients and 140 healthy subjects (HS) were included. The MeS patients were defined with National Cholesterol Education Program, Adult Treatment Panel III criteria. All participants included were clinically evaluated by Physician, dentist and nutriologist. In addition, blood samples were obtained to quantify sera levels of glucose, triglycerides, lipoproteins and insulin using standard methods. Statistical analysis consists of descriptive and inferential statistic using SPSS v.11.5 software. A p value < 0.05 were considered significant.

Results: The age was 49±11 (mean ±SD) yrs and 45±8.6 (mean ±SD) yrs in MeS and HS respectively. 62% HS and 56% MeS were females. The MeS components more prevalent in patients with MeS plus PD were waist circumference >90 cm and low concentrations of cHDL presents in 100% and 91% of patients studied, respectively. In MS patients 67% showed periodontitis versus 37% in HS (p< 0.001), OR 3.46 and RR 1.87 95% CI. Gingivitis was identify in 33% of MS patients versus 63% in HS (p< 0.001), OR 0.29 and RR 0.53 95% CI.

Conclusions: Metabolic Syndrome is associated to periodontal disease in Mexicans adults.

SOCIOECONOMIC STATUS AND METABOLIC SYNDROME IN IRANIAN POPULATION(IHHP STUDY)

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Aims: The aim of this study is to analyze the relationship between socioeconomic status and both metabolic syndrome factors and SES variables.

Methods: A cross-sectional survey examined a random sample of men and women resident in two provinence districts participating in the Isfahan Healthy Heart Program (IHHP) in 2000-2001. Participants completed a questionnaire, underwent anthropometric and blood pressure measurements, and provided a blood sample. Two indicators of SES were used: education and SES statues scale, SES statues scale were measured by income, kind of job. Linear regression was employed to analyse the relation between SES and total and high-density lipoprotein (HDL)cholesterol, body mass index (BMI), waist-hip ratio (WHR) and height. Logistic regression was used to assess the association between SES and smoking and hypertension.

Results: Our study showed that the multivariable association of metabolic cardiovascular risk factor and also pressure with different SES variable high blood pressure is lower associated with lower education level of lower income and no car ownership. But having high TG and low LDL associated higher in come. Also low HDL is higher in lower educational level but high

TG is inversely associated with car ownership low LDL doesn't have any significant association with SES variable.
Conclusions: While in Iran there have been numerous efforts to persuade the population to adopt a healthier lifestyle, these efforts have targeted only those who are among the most economically disadvantaged, and these efforts have not been as effective for those who are among the most economically disadvantaged.

THYROTROPIN AND THYROXINE ARE ASSOCIATED WITH FASTING INSULIN AND INSULIN RESISTANCE IN EUTHYROID IMPAIRED GLUCOSE TOLERANT SUBJECTS

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Objective: To investigate the relationship of thyroid hormones and insulin secretions in glucose homeostasis in impaired glucose tolerant and type 2 diabetic subjects, with normal thyroid functions.

Methods: Retrospective cross sectional analysis was carried out on (n = 266) impaired glucose tolerant, type 2 diabetics and normal glucose tolerant subjects. Thyrotropin (TSH), total triiodothyronine (TT3), total thyroxin (TT4) and insulin were assessed by enzyme linked immunoassays (ELISA). Fasting plasma glucose and HbA1c were measured by glucose oxidase and low pressure cation exchange chromatography. Homeostasis model of assessment (HOMA-IR) was employed to assess the level of insulin resistance. Anthropometric measurement and habits were recorded.

Results: Serum TT3 levels were significantly lower in the IGT subjects. TT4 and TSH were higher in IGT subjects as compared to control and diabetics. IGT subjects were more hyperinsulinemic and insulin resistant as compared to diabetics. There was a significant positive correlation of TSH with BMI only in control group ($r = 0.351$; $P < 0.05$). Correlation of insulin with TSH was significant ($r = 0.457$) in IGT subjects. In multiple regression analysis TSH, TT4 contributed significantly to the variance of fasting insulin in IGT subjects. Pathophysiology of chronic hyperglycemia and persistent insulin resistance suppressed the true picture of thyroid hormone status in diabetic subjects.

Conclusion: T4 and TSH are associated with insulin secretions in IGT subjects. Impaired glucose tolerant subjects can be targeted for better therapeutic options.

The study was approved by ethical committee of the hospital.

INCIDENCE OF HYPERINSULINAEMIA ON A HYPERTENSIVE OBESE POPULATION

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Aims: Insulin-resistance is the corner-stone for MetS so the correlation between IRI values, basal and reactive and TA (arterial hypertension), systolic and diastolic was made.

Cases and methods: Our study was made on 187 obese patients. The aim of the study was the correlation between reactive IRI on OGTT (oral glucose tolerance test) and arterial hypertension (TA), TAS (systolic) and TAD (diastolic). After OGTT we distributed the subjects on three groups. The first group with normal values on OGTT included 49 cases, the second group: 52 cases, 48%, had basal glycoregulation disturbances. The third group: 128 cases, about 81% of cases had glycoregulation disturbances significant for diabetes.
Results and discussion: The first group has BMI=34,2kg/mp, basal IRI=103+/-63pmol/l, reactive IRI=425+/-82pmol/l, TAS with low correlation. The second group has BMI = 36,6kg/mp, IRI=209+/-30pmol/l, reactive IRI=815+/-42pmol/l, AT is significant correlated with reactive IRI ($p < 0, 0005$) and TAS ($p < 0, 01$). The third has BMI = 39,7kg/mp, basal IRI = 406+/- 120 pmol/l, reactive IRI=957+/-pmol/l. TAS is significant correlated with reactive IRI ($p < 0, 0001$) and the same for TAD ($p < 0,001$).

Conclusions:

1. Hiperinsulinaemia is present at 138 cases with essential hypertension.

2. Hiperinsulinaemia appears earlier than glycoregulation disturbances (95 cases-50%).

3. We marked that arterial hypertension sets up on first group too (with normal IRI) and rise as incidence depending of reactive IRI.

Keywords: Android shape obesity, arterial hypertension, insulinemia, basal and reactive.

THE CLUSTERING OF COMPONENTS OF METABOLIC SYNDROME IN A POPULATION-BASED STUDY -THE TAICHUNG COMMUNITY HEALTH STUDY (TCHS)

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Background: To evaluate the relationship among the different components of metabolic syndrome for the ensuing development of the primary prevention program.

Methods: 2359 community-based voluntary participants were randomly enrolled. All subjects were having the general anthropometric data collected, fasting blood samples were taken and then metabolic variables were measured. Based on the criteria of metabolic syndrome (MetS) mentioned in the ATP III, subjects were classified under 8 groups, MetS with waist component, waist required and non-waist required; MetS without waist component, with 3 other components and with more than 3 components; Non-MetS with waist component, with one other component and without any other component; Non-MetS without waist component, with other component(s) and without any other component.

Results: The case and percentage distributions of MetS in different ranges of body mass index (BMI) in 8 groups in this cohort were demonstrated. There were 38.5% participants defining as having MetS. Among them, 9.2% was waist required, 13.4% non-waist required, whereas 15.9% was MetS without waist component. In addition, the percentage distributions of each different component of MetS (TG, HDL-C, glucose, waist and blood pressure) in different ranges of BMI in these 8 groups were shown. There was no significant relationship between percentage distributions of each individual component of MetS and different ranges of BMI demonstrated by trend test.

Conclusion: According to those cross-sectionally population-based results, the development of the clustering of each component to eventually form MetS might not be necessarily parallel with the increasing of BMI.

PREVALENCE OF METABOLIC SYNDROME IN WORKING POPULATION OF ST.PETERSBURG SBERBANK

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Objective: The study addresses prevalence of metaboloc syndrome (MS) in a selected population of subjects working in bank office according to different criteria.

Methods: 1600 subjects from 20 to 65 years old (340 males and 1260 females) occupied in Sberbank offices were screened. The special questionarie was filled including lifestyle, heredity, medical history, and medication. Waist circumference (WC), body weight, height, vital signs (mean blood pressure on right arm and resting heart rate) were registered. Fasting plasma glucose and serum triglycerides and high density lipoproteins were measured.

Results: The prevalence of MS was 19,4% according to IDF2005 criteria and 17,6% accoring to ATP III (2005) criteria. In males the prevalence was significantly higher (39,4% and 35,2% respectively, $p< 0,05$) compared to females (13,9% and 12,7%, respectively). These discrepancies were maimly due to high prevalence of hypertension in males (67%). The prevalence of MS by both criteria increased with age and was higher in subjects with sedentary lifestyle and in smokers. The correlation between two criteria was high (Spirman coefficient 0,79, $p< 0,01$, kappa coefficient of concordance 0,78, $p< 0,01$). Higher prevelence by IDF criteria was explained by lower thresholds for WC and relative increase in abdominal obesity prevalence (45,6% according to IDF and 25,6% according to ATP, $p< 0,05$).

Conclusions: The MS is highly prevalent in subjects of relatively young age working in bank office. Extremely high prevelence of hypertension in males and abdominal obesity in both sexes was observed. High prevelence of MS component was related to sedentary lifestyle.

DEVELOPING A SYSTEMIC INTERVENTION TECHNIQUES FOR DIABETES AND METABOLIC SYNDROME

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Aim: Developing a systemic intervention techniques and procedures for diabetes.

Methods: A program of three-year community-based life-style intervention for diabetes was initialed. The intervention was conducted by integrating a predictive mathematic model for diabetes and a daily energy monitor technique. The end point would be diabetic incidence comparing between two groups.3858 High risk subjects were screened by combined with the predictive mathematic model and IDF criteria of metabolic syndrome and divided into intervention and control groups. The effects of intervention were also assessed by the same mathematic model.

Results: Systemic intervention techniques with screening, intervention, monitor and assessment were established in 18 centers all over China. The daily energy balance was directed according to record of diet diary and energy expenditure every week. Exercise-induced energy expenditure, indicated clearly by the energy monitor, increased from 200-300 to 400-600 kilocalorie per day in first month. Body weight as well as indicators of blood test (FPG, TC, and TG) decreased comparing with baseline after 6 months intervention in more than 70% subjects. The risk level, assessed by the mathematic model, decreased 6 months later due to the energy expenditure in one unit of time but not total energy expenditure.

Conclusion: Three important techniques of intervention for diabetes, namely screen, monitor and assessment, was developed. With the help of these techniques,

1) life style intervention could be conducted regularly and quantitatively;

2) energy expenditure in one unit of time was the key factors of exercise-induced effects.

WEIGHT CHANGE AND INCIDENT METABOLIC SYNDROME IN IRANIAN MEN AND WOMEN; OVER 3 YEARS FOLLOW-UP STUDY

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Aims: To define the effects of weight change (including weight loss) on incident MetS and its components.

Methods: A total of 1492 men and 2087 women aged ≥ 20 years with BMI>18.5 kg/m^2 were followed over 3 years. Logistic regression analysis was used to estimate the odds ratio (OR) of MetS and its components (the ATP III definition) associated with sex-stratified quintiles of percent weight change after adjustment of age, baseline weight, smoking, physical activity, education and antidiabetes, antihypertension and antilipid drug usage.

Results: There was 20.6% (95% CI, 19.8-21.4) age-adjusted incident MetS (18.6% male vs. 23.6% women). In both genders there was a strong linear trend of weight gain and worsening of all the MetS parameters except for the FPG level. In men, mild weight gain (WG) predicted high waist circumference (WC) and high triglyceride; medium WG predicted MetS (OR 2.5, 95% CI 1.4-4.3), high WC and high blood pressure (BP); large WG predicted MetS and its components except high FPG. In women, mild WG predicted MetS (OR 2.5, 95% CI 1.4-4.3), high WC and high BP; medium WG predicted Mets, high WC and high triglyceride; Large WG predicted MetS and its components except low HDL-cholesterol. Mild weight loss had protective effect on high WC in both genders and MetS in men (OR 0.5, 95% CI 0.26-0.97, P=0.04).

Conclusions: Weight change showed different effects on MetS in men and women. In women mild WG predicted MetS, however mild weight loss was protective against MetS in men and high WC in both genders.

HYPERGLYCEMIA IS ASSOCIATED WITH METABOLIC SYNDROME IN A TAIWANESE METROPOLITAN ADULT POPULATION

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Objective: The objective of this study was to assess the association between metabolic syndrome with hyperglycemia (impaired fasting glucose [IFG]) and diabetes in a Taiwanese metropolitan adult general population.

Methods: We did a cross-sectional survey in a representative random sample of 2,350 Taiwanese adults aged 40 years and over who lived in a metropolitan city, Taiwan in 2004-05. Metabolic syndrome was defined

according to the criteria of American Heart Association and National Heart Lung and Blood Institute (AHA/NHLBI).

Results: The prevalence of metabolic syndrome in individuals with normal glycemia (NG), IFG, and diabetes was 22.11%, 62.73%, and 83.28%, respectively. Number of metabolic syndrome components was significantly higher in diabetic participants (1.44 components higher compared to NG individuals, p< 0.001) and in those with IFG (2.06 components higher compared to NG individuals, p< 0.001). After adjusting for age, gender, smoking, alcohol drinking, central obesity, BMI, and percent body mass fat, IFG was associated with an OR of 7.01 (95% confidence interval [CI]: 5.39, 9.10) and diabetes was associated with an OR of 19.21 (95% CI: 12.95, 28.51) for metabolic syndrome.

Conclusions: Our findings show that hyperglycemia is associated with increased prevalence of metabolic syndrome. This association is consistent in diabetic individuals, and also extends to those with IFG.

AN INNOVATIVE SCREENING PROGRAM FOR PREVENTION OF METABOLIC SYNDROME: A PILOT STUDY

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Metabolic syndrome (MS) is a combination of genetic and/or acquired pathological conditions. People with MS are at increased risk of developing cardiovascular diseases and diabetes. Some studies estimate the prevalence in Italy up to 20% of population. Prevention programs are essential for controlling and reducing the underlying risk factors.

In September 2008, we started a prevention program in two small Italian towns aimed at estimating how lifestyle, nutritional, socio-economical and environmental variables can influence MS in "apparently" healthy people.

This pilot prevention program, supported by "Provincia di Milano" and ANCeSCAO Association, was performed using a mobile laboratory, "La Sanità Itinerante" ("Mobile Healthcare", developed for risk disease prevention and equipped for specific screening programs - medical check ups as well as for collection, testing and preservation of biological specimens).

A total of 297 healthy subjects (142 M and 155 F, aged 60.5 ± 11.2 years) spontaneously presented at screening. They were visited by the clinician team, enrolled and tested according to NCEP diagnostic panel: serum triglycerides, HDL-cholesterol and glucose concentrations (Modular analyser, Roche), waist circumference and blood pressure.

Interestingly only 55 subjects (18M, 37 F; 18%) did not show any risk factor whereas 102 (55 M, 47 F; 34%) showed MS with 3 or more risk factors, the remaining 48% showed at least one/two altered indexes.

These preliminary data demonstrate a dramatic increase in the frequency of MS in "apparently" healthy subjects, and a urgent need of prevention programs for an early MS detection in our country.

SUBCLINICAL HYPOTHYROIDISM IS A NEW COMPONENT OF METABOLIC SYNDROME

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It is well known today that truncal obesity and diabetes mellitus type 2 (DM2) are the main components of metabolic syndrome. We investigated large group of heart ischemic disease patients (n=936). Elevation of TSH level (so called subclinical hypothyroidism) was associated with higher body mass index (BMI) and DM2. Among patients with obesity one in three had DM2. In patients with DM and obesity the level of TSH was reliably higher (3.6 ± 0.3 IU/l) in comparison with patients without obesity(1.9±0.1) p=0.006. Based on this fact it was actual to study the level of insulin resistance index (HOMA-IR) in patients with different BMI and to compare the obtained data with TSH concentration.

Methods: 73 patients were included in our study. Heart ischemic disease was confirmed by the results of coronarography.. Fasting blood samples were taken for measuring of TSH level, glucose and insulin concentration. HOMA-IR was calculated as fasting insulin (mU/l) times fasting glucose (mmol/l) divided by 22,5. Patients with diabetes were excluded from the study.

Results: Midde age of our patients was 57,23±0,48 years, BMI was 28,23±2,19 kg/m2 and TSH level was 2,61±0,74 IU/l. In accordance with BMI all patients were divided in 3 groups: I - normal weight, II - weight abudance, III - obesity. TSH level was reliable higher in patients with obesity (3,05±1,14 IU/l) and weight abundance (2,73±0,26 IU/l) than in group with normal weight (1,52±0,34 IU/l) (p 0,02 and 0,01). Age was nearly the same in all groups. HOMA-IR was the highest in the group of obesity (4,67±1,12). In group I and II HOMA-IR was statistically lower: 1,30±0,26 and 1,52±0,74 (p 0,002 and 0,05).

Conclusion: In patients suffering from heart ischemic disease and obesity TSH level and HOMA-IR index were statistically higher than in patients with normal weight. We can propose that mild thyroid failure can potentiate insulin resistance in metabolic syndrome patients.

HOLTER ECG FINDINGS DURING GASTROSCOPY IN PATIENTS WITH ATRIAL FIBRILLATION AND METABOLIC SYNDROME

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Introduction: Atrial fibrillation is a significant indicator for an increased incidence of strokes and mortality. The reported incidence of dysrythmias during endoscopy rises sharply with age and presence of cardiopulmonary diseases. Therefore is gastroscopy for the patients with CAD (coronary artery disease) and heart failure a potentially dangerous procedure. For the clinical use of warfarin or aspirin it is important to exclude possible contraindications of this therapy, e.g. peptic ulcer.

Aim of the study: To document the incidence of electrocardiographic changes during elective upper gastrointestinal endoscopy (dysrhythmias and ischemia) by Holter ECG monitoring at patients with atrial fibrillation and metabolic syndrome.

Patients and methods: We investigated 30 patients, 19 man and 11women, mean age 71 years (range 49 - 82 years) with atrial fibrillation before starting anticoagulant therapy with Warfarin. Holter ECG equipment Marquette - Hellige,3-channel device, with mean monitoring time of 22 hours was used. Gastroscopy was performed with an Olympus GIF Q145 videoendoscope with topical lidocain spray anesthesia.

Results: All the patients had during the endoscopy a typical finding of atrial tachyfibrillation with rapid ventricular response. In 8 patients (26,7%) endoscopic procedure induced complex cardiac dysrythmias and in 7 patients (23,3%) also significant myocardial ischemia.

Conclusions: Gastroscopy induced complex cardiac dysrythmias in one quarter of the investigated patients. In 23% of the patients endoscopic procedure induced also significant myocardial ischaemia. These findings can evoke serious hemodynamic consequences.

Higher age, preexisting cardiac and pulmonary diseases and metabolic syndrome are important risk factors of possible cardiovascular complications of gastroscopy.

THE RELATION OF ENLARGE WAIST ENLARGED TRIGLYCERDEMIC PHENOTYPE WITH DIABETES AMONG INDIVIDUALS WITH FAMILY HISTORY OF DIABETES

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Background: Studies have used antropometric measures along with biochemical indicators as screening tools for chronic diseases. Few studies have assessed the relation of EWET (Enlarged waist Enlarged triglycerdemic) phenotype with diabetes, particularly among individuals with family history of diabetes. This study aimed to evaluate the association of EWET phenotype with diabetes among individuals with family history of diabetes.

Method: Antropometric and biochemical measurments were assessed in a pouplation - based cross - sectional study of 332 male and 991 female Isfahani adults aged 35-55 year. The EWET phenotype was defined as serum trigcylglycerol concentrations ≥ 150 mg/dl and waist circumference ≥ 88 cm in women and ≥ 102 cm in men.

Result: The prevalence of EWET phenotype was 9.6% among men and 23.6% among women. Individuals with the phenotype had significantly higher antropometric measure as compared to other groups. After control for age and physical activity, men with EWET phenotype were significantly more likely to have high serum triglyceride levels (P< 0.001), chol (P< 0.001), sistolic BP (P< 0.01) and diastolic BP (P< 0.001). After aditional control for BMI the significant associations remained except for low HDL Cholestrol women with EWET phenotype had significantly adverse metabolic risks as compared to othe phenotypes, either before or after control for BMI (P< 0.001). Individuals with the phenotype were more likely to have diabetes and IGT.

Conclusion: Our findings showd a significant association between EWET phenotype and diabetes. This phenotype could be used for early identification of diabetes and IGT.

ROLE OF LEPTIN IN DEVELOPMENT OF METABOLIC SYNDROME IN EGYPTIAN OBESE PATIENTS

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Objective: Obesity and its complications including metabolic syndrome has been increased in children and adolescents recently. Leptin is known to play an important role in the pathogenesis of obesity.

Methods: The objective of this study was to evaluate the relationship between leptin and and the development of metabolic syndrome in Egyptian obese patients. A cross sectional study was carried out in 30 obese patients. All patients have BMI < 30 Kg/m^2. Anthropometric variables measurements, blood pressure, fasting plasma glucose, triglyceride, high-density lipoprotein cholesterol and serum leptin were obtained from the study sample.

Results: Serum leptin levels were significantly higher in females in comparison to males. Serum level of leptin were higher in patients with metabolic syndrome in comparison to obese patients without metabolic syndrome and control group.

Conclusion: Leptin appear to have a major role in development of metabolic syndrome, and it was strongly associated with obesity parameters. More studies evaluating the relationship between leptin and metabolic syndrome in various ethnic groups are recommended.

METABOLIC SIDE EFFECTS OF "*RISPERIDON*"

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Introduction: "*Risperidon*" is a serotonin-dopamine antagonist known as novel antipsychotic which according to many literatures is the drug of choice for treatment of schizophrenia and other psychotic disorders. Although it has fewer and a favorable profile of side effects, but some metabolic adverse effects have reported in patients receiving "*risperidon*".

Method: 38 patients diagnosed schizophrenia(according to DSM-IV-R)who experienced the first episode of their illness and received "*rispridon*" encountered in an open clinical trial for 12 weeks.

Results: Increased BMI reported in 62% of patients (especially in women). The average weight gain was 4.8 ± 0.9 kg.

Increased serum "prolactin" also was shown in 32% of the patients.

No changes in fasting blood sugar or serum lipid profile was observed in this 12 week trial.

Conclusion: "*Risperidon*" , and probably other antipsychotics, may be associated with some metabolic adverse effects that necessitates careful observation of patients for BMI as well as serum level of glucose, lipids and some hormones such as "prolactin".

Keywords: Rispridon, antipsychotic, metabolic syndrome, BMI.

THYROID GLAND IN METABOLIC SYNDROME

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The medical examination was carried out among 92 women with Type 2 Diabetes, who had been sorted into the 1st group - 71 patients having Type 2 Diabetes with metabolic syndrome, and the 2nd - control group, comprised of 21 patients with Type 2 Diabetes without metabolic syndrome. The anthropometrical, general clinical, laboratory-biochemical, and US examinations were performed among the patients.

The examination results of patients in the 1st group that have metabolic syndrome detected a more pronounced increase in body weight, BWI indicator, vital statistics (waistline/ measurement round hips), rise in both systolic and diastolic AP, significant hyperinsulinemia, cholesterol metabolism disturbance - TC, VLDL, LDL, TG, and HDL level reduction. According to US data, among the women with MS the following information had been gathered: structural changes were revealed noticeably often, increase in volume parameters as well as disorder in hypophysis-thyroid gland functional condition and autoimmune processes with regard to the thyroid gland - significant increase of TSH level and T3 and free T4 levels reduction characterizing the hypothyroidism phenomena, and also rise of antithyreoperoxidase and antithyreoglobulin levels characterizing autoimmune thyroiditis phenomena.

PREVALENCE OF METABOLIC SYNDROME AMONG HYPERTENSIVE PATIENTS ATTENDING A PRIMARY CARE CLINIC IN KUWAIT

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Objective: To determine the prevalence of metabolic syndrome among hypertensive patients using the criteria of the National Cholesterol Education Program´s Adult Treatment Panel III in a primary care health center in Kuwait.

Subjects and methods: A population of 250 Kuwaiti hypertensive patients (129 males and 121 females) over the age of 40 were screened for metabolic syndrome by determining body mass index (BMI), waist circumference, levels of fasting plasma glucose and fasting plasma lipids (serum triglycerides, total cholesterol and high-density lipoprotein cholesterol). The study was carried out in the Mishref Family Practice Health Center, Kuwait, from January to July 2001.

Results: The total number of patients who met the criteria for metabolic syndrome was 85 (34%), 55% of them were males and 45% females. Prevalence of the syndrome was 28.2% among 40- to 55-year-olds and 41.9% in those above the age of 55 years. Among the 250 hypertensive patients, type II diabetes mellitus was found in 52.8% (54% males and 46% females), impaired fasting glucose in 8% (70% males and 30% females), high plasma triglycerides in 44.8% (53% males and 47% females) and low high-density lipoprotein cholesterol in 63.2% (54% males and 46% females). Obesity measured as BMI = 30 kg/m(2) was noted in 46% (43% males and 57% females) and increased waist circumference in 58% (44% males and 56% females).

Conclusion: The prevalence of metabolic syndrome is high among hypertensives attending primary health care centers in Kuwait.

PREVALENCE OF METABOLIC SYNDROME AND ITS EFFECT ON RESPONSE TO AMLODIPINE BESYLATE IN PRIMARY CARE HYPERTENSIVE PATIENTS

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Background: Metabolic syndrome (MetS) in the hypertensive population is much more prevalent than that in general population. In this study, we aimed to assess the prevalence and the characteristics of MetS in patients with essential hypertension in a primary care setting and to compare the efficacy of amlodipine in hypertensive patients with or without MetS.

Method: Essential hypertensive patients who were treated in primary care clinics and are not at hypertensive goal according to JNC 7 guideline were enrolled.

Results: Of 7,622 patients, the prevalence of MetS in population with hypertension was estimated as 61%. MetS was more prevalent in females than in males. The most common component of MetS (other than high BP) was high triglyceride (58.3%) followed by low HDL-cholesterol (47.6%), abdominal obesity (43.1%), and high fasting glucose (37.3%). Interestingly, low HDL-cholesterol was almost twice more common in females than in males (79.9% versus 43.6%), whereas in males, high triglyceride (81.3% versus 75.5%) and high fasting glucose (60.8% versus 51.7%) were more common. Hypertensive patients with MetS were associated with more cardiovascular diseases and higher systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP) than those without MetS. Eight weeks of amlodipine treatment exerted a similar ranges of blood pressure lowering regardless of MetS status.

Conclusion: High prevalence and prognostic significance of MetS makes its evaluation and tight control essential for optimal care for hypertensive patients. A calcium antagonists, amlodipine besylate, exerted a consistent blood pressure lowering effect, regardless of MetS status.

THE BIOCHEMICAL MARKERS OF CORONARY HEART DISEASE CORRELATE BETTER TO METABOLIC SYNDROME DEFINED BY WHO IN KOREAN TYPE 2 DIABETES PATIENTS

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Background: Metabolic syndrome (MetS) is constellation of cardiovascular risk factors. There are three typically used definitions of MetS proposed by WHO, IDF and NCEP-ATP III. We conducted this study to compare the associations of MetS by WHO, IDF and NCEP-ATP III definition to various metabolic markers of coronary heart diseases in Korean type 2 diabetes patients.

Methods: We enrolled 151 Korean type 2 diabetes patients in one hospital. Anthropometric and biochemical parameters, including high-sensitivity C-reactive protein (hsCRP), homocysteine, uric acid were measured. And then, we divided MetS group from non-MetS group according to three other definitions.

Results: Serum hsCRP level was higher in those with MetS group than non-MetS group by WHO definition (0.33±0.36 mg/dl vs 0.18±0.26 mg/dl, $p< 0.001$). But, there are no difference in MetS group and non-MetS group by IDF and NCEP-ATPIII definition.(By IDF, 0.28±0.31 mg/dl vs 0.25±0.34 mg/dl, $p=0.64$; By NCEP-ATP III, 0.28±0.33 mg/dl vs 0.22±0.32 mg/dl, $p=0.41$). Uric acid and homocysteine levels were higher in those with MetS by WHO definition ($p< 0.05$). Similarly, analyses according to IDF and NCEP ATP III definition showed no significant difference.

Conclusion: In conclusion, WHO definition of MetS has a stronger relationship with the biochemical markers of coronary heart disease in Korean type 2 diabetes patients.

HYPERTRIGLYCERIDEMIA/HYPERACIDEMIA: A CAUSE AND CONSEQUENCE OF HYPERINSULINISM/INSULIN RESISTANCE

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Hypertriglyceridemia and hyperacidemia could be cause and consequence of hyperinsulinism/insulin resistance.

Objective: To diminish triglycerides and free fatty acids levels to break the vicious circle.

Design and methods: Twenty-six patients with primary hypertriglyceridemia received, after six months of a non-pharmacological treatment, 500 mg of etofibrate retard. Before and after six months of treatment were determined: total C and TG, HDL-C, LDL-C, apos A1 and B, FFA, and glycemia and insulinemia during an OGTT. For statistical analysis ($p< 0,05$) were applied the tests: Chi-Square, Friedman, Nemenyi, T-Test, U-Mann Whitney, Wilcoxon, and the trapezoidal rule. Using the HOMA index (cut-off point = 2,5), were obtained two groups, thirteen patients each; nine indexes of insulin secretion and nine indexes of insulin resistance were calculated. All patients had from three to seven metabolic disturbances.

Results: After treatment, total TG, FFA and C/HDL-C ratio diminished (40%, 19% and 20%, respectively), and apo AI increased (32%). Glycaemia, insulinemia, and total glycemic and insulinemic areas under the curve, diminished during the OGTT ($p< 0,05$). One insulin sensitivity index

and one insulin resistant index improved in the more sensitive group; four insulin sensitivity indexes and seven insulin resistance indexes improved in the less insulin sensitive group (p< 0,05). There were not differences in the 24 hours of a typical day diet recalls.

Conclusions: Etofibrate improved lipid profile, glucose tolerance, insulinemia and insulin sensitivity. Lipids improvement could break the vicious circle hypertriglyceridemia-hyperacidemia-hyperinsulinism-insulin resistance. Etofibrate is effective in the treatment of the dyslipidemia of the insulin resistance syndrome.

LIPOPROTEIN AND GLUCOSE PARAMETERS AT HIGH TRIGLYCERIDES AND LOW HDL CHOLESTEROL LEVELS

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High TG and low HDL C levels are integral features of metabolic syndrome and type 2 diabetes mellitus.

Aim: To reveal the relationship between parameters determined atherogenicity of high TG and low HDL C combination and glucose utilization abnormalities, if any. Seventy subjects from cohort of 500 Moscow residents randomly selected from free-living population aged 55-84, were enrolled into the study. Group I (n=35) - subjects with high TG level >=1.7 mmol/l and low HDL C < 1.0 mmol/l; group II (n=35) - randomly selected subsample with TG (ME, 1.0) and HDL C (1.3 mmol/l). In group I, apo B/AI ratio and apo AII level were higher: 1.11 vs 0.72; p< 0.001, and 38 vs 33 mg/dl; p< 0.01), respectively; HDL-mediated reverse cholesterol transport activity was lower: apo AI level (142 vs 155 mg/dl; p< 0.02), HDL phospholipids concentration (101 vs 130 mg/dl; p< 0.02); cellular cholesterol efflux (18.8 vs 21.2%; p< 0.02). No differences in fasting glucose concentration and HbA1c between groups were found: 6.0 vs 5.8 mmol/l; p=0.222, and 6.0 vs 5.8%; p=0.127. Group I had higher fasting insulin (11.8 vs 5,4 uU/ml; p< 0.06) and HOMA-IR (1.6 vs 0.8; p< 0.001) with identical HOMA-%B.

In conclusion, the atherogenic shifts in lipid and apolipoprotein parameters associated with disturbed glucose utilization in high in subjects with high TG and low HDL C might be regarded as biomarkers of high risk of atherosclerosis in metabolic syndrome and type 2 diabetes mellitus.

PREVALENCE OF METABOLIC SYNDROME ACCORDING TO ATP III AND IDF DEFINITION IN SEMNAN, IRAN

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Aims: The clustering of central obesity, dyslipidemia, hypertension, and hyperglycemia known as metabolic syndrome. The risk of cardiovascular diseases with this syndrome is higher than with each of its components alone. This study was performed to determine the prevalence of metabolic syndrome and its components in adults aged 30 years and older in Semnan province, IRAN, according to the International Diabetes Federation (IDF) definition and Adult Treatment Panel III (ATP III) criteria.

Methods: This survey was conducted in a sample population of 3799 people 30-70 years old, between October 2005 and February 2006 in the province of Semnan. A multistage clustered sampling was performed. Evaluation of anthropometric variables, blood pressure, fasting blood glucose and lipids was performed.

The prevalence of metabolic syndrome was calculated according to the standard criteria of IDF and ATP III.

Results: There were 3799 individuals' aged 45.8 ± 10 years. According to the ATPIII and IDF definitions, the prevalence of metabolic syndrome was, respectively, 25.1%, and 35.8%. In both definitions prevalence of metabolic syndrome was significantly higher in women than men (P< 0.001). High blood pressure and adiposity were the criteria found most frequently among metabolic syndrome holders irrespective of the metabolic syndrome definitions.

Conclusion: We identified a high prevalence of metabolic syndrome in this population. In view of correlation between metabolic syndrome and cardiovascular disease, it must be the priority for interventional preventive measures.

THE IMPACT OF SHIFT WORK ON THE DEVELOPMENT OF METABOLIC SYNDROM

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Aims: To estimate the impact of shift work on the incidence of metabolic syndrome (MS).

Methods: 300 men were involved in this study. 149 of them worked in night-shifts twice or three times a week and the others worked at the day time. An average age of these groups was 47 years old. The factors of risk such as smoking, alcohol consumption, low educational level and physical activity were the same in both groups. The diagnosis of MS was done according to International Diabetes Federation definitions.

Results: The metabolic syndrome incidence was much greater in night-shift workers than in others workers (36,3% and 10,2 % respectively).

Conclusions: This study shows that the night shift work may be one of the new factors of developing MS.

ALCOHOL CONSUMPTION AND THE PREVALENCE OF METABOLIC SYNDROME: A META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: In the past two decades, the metabolic syndrome has given rise to much clinical and research interest. The broad overlap of alcohol consumption with different components of metabolic syndrome makes alcohol-metabolic syndrome relationship a controversial topic.

Objectives: To support the evidence available about the relationship between alcohol consumption and metabolic syndrome as a comprehensive clinical entity, as well as to identify the gender-specific dose response, by performing a meta-analysis.

Methods: Manual and computer searches in different bibliographic databases were performed to identify the relevant scientific publications, on the relation between alcohol consumption and metabolic syndrome. Alcohol intake was converted into a same unit (g/day) and then categorized using standard classification in order to provide relevant comparisons. Fixed and random effects models were used to aggregate individual Odds Ratios and to derive pooled estimates and 95% Confidence Intervals.

Results: Fourteen relevant publications were identified on the relation between alcohol consumption and the prevalence of metabolic syndrome. 7 studies were included in the meta-analysis. The results showed that alcohol

consumption of less than 40 g/day in men and 20 g/day in women significantly reduced the prevalence of metabolic syndrome.

Conclusion: "Responsible alcohol intake" appears to be associated with a reduced prevalence of metabolic syndrome. Favorable metabolic effect seemed to be restricted to alcohol consumption of less than 20 g/day among women, and of less than 40 g/day among men. These findings support the actual recommendations regarding alcohol consumption among apparently healthy people.

METABOLIC SYNDROME IN SUBJECTS WITH TYPE 2 DIABETES

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Aims: Type 2 diabetes is often associated with a clustering of other cardiovascular risk factors known as the metabolic syndrome (MS). The aim of the present study was to estimate the prevalence of different MS components in subjects with type 2 diabetes.

Methods: 195 patients with type 2 diabetes were included in the study (males/females: 99/96, mean±SD age: 64.8±9.9 years old). MS presence was defined according to the International Diabetes Federation criteria. All the subjects fulfilled the criterion about diabetes existence.

Results: 174 out of 195 (89%) patients (pts) were identified as having the MS. The mean±SD values of the main anthropometric-metabolic parameters of the study population were as follows: Waist circumference: 108.4±12.5 cm, systolic blood pressure: 148.6±18.6 mmHg, diastolic blood pressure: 87.5±9 mmHg, triglycerides: 160.2±84.3 mg/dl, HDL-cholesterol: 46.5±13.7 mg/dl, HbA1c: 8.1±1.5%. We observed the following prevalence of MS components: central obesity-170 pts (98%), elevated blood pressure-158 pts (90.8%), high triglycerides-83 pts (48%), low HDL-89 pts (51%). 65 pts (37%) had at least 3 MS components, 66 pts (38%) had 4 MS components and 43 pts (25%) had 5 MS components. MS was quite more common in women compared to men (95/96 vs. 79/99 respectively, $p< 0.001$).

Conclusions: A particularly high prevalence of MS was observed among diabetic subjects. Moreover, 1 in 4 pts with type 2 diabetes fulfilled all the MS criteria in our study. Central obesity and hypertension were the most common MS components.

PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Purpose: To assess the frequency and factors associated with metabolic syndrome in adult female patients with rheumatoid arthritis (RA).
Methods: During October and March 2006, 100 consecutive adult female patients seen during their scheduled appointment at the out-patient rheumatology clinic and meeting the College of Rheumatology. Classification criteria for RA were invited to participate in this study. Sociodemographic, menopausal status, personal history of coronary heart disease, and physical activity were evaluated. According to the National Cholesterol Education Program Adult Treatment III (NCEP/ATP III), metabolic syndrome was defined

Results: Seventy five RA patients with a mean age of 47±10 years were included in this study. 45% had a normal weight, 32% were overweight, and 23% were obese. The frequency of metabolic syndrome in RA patients was 17%. Metabolic syndrome was significantly associated with greater age, less education, lower income. In RA patients, metabolic syndrome was significantly associated with a shorter treatment period with methotrexate, with pain, and with health assessment questionnaire scores. By multivariate logistic regression, the only statistically significant predictor of metabolic syndrome was lower income.

Conclusions: The frequency of metabolic syndrome in RA patients associated with lower income. In RA patients, metabolic syndrome was related with pain and functional status, suggesting disease activity. A better control of disease activity may reduce the presence of metabolic syndrome and the risk of cardiovascular disease.

THE FRENCH REVOLUTION, THE FRENCH PARADOX AND THE METABOLIC SYNDROME

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Aim: To test the hypothesis that the French Paradox - the low rates of Cardiovascular disease in Metropolitan France, in a population with moderately high levels of animal fat consumption, serum total cholesterol and high density lipoprotein cholesterol concentrations, blood pressure, and (in men) smoking - can be explained in terms of demographic and dietary changes, and recent human evolution since, and in at least one respect because of, the French Revolution.

Background: None of the putative causes of the French Paradox - red wine consumption, a Mediterranean diet, lagged mortality and biased mortality registration - fully explain this phenomenon.

The evolutionary paradox of the high prevalence of the Polycystic Ovary syndrome, a heritable cause of ovarian infertility strongly linked to the Metabolic Syndrome provides the basis for a new hypothesis proposing that adaptations to an agrarian diet, particularly increased insulin sensitivity, were constrained throughout the entire agrarian period by ovarian infertility. This constraint, it is proposed, was released with improvements in nutrition in the 18th and 19th century and effected rapid changes in the prevalence of this Agrarian genotype through a mechanism of fertility selection.

Methods: The remarkable longitudinal record of anthropometry, fertility, mortality, dietary composition and a recent age-period -cohort analysis of cardiovascular mortality in France provide an opportunity to test this hypothesis.

Conclusion: Very early declines in fertility, accelerated by the French Revolution, and patterns of mortality from cardiovascular disease, which began to decline in all men in France born after 1860 are consistent with this hypothesis.

ANKLE-BRACHIAL INDEX IN PATIENTS WITH DIFFERENT COMPONENTS OF THE METABOLIC SYNDROME

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Objective: The objective of the present study was to investigate the subclinical peripheral vessel disease according to ankle-brachial index (ABI) in patients with various components of metabolic syndrome (MS) and its relation to other target organ damage.

Material and methods: The study included 48 subjects (37 women and 11 men from 26 and 69 years old (mean age 48,8±0,89 years). 17 subjects were smoking. Anthropometric parameters (body mass index, waist circumference, hip circumference) and blood pressure values were obtained. Serum lipids, fasting plasma glucoses and 2-hour glucose during glucose tolerance test were measured. Echocardiography with left ventricular mass assessment, carotid vascular ultrasound were performed. ABI was measured by portable device Smartdop 30lx.

Results: ABI was lower than 0,9 in 26 patients (54%). Inverse relation of ABI and age was observed (r=-0,42, p< 0,05) as well as smoking duration (r=-0,4, p< 0,05). The postprandial glycaemia level also negatively correlated with ABI (r=-0,48, p< 0,01). Lipid level was strongly associated with ABI level. All subjects were divided on two groups according to presence of dyslipidemia. 26 subjects (1st group) had dyslipidemia and/or hypertriglyceridemia. In 22 subjects lipid profile was normal. Mean value of ABI in the 1st group was significantly lower compared to second group (0,85±0,27 and 1,05±0,3, p< 005). Intima-media thickness (IMT) was related to ABI value (r=-0,46, p< 0,05).

Conclusions: ABI reduction is highly prevalent in subjects with metabolic risk factors and is related to lipid and glucose abnormalities. It is also related to carotid atherosclerosis indicating system vascular involvement in the process.

ASSOCIATION BETWEEN SYMPTOMS OF ATHEROSCLEROSIS AND METABOLIC SYNDROME, DEFINED ON IDF AND NCEP ATP III CRITERIA

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Objective: To study association between metabolic syndrome (MS), defined on two types of criteria, and symptoms of atherosclerosis.

Methods: Epidemiological survey included random sample of men and women aged 30-69 (Cheboksary, Privolzhsky region). The response was 88,7%, survey was completed by 1572 participants. All participants filled the questionnaire (social status, lifestyle, smoking, family history of cardiovascular diseases, other chronic diseases), they all were measured blood pressure, heart rate, resting ECG, waits circumference, height, weight, plasma lipids, glucose tolerance test, index HOMA IR.

Results: According to the NCEP ATP III criteria MS was revealed in 15,6% of adult population of one Russian city (13.6% in women and 18.5% in men), according to the IDF criteria MS was in 26.6% participants (27,0% in women and 25,8% in men). The prevalence of MS, defined on IDF and NCEP ATP III criteria increased with the age. Mean SCORE risk was 3.48±0.37% in men and 1.96±0.20% in women.

Participants with MS on NCEP ATP III criteria had the following prevalence of cardiovascular diseases (angina - 22%, history of myocardial infarction -2%, cerebral atherosclerosis - 22.8% stroke history - 2.6%). Mean SCORE risk was 2.84±0.37% in men and 1.73±0.20% in women. IDF criteria associated with less (nonsignificant) prevalence of cardiovascular events.

Conclusions: In random sample of the working age population in one the Russian cities prevalence of MS defined on IDF criteria is two time higher compared with MS, defined on NCEP ATP III criteria. More strict IDF criteria associate with nonsignificant decrease of cardiovascular events.

ASSESSMENT OF QUALITY OF LIFE IN METABOLIC SYNDROME PATIENTS

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Aims: To describe quality of life (QOL) and disease-specific symptoms of patients with metabolic syndrome (MetSyn).

Methods: Prospective randomized study included 84 male and female patients of average age 58. QOL was estimated using Ferrans and Powers Quality of Life Index (QLI). Possible range is from 0 to 30. QOL overall and QOL in four domains (health and functioning, social and economic, psychological/spiritual, and family) were calculated. Data was analyzed using an independent t-Test. Correlation analysis was made to examine relationships between QOL on each scale of the QLI questionnaire, and dominant syndrome: obesity (waist >102 cm in men, >88 cm in women), high blood pressure (≥140/90 mmHg), and high fasting glucose level.

Results: QOL was decreased in all groups (14.6). The mean overall score for obesity group (n = 28) was 15.6, mean score for high blood pressure group was 19.1 (n = 29), mean score for high glucose group was 9.2 (n=27). Statistically reliable correlation between low QOL and prevalence of obesity in male patients was revealed, p=0,004, the lowest points showed "social and economic", "psychological/spiritual" domains. In female patients was revealed correlation between low QOL and prevalence of high fasting glucose (p=0.01), the lowest points showed "health and functioning", "social and economic" domains.

Conclusions: MetSyn impacts QOL. Male patients with prevalence of obesity have the lowest QOL, female patients - with prevalence of high glucose. The most sensitive QOL domain is social and economic; it is followed by psychological/spiritual (healthcare, personal faith, life goals).

PREVALENCE OF METABOLIC SYNDROME IN YOUNG ASPIRINGS TO AUTONOMOUS UNIVERSITY OF SAN LUIS POTOSI, MEXICO

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Background: Metabolic syndrome is defined as a set of abnormal parameters that include: high blood pressure, hyperglycemia, overweigh and/or obesity, insulin resistance and others, alteration at in the present we found in very early ages.

Objective: To estimate the prevalence of Metabolic Syndrome in young aspirings to Autonomous University of San Luis Potosi, México.

Material and methods: Was realized in 8376 youth aspiring (3923M and 4453W) to Autonomous University of San Luis Potosi, México; who were ranged from 16 to 39 years both sexes and healthy subjects. We measured age, gender, weight, height, BMI, systolic and diastolic blood pressure,

waist circumference and we determined fasting glucose in blood sample. Metabolic syndrome was classified according WHO and ATPIII criteria.

Results: According WHO criteria we found 86.2% healthy subjects and 13.8% (9.2%M, 4.6%W) with metabolic syndrome. According ATPIII criteria we found 86% healthy subjects and 14% (9.6%M, 4.4%W) with metabolic syndrome.

Conclusions: The presence of metabolic syndrome in this population it is a risk factor to develop cardiovascular diseases, which is modifiable to consider a change lifestyle and it is required continuing check up also to implement preventive measures.

RELATIONSHIP BETWEEN SERUM FETUIN-A LEVEL AND INSULIN RESISTANCE IN JAPANESE MEN

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Aims: Fetuin-A, also known as alpha2-Heremans Schmid glycoprotein (AHSG), is an abundant plasma protein that is synthesized predominantly in the liver. Fetuin-A inhibits the insulin receptor autophosphorylation that is mediated by its intrinsic tyrosine kinase activity. In this study, we examined association between serum fetuin-A level and insulin resistance in Japanese men.

Methods: We recruited 300 unrelated Japanese men who had health examinations without known chronic disease including diabetes mellitus or history of regular drug use. By 75g oral glucose tolerance test, the study population was found to consist of 194 normal glucose tolerance (NGT), 91 impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG), and 15 diabetes mellitus. Serum fetuin-A concentrations were measured using an ELISA kit (BioVender, Brno, Czech Republic).

Results: Serum fetuin-A concentrations were correlated positively with fasting insulin levels ($r=0.269$, $P < 0.001$), HOMA-IR ($r=0.274$, $P < 0.001$) and LDL-cholesterol ($r=0.172$, $P < 0.01$), and negatively with HDL-cholesterol concentrations ($r=-0.191$, $P < 0.001$). Fetuin-A concentrations were also correlated positively with serum leptin ($r=0.150$, $P < 0.01$) and negatively with adiponectin concentrations ($r=-0.208$, $P < 0.001$). Stepwise regression analyses confirmed that fetuin-A concentration was an independent contributor to fasting insulin level and HOMA-IR, independently of body mass index, triglyceride, LDL-cholesterol, leptin and adiponectin concentrations.

Conclusions: Our data suggest that the increased serum fetuin-A is associated with insulin resistance and an atherogenic lipid profile in Japanese men.

HOMEOSTASIS MODEL ASSESSMENT OF INSULIN RESISTANCE IN RELATION TO ORAL GLUCOSE TOLERANCE TESTING IN DETERMINATION OF HYPERINSULINEMIA

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Aim: To investigate the clinical applicability of homeostasis model assessment of insulin resistance (HOMAIR) in relation to oral glucose tolerance testing (OGTT) in determination of hyperinsulinemia.

Methods: The study included 79 subjects who underwent 2-hour 75 g OGTT during which basal and stimulated values of serum insulin were determined and HOMAIR indices were calculated. Based on the presence of basal and/or stimulated hyperinsulinemia, two groups were created: normoinsulinemic (NI) subjects (n=42) and subjects with hyperinsulinemia (HI) (n=37).

Results: Although subjects showing any carbohydrate metabolism abnormality were excluded, the HI group showed statistically significant higher postprandial glucose values (5,99 ± 1,00 mmol/l vs. 4,9 ± 0,94 mmol/; p< 0,001) and body mass indices (31,83 ± 7,55 kg/m^2 vs. 24,68 ±4,04 kg/m^2; p< 0,001) in relation to the NI group. The values of HOMAIR were 2,09 ± 0,76 in the NI group and 5,82 ±4,87 in the HI group (p< 0,001). There was a significant correlation of HOMAIR with the stimulated insulin values in the HI group (p=0,02).

Conclusions: The correlation of HOMAIR with the stimulated insulin values indicates that HOMAIR is a relevant index of hyperinsulinemia that can be easily applied in clinical practice. The results imply the role of adiposity and minor glucose metabolism abnormalities in the development of hyperinsulinemia.

METABOLIC SYNDROME IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Objective: It was previously shown that patients with primary hyperparathyroidism (PHPT) are insulin resitant, and often clinically presented with features of metabolic syndrome (overweight, dyslipidaemia, diabetes and hypertension). The aim of our study was to evaluate the frequency of metabolic syndrome in newly diagnosed patients with PHPT and the effect of surgical treatment on it.

Material and methods: In 41 patients with PHPT (age: 56.73±10.59 years, BMI 26.34±4.24 kg/m2), fasting plasma glucose, insulin and lipid levels were determinated before and 4 months after surgery. Insulin sensitivity was evaluated using HOMA index.

Results: On initial presentation in 11 patients (26.82%) metabolic syndrome was diagnosed (using IDF classification), and in 7 (17.07%) patients type 2 diabetes was diagnosed (4 of them were previously diagnosed). Hypertension was observed in 19 patients (46.24%), and dyslipidaemia was observed in 17 patients (41.46%). Surgical treatment was performed in 28 patients (in all with metabolic syndrome). In patents with metabolic syndrome there was no change in BMI (28.33±2.46 vs. 28.45±2.92 kg/m2, p>0.05), HDL (1.01±0.05 vs 0.96±0.07, p>0.05), TG (2.26±0.21 vs. 2.53±0.39 mmol/l, p>0.05), and HOMA index (4.43±3.03 vs. 4.97±2.27, p>0.05) 4 months after operation. In conclusion, there was increased prevalence of metabolic syndrome and type 2 diabetes in our group of patients with PHPT.

THE RELATIONSHIP OF THE REDUCTION OF INSULIN RESISTANCE WITH SERUM URIC ACID LEVELS IN PATIENTS WITH METABOLIC SYNDROME

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Background and aims: The aim of our investigation was to study the relationship of the reduction of insulin resistance with serum uric acid and other metabolic parameters in patients with metabolic Syndrome (MS) during insulin sensitizing therapy (metformin and thiazolidindiones).

Materials and methods: 30 patients with MS (10 males, 20 females, mean age - 35.5 ± 9.7 years) have been investigated by all metaboolic parameters and serum UA levels. Exclusion criterion was a gout. Investigated group was divided on 2 groups: group 1 - 18 patients HOMA-IR of which decreased less than 50% (7.8%±30.6%); group 2 - 12 patients HOMA-IR of which decreased greater than or equal to 50% (62.4%±10.6%).

Results: The mean value of UA in group 1 was non-significantly decreased from 6.6±1.7 mg/dl to 5.9±1.7 mg/dl. The percentage of hyperuricemia cases was decreased from 55.6% to 33.3%. The decrease of UA levels in group 2 was significant (from 5.8±0.4 mg/dl to 5.0±0.5 mg/dl, p< 0.001). After 6 months all patients in this group had normal serum levels of UA. The percentage decrease of UA levels in group 2 was 14.6%±11.8%, the same parameter in group 1 was - 10.0%±12.9%. PPG, basal C-peptide, and lipids also decreased significantly. Such a improved change in group 1 did not observed.

Conclusion: Obtained results shown that during insulin-sensitizing therapy changes in UA levels and other metabolic parameters significantly depend on the degree of the reduction of insulin resistance.

PREVALENCE OF METABOLIC SYNDROME IN AÑU ETHNIC GROUP FROM MUNICIPIO PAEZ, ZULIA STATE, VENEZUELA

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Objective: MS is a major risk factor for cardiovascular disease. It has been poorly studied among Indian groups; by which the main purpose of this research is to determine MS prevalence in Añu population from Zulia state, Venezuela.

Materials and methods: 136 healthy adults of both sexes were selected randomly whom a clinical history was made. Lipid profile was determined and MS diagnosis was done according to the International Federation of Diabetes criteria (IDF). The variables behaviour was determined using the Z-test of Kolmogorov-Smirnov by which results are shown as median or mean according to the case.

Results: Median of abdominal circumference was 89,74 ± 15,43cm. (Males: 101,7 ± 13,9cm.; Females: 85,5 ± 13,7cm.) showing that 70,6% of the population presents central obesity. Triacilglycerid levels showed a median of 98mg/dl, however 22,8% of individuals showed levels higher than 150mg/dl. 79,4% showed low levels of HDL-col with a median of 39,1 ± 10,6mg/dl (Men: 34,4 ± 9,1mg/dl; Women: 40,8 ± 10,6mg/dl). Median of arterial pressure was 130/90 mmHg, showing arterial hypertension in 40,4% of the sample. Serum glucose showed a median of 91mg/dl and 14% of the studied cases are over 100mg/dl. 39,7% of the Añu's population present the minimal criteria for SM, and the most common positive criteria was central obesity, arterial hypertension and low levels of HDL-col.

Conclusions: 39,7% of the Añu's population presents SM according to IDF criteria. Is it necessary to carry out studies relating the presence of SM with cardiovascular disease in this Indian population.

ELEVATED SERUM TRIGLYCERIDES IS THE STRONGEST SINGLE INDICATOR FOR THE PRESENCE OF METABOLIC SYNDROME IN PATIENTS WITH TYPE 2 DIABETES

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Background: Our aim was to identify one single clinical parameter, which could effectively predict the presence of MS in patients with type 2 diabetes.

Methods: We studied all patients with type 2 diabetes who attended our Diabetes Outpatient Clinic during a three-month period. Waist circumference, blood pressure and serum lipids were measured. Establishment of MS diagnosis was based:

<ol style="LIST-STYLE-TYPE: lower-alpha">
on National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria and
on International Diabetes Federation (IDF) criteria.

Receiver operating characteristic (ROC) analysis was applied in order to identify the clinical parameter with the highest predictive capability for MS. Among the 500 participating patients (231 males, 269 females), MS was diagnosed in 364 patients (72.8%) according to the NCEP ATP III criteria and in 408 patients (81.6%) according to the IDF criteria.

Results: For the NCEP ATP III classification, serum triglycerides (in the overall population), waist and HDL (in female population) demonstrated the highest predictive capability for MS (AUCs:0.786, 0.805 and 0.801, respectively). For the IDF classification, no single parameter reached an AUC > 0.800 in the overall population. In females, HDL displayed a satisfactory predictive capability for MS with an AUC which was significantly higher than the one in males (0.785 vs. 0.676, respectively, p < 0.05).

Conclusion: Elevated serum triglycerides strongly indicate the presence of MS in patients with type 2 diabetes. In female patients with type 2 diabetes, central obesity was the second stronger predictor of MS besides hypertriglyceridemia.

LEPTIN IN INSULIN-RESISTANT OTHERWISE HEALTHY ELDERLY PERSONS

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Aims: Adipose tissue - derived hormones are proposed to mediate biochemical status between abdominal fat and other tissues. Aging is considered to increase insulin resistance. The analysis of leptin level in the blood of non-diabetic elderly persons could facilitate diabetes prevention in elderly. The aim of the study was to estimate leptin concentration of healthy elderly patients with or without insulin-resistance.

Methods: Elderly (WHO criteria), both females and males, with no acute or severe chronic disorder were assessed waist, BMI, body fat composition, blood pressure. During OGTT fasting, Glu0' and 2h-glycemia, Glu120' were determined, then type 2 diabetes was excluded. Total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides (bioMérieux); Insulin (Biosource) and Leptin (R&D Systems) were measured fasting. According to insulin/Glu0´ ratio, IR we divided subjects into insulin-resistant, I-R (IR > 0,3; n=27; age 72±1) and insulin-sensitive, I-S (IR < 0,3; n=19; age 70±1). All data are shown as median±SEM.

Results:

1. I-R group was characterized by increased BMI and body fat comparing with I-S, however both groups did not differ in waist, blood pressure, plasma lipid profile and glucose.
2. Increased Leptin (32997 ± 4874 pg/ml vs 15528 ± 3222 pg/ml) (p< 0,04) was observed in I-R in comparison with I-S.
3. In I-S group a positive correlation Leptin&Glu0' (R=0,48, p< 0,05) whereas in I-R group positive correlations: Leptin&BMI

(R=0,5, p< 0,02) and Leptin&Body Fat (R=0,54, p< 0,005) were found.

Conclusion: Different metabolic factors seem to contribute serum leptin concentration of non-diabetic elderly in the presence or absence of insulin resistance.

IDENTIFYING PEOPLE WITH METABOLIC SYNDROME IN PRIMARY CARE BY SCREENING WITH A MAILED TAPE MEASURE. A SURVEY IN 14,000 PEOPLE IN THE NETHERLANDS

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Aims: To determine the feasibility and performance of population-based screening for metabolic syndrome in primary care in a Dutch city.

Methods: Survey in 14,000 people on the list of primary care physicians in IJsselstein, a small city (n=33,000) in the middle of the Netherlands. All adults between 20 and 70 years on July 1st, 2006, not known with diabetes, hypertension, dyslipidemia, or metabolic syndrome, were asked to measure their waist circumference using a home mailed tape measure. Participants with a high waist circumference (>88 cm for women; >102 cm for men) were invited for assessment of other factors defining metabolic syndrome according to the NCEP/ATPIII criteria.

Results: 11,862 subjects were invited, of whom 6,843 (58%) measured their waist circumference. 2,004 measured a waist circumference >88/102 cm and 1,721 participated in all examinations. In 473 metabolic syndrome was detected. The number of metabolic syndrome patients detected in people younger than 30 years was very low (n=16). The sensitivity of the used screening method was 77%, the negative predictive value 96%.

Conclusions: A primary care physician-driven population screening with self-measurement of WC can identify adults with metabolic syndrome. Especially cases aged 30-60 years, who do not visit the primary care physician often, will be detected. The negative predictive value of 96% indicates that with the used screening method and cut-off point for waist circumference the majority of people with metabolic syndrome are identified. This procedure creates possibilities for targeted screening, prevention and treatment of people who are at an increased cardiovascular risk.

DECREASE OF HEPATIC CYTOSOLIC PLA_2 EXPRESSIONS IN METABOLIC SYNDROME. EFFECTS OF DIETARY A-LINOLENIC ACID

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Metabolic syndrome (MS) is characterized by insulin resistance, obesity and dyslipidemia, among them, impairments of poly-unsaturated fatty acid (PUFA) metabolism. However, the relationships between MS and PUFA metabolism disturbances remain unclear, and the PUFA signaling enzymes (phospholipases A_2, PLA_2) as well as the PUFA biosynthesis enzymes (delta-6 desaturase, D6D, and elongases) may be involved. Moreover, insulin resistance can be modulated by dietary lipids, and more specifically by omega-3 PUFA.

Because the liver has a central role in glucose and lipid metabolisms, we investigated hepatic modifications of PUFA signaling and biosynthesis during the establishment of MS. For that, three-months-old fatty Zucker rats were used as model of MS - in comparison with their lean littermates - and were fed a control or a linseed oil diet from gestation until sacrifice.

Our results showed, in animals fed the control diet, a strong inhibition of $cPLA_2$ IV and VI gene expression in the liver of insulin resistant rats, compared to lean. Expressions of D6D as well as of elongase 2 were increased in the fatty Zucker rats, independently of SREBP-1c activation.

The α-linolenic acid rich diet significantly decreases glucose intolerance and tends to abolish the PUFA signaling and biosynthesis perturbations observed in fatty Zucker rats fed the control diet.

In conclusion, this study evidenced for the first time a perturbation of hepatic $cPLA_2$ enzymes in insulin resistant Zucker rats. These observations may suggest a new role for these enzymes in metabolic syndrome.

A COMMON VARIANT IN THE FTO GENE IS ASSOCIATED WITH BMI BUT NOT WITH METABOLIC SYNDROME IN CZECH MALES

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Aims: Obesity and metabolic syndrome are the serious health problem worldwide and are associated with increased risk of heart disease, and type 2 diabetes mellitus. Obesity has an important genetic component estimated on 40-60%. FTO („fat mass and obesity related gene", exact function unknown) gene and its variants has been recently associated with the BMI and waist determination in west European populations. We have analyzed the association between the FTO gene variant rs17817449 BMI and metabolic syndrome in middle European - Slavic population.

Methods: FTO variant rs17817449 (G>C) was analyzed by PCR-RFLP in 1191 adult (25-65 years old) males selected according the MONICA protocol. The presence of metabolic syndrome was analysed according the NCEP-ATP III kriteria. FTO genotype and all parameters were available in 1063 (89.2%) of males.

Results: Genotype frequencies in Slavic population were similar to the previously described west European populations (GG - 18%; GT - 50%; TT - 32%). FTO rs17817449 variant was significantly associated with BMI (kg/m^2) (GG - 28.7±3.7; GT - 28.3±4.1; TT - 27.8±3.9; P=0.014). But the FTO genotype frequencies did not significantly differ (P=0.549) between males with (N = 275) and without (N = 788) metabolic syndrome.

Conclusions: FTO variants have an effect on BMI, but not on metabolic syndrome development in Czech males.

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RATES OF METABOLIC SYNDROME AMONG SCHIZOPHRENIA PATIENTS TREATED WITH OLANZAPINE, QUETIAPINE, RISPERIDONE, OR ARIPIPRAZOLE AT 26 WEEKS; A POOLED ANALYSIS OF THREE RANDOMIZED CLINICAL TRIALS

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Background: It is well known that the prevalence of metabolic syndrome among patients with schizophrenia is typically double that of the general population. Further, certain atypical antipsychotic agents have been associated with weight gain, hyperlipidemia, and hyperglycemia: all components of the metabolic syndrome. We compared the 26 week rates of

metabolic syndrome (ATP-III) among schizophrenia patients treated with one of four atypical antipsychotics using pooled data from three randomized clinical trials.

Methods: Patient-level data from three randomized clinical trials (CN138-002, 003, and 152) were used for the analysis. Rates of ATP-III defined metabolic syndrome were assessed after 26 weeks of exposure to one of the following atypical antipsychotic agents: olanzapine, quetiapine, risperidone, and aripiprazole. A longitudinal repeated measures mixed model design was employed, adjusting for baseline levels, time, and treatment. Relative risk estimates were obtained for three agents with aripiprazole as referent.

Results: In the olanzapine controlled trials, 26 week rates of metabolic syndrome for olanzapine versus aripiprazole were 41.4% ±3.5 (n=176) versus 24.4% ± 3.1(n=221), respectively; RR = 1.70 (P< 0.0001). For quetiapine, metabolic syndrome rates were 25.4%±4.7 (n=54) and 15%±2.3 for aripiprazole (n=164); RR = 1.69 (p=0.03). For risperidone, metabolic syndrome rates were 16%±4.4 (n=51) and 15%±2.3 for aripiprazole (n=164); RR = 1.07 (p=0.83).

Conclusions: Among schizophrenia patients treated with atypical antipsychotics, olanzapine and quetiapine appear to be associated with the highest rates of metabolic syndrome relative to aripiprazole. Rates were similar for both risperidone and aripiprazole.

THE RELATIONSHIP BETWEEN ANDROGEN DEFICIENCY AND METABOLIC SYNDROME

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Aims: The aim of the study was to determined whether lower testosterone level is associated with the development of metabolic syndrome in men with diabetes type 2.

Methods: 114 men with DT 2 age from 45-60 years (M±SD 54,0±4,63) were analyzed. The level of total testosterone (TT), SHBG, total cholesterol (TC), LDL, VLDL, HDL, triglycerides (TG) were assessed. Body mass index (BMI) and waist/hip ratio (WHR) were calculated. Metabolic syndrome (MS) was diagnosed based on the NCEP III/IDF definition. Control group included 25 healthy men age from 45-60 years.

Results: The mean of duration of DT2 was 8,52±5,89 years. The ÒÒ level was lower in diabetic men compared with control group men (6,05±2,65 vs. 11,8 ± 5,14 nmol/l). Patients were divided into two groups: 1 - 57 with testosterone deficiency (TT were in low normal limits 5,9 nmol/l) and 2 - 32 with normal testosterone concentration. According NCEP III/IDF definition prevalence of metabolic syndrome was: 88% patients in 1 group and 24% - in 2 group. The levels of TG, VLDL, waist circumference, BMI were significantly higher in 1 group compared to 2 group (p=0,0002, p=0,002, p=0,006, p=0,036, respectively).There was inverted correlation between the TT and BMI (r=-0,35, p< 0,05), WHR (r=-0,31, p< 0,05), TG (r=-0,31, p< 0,05), VLDL (r=-0,32, p< 0,05).

Conclusions: Men with MS and DT2 have a higher incidence of hypotestosteronaemia. Triglycerides concentration, BMI and waist circumference are sensitive parameters to reflect the influence of androgen deficiency on risk of the metabolic syndrome.

THE DISORDERS OF TRANSPORT IN CELLS OF THE FREE FATTY ACIDS IN PATOGENEZE METABOLIC SYNDROME

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Studied the composition of blood plasma free fatty acids (FFA) and of blood erythrocytes fatty acids in metabolic syndrome (MS) patients.

Examined 22 patients with MS. The MS was diagnosed according to the criteria offered by the experts of the USA National Education Program on cholesterol [Third Report of the National Cholesterol Education Progam Expert Panel on Detection, Evaluation and treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication. 2001]. The methyl ethers of fatty acids analysis was executed on the gas-liquid chromatograph Shimadzu GC-17A (Japan). The results were stated in relative % from the total fatty acids sum.

In the MS patients with the normoinsulinemia and in the MS patients with the insulin resistance the lauric, myristic and palmitic saturated acids level decrease of blood plasma was detected. Against the saturated FFA relative amount decrease the content of polyunsaturated fatty acids (linolic, linolenic, arachidonic acid) increased. However in the erythrocytes the saturated fatty acids level increased, polyunsaturated fatty acids level decrease was detected. In the MS patient with the insulin resistance the disorders of the fatty acids level in the erythrocytes were more vivid than in the MS patient with the normoinsulinemia.

The findings testify about the disorder of transport in blood and the carrying over by FFA in the cells in the MS patient. Thus, a significant factor of increased risk of MS development and burdening is the FFA transport failure.

DIFFERENT MECHANISMS FOR IMPAIRED FASTING GLUCOSE AND IMPAIRED GLUCOSE TOLERANCE ON INSULIN SECRETION AND RESISTANCE

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Aims: To investigate the metabolic profiles according to glucose tolerance status.

Methods: We conducted cross-sectional analysis of 260 Korean subjects with risk factors of type 2 diabetes, but without a history of diabetes. After oral glucose tolerance tests, the subjects were classified into the following groups:

1. normal glucose tolerance (NGT; n=107);
2. isolated impaired fasting glucose (IFG; n=27);
3. isolated impaired glucose tolerance (IGT; n=51);
4. combined IFG and IGT (IFG/IGT) (n=46); and
5. combined fasting and 2-hr hyperglycemia (diabetes; n=29).

The homeostasis model assessment indexes of beta cell function (HOMA-β) and insulin resistance (HOM-IR) and post-glucose loading insulin increment were calculated.

Results: The beta cell function and insulin sensitivity (value 1/HOMA-IR) in diabetes had the lowest than those in the other groups. HOMA-β and 1/HOMA-IR in IFG and IFG/IGT were lower than those in NGT or IGT (IGT vs. IGT and IFG/IGT, P< 0.05, respectively, in HOMA-β; NGT vs. IFG/IGT, P< 0.05 in 1/HOMA-IR). The insulin increment after glucose loading was the highest in IGT, and progressively decreased to NGT, IFG, and diabetes in order. On the curve plotting HOMA-β and 1/HOMA-IR, IGT showed similar pattern to NGT. However, the curves of IFG and IFG/IGT were plotted between NGT and diabetes.

Conclusions: IFG and IFG/IGT showed more reduced basal insulin secretion and insulin sensitivity compared with NGT and even IGT.

Therefore, the subjects with IFG, regardless of IGT, could be progressed more rapidly to overt diabetes, compared with IGT.

DECREASED LEG GLUCOSE UPTAKE DURING EXERCISE CONTRIBUTES TO THE HYPERGLYCEMIC EFFECT OF OCTREOTIDE

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Aim: During prolonged infusion of somatostatin there is an increase in arterial glucose concentration, and this increase persists even during prolonged exercise. The aim of the study was to measure glucose uptake in the leg muscles during octreotide infusion before and during leg exercise.

Material and methods: 8 healthy male subjects were investigated twice during fasting: during 3 h infusion of octrotide (30ng/kg/min) or sodium chloride with exercise at 50% of max VO_2 in the last hour. Glucose uptake in the leg was measured by Fick's principle by blood sampling from an artery and a femoral vein. Blood flow in the leg was measured by the indicator (ICG) dilution technique.

Results: After an initial decrease during rest, octreotide infusion resulted in a significant increase in arterial glucose concentrations compaired to placebo conditions during exercise (7,6±0,6 versus 5,6±0,1 mmol/l, mean±SEM). During rest octreotide did not change the leg glucose uptake (59±10 versus 55±11 µmol/min). In contrast leg glucose uptake was significantly lower during exercise compared to placebo conditions (208±79 versus 423±87 µmol/min). During exercise leg oxygen uptake was not different in the two experiments (20.4±1.3 versus 19.5±1.1 µmol/min).

Conclusion: Despite the same leg oxygen consumption, infusion of octreotide decreased leg glucose uptake during exercise. This indicates that the hyperglycemic effect of octreotide partly is due to this reduced leg glucose uptake. Furthermore the results suggest that a certain level of circulating insulin is necessary in order to obtain sufficient stimulation of glucose uptake in the exercising muscles.

IDENTIFYING PRE-DIABETES IN YOUTH WITH OBESITY

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One in four children with obesity in clinical programs have pre-diabetes, and impaired glucose tolerance (IGT) is much more common than impaired fasting glucose (IFG). The Canadian and American Diabetes Associations (CDA/ADA) recommend screening for dysglycemia using fasting plasma glucose (FPG) in obese children ≥10 y at high risk for Type 2 diabetes mellitus (T2DM) based on family history, ethnicity and clinical indicators.

Objectives: To examine the sensitivity and specificity of current screening criteria to identify pre-diabetes and to examine models for predict ing IGT utilizing clinical assessment and fasting blood work.

Methods: In 174 obese children age 11.7±2.69 y, enrolled in a longitudinal study, baseline assessment included anthropometry, blood pressure, fasting glucose, HDL-cholesterol, triglyceride, insulin, 2 hour glucose and family history of T2DM.

Results: Twenty-four percent of these children (BMI-Z score 2.28±0.37, body fat 41.3±4.85%), have pre-diabetes (5.2% IFG, 15.7% IGT, 3.5% IFG + IGT). Current screening criteria have low sensitivity (33.3 (19.6-49.5) %) but reasonable specificity (77.1 (68.9-83.9)%) to identify pre-diabetes. Logistic models and ROC curves to predict IGT were developed. The model with the greatest diagnostic performance (AUC 0.720) included age, BMI, systolic blood pressure, HOMA-IR and fasting triglyceride. Sensitivity was 80% with specificity of 60%.

Conclusion: Current screening criteria for assessing glycemic status in obese children have low sensitivity to identify pre-diabetes. We propose a model with improved sensitivity and specificity using simple clinical parameters.

Sources of support: Canadian Institutes of Health Research (CIHR); Population Health Research Institute; Heart and Stroke Foundation of Canada.

PREDICTIVE FACTORS OF WORSENING GLUCOSE TOLERANCE AFTER 2-YEAR BEHAVIORAL INTERVENTION PROGRAM

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Aims: The aim of this study was to identify predictive factors for change of glucose tolerance status following 2-year behavioral prevention program in a high cardiometabolic risk population.

Methods: 295 subjects (59.7% women), > 30 years old, completed the 2-year intervention program based on healthy diet and physical activity orientations. Characteristics of those who maintained or regressed the glucose tolerance status (non-progressors) were compared with those who progressed (progressors) after the intervention. Logistic regression was used as non-progressors as a dependent variable.

Results: Characteristics of the non-progressors (72.5%) and progressors had a similar evaluation after the intervention, except for greater decrease in fasting (-4.5±11.0 vs. 7.1±12.6 mg/dl, p0.000) and 2-hour plasma glucose (-1.0±31.6 vs. 46.6±43.2 mg/dl, p0.000) and HDL-cholesterol (-5.2±8.7 vs. -2.0±10.8 mg/dl, p0.036), and lower levels of C-reactive protein (0.20±0.38 vs. 0.27±0.43 mg/dl, p0.006) in the non-progressor group. In logistic regression model, lower levels of C-reactive protein at baseline and change in total cholesterol after the intervention period were independently associated with maintenance or regression of glucose tolerance status, adjusted for insulin and age. The significance of the variables did not change when changes in BMI or in waist after the intervention was included in the final model.

Conclusion: Based on the CRP values, we suggest that lower inflammatory status may be beneficial on the prevention of worsening glucose metabolism, independent of body adiposity. Reduction in total cholesterol after 2-year intervention program was also associated with a better glucose tolerance status. This may be reflecting compliance to lifestyle modification.

DOES INTENSIVE PROGRAM OF LIFESTYLE CHANGES INTERFERE IN QUALITY OF LIFE OF INDIVIDUALS AT RISK FOR TYPE 2 DIABETES?

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Lifestyle changes prevent type 2 diabetes but it is not a consensus whether strict recommendations are beneficial for quality of life (QoL).

Multiprofessional approach improves patients knowledge about diabetes which can minimize complications; we do not know how limitations in their routine, imposed by intervention programs, affect QoL. We assessed QoL of pre-diabetic individuals submitted to 2 types of 18-month DM prevention programs: traditional or intensive. The intensive program was based on multiprofessional psychoeducative group sessions. QoL was obtained by the Short Form-36 (SF-36) Health Survey, including 8 domains, scaled from 0-100. Preliminary results of 68 individuals (31% men; 58.1±12.4 yrs) are reported. Baseline and 3-month mean values of each domain were compared. Intensive group had higher weight loss than the traditional. SF-36 results are below:

		Intensive			Tradicional	
SF-36 domains	Baseline	3-month	p	Baseline	3-month	p
Physical functioning	76.4 ± 19.6	83.9 ± 14.8	<0.001	78.4 ± 24.3	82.1 ± 19.4	0.155
Role - physical	75.5 ± 33.5	82.6 ± 31.1	0.199	68.2 ± 37.9	72.7 ± 34.4	0.628
Body pain	60.5 ± 22.1	63.7 ± 24.9	0.341	59.6 ± 25.3	62.0 ± 29.2	0.674
General health	70.1 ± 18.6	77.1 ± 17.2	0.005	69.0 ± 20.1	70.3 ± 17.1	0.667
Vitality	60.4 ± 21.6	69.5 ± 19.2	0.001	60.5 ± 23.1	63.9 ± 22.4	0.288
Social functioning	69.8 ± 25.4	79.9 ± 25.2	0.004	73.3 ± 28.7	78.9 ± 23.9	0.313
Role - emotional	55.8 ± 40.4	76.8 ± 32.8	0.002	62.1 ± 40.2	72.7 ± 26.5	0.129
Mental health	66.1 ± 20.0	72.6 ± 14.9	0.003	63.1 ± 23.7	70.2 ± 21.3	0.069

Intensive intervention program on lifestyle improves patient perception of health. Such program may have enhanced awareness about the importance of self-care for sustained well-being.

GENDER DIFFERENCES IN LOW-GRADE INFLAMMATION AND ADIPONECTIN IN NORMAL GLUCOSE TOLERANCE, PRE-DIABETES AND TYPE 2 DIABETES

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Aims: Women with pre-diabetes and type 2 diabetes (T2DM) are at increased, relative risk for cardiovascular disease (CVD) compared to men. The reason for this is unknown. We studied gender differences in low-grade inflammation, by high-sensitivity C-reactive protein (hs-CRP) and interleukin-1 receptor antagonist (IL-1 Ra), and adiponectin in normal glucose tolerance (NGT), pre-diabetes and T2DM subjects.

Methods: Population-based study of 411 middle-aged men and 512 women Pieksämäki, East-Finland. They underwent a 75-g oral glucose tolerance test and measurement of adiponectin, hs-CRP, IL-1 Ra. WHO diagnostic criteria for diabetes, pre-diabetes (IFG+IGT) were used. Statistical comparisons between groups were performed by bootstrap-type analysis of covariance.
Results: Mean body mass index was 26 kg/m² in both genders. In NGT group no difference was found between genders in hs-CRP and IL-1 Ra. In subjects with pre-diabetes or T2DM women had significantly higher levels of both hs-CRP and IL-1 Ra compared to men. Women-to-men-ratio of these markers increased linearly (for hs-CRP P=0.019 and IL-1 Ra P=0.013) from NGT to T2DM. Adiponectin levels were absolutely higher in women, but ratio of adiponectin between women to men decreased linearly (P=0.011) across NGT 1.61(95% CI 1.48 to 1.75), pre-diabetes 1.57 (1.36 to 1.83) and T2DM 1.16 (0.87 to 1.53).

Conclusions: Ratio of adiponectin level between women to men decreased across subjects with NGT, pre-diabetes and diabetes, and the ratio of inflammatory markers increased same time. Increased inflammatory stress in women, possibly started by relatively higher adiponectin decline, may explain why women with pre-diabetes and diabetes have excess CVD.

HBA1C, BUT NOT FASTING GLUCOSE OR INSULIN, IS INDEPENDENTLY ASSOCIATED WITH PHYSIOLOGICAL PARAMETERS OF WORSENING GLYCAEMIC METABOLISM POST-TRANSPLANTATION - A MULTIVARIATE ANALYSIS

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Aims: Hyperglycaemia is common post-transplantation. The hyperbolic equilibrium between first-phase insulin secretion (FPIS) and insulin sensitivity (IS) is termed the disposition index (DI). In the context of insulin resistance, declining FPIS reflects the first stage of diabetes as the DI is lowered. Early identification of these defects is desirable. We conducted multivariate analysis to determine variables which could be utilised as simple markers of these physiological parameters post-transplantation.

Methods: FPIS, IS and DI was calculated by minimal model analysis from intravenous glucose tolerance tests. Second-phase insulin secretion (SPIS) was calculated from meal tolerance tests. 80 tests were conducted in non-diabetic, tacrolimus treated renal transplant recipients with clinical/biochemical analysis. Linear regression model was used for univariate analysis and statistically significant variables entered into a multivariate model for analysis.

Results: HbA1c independently correlated with first phase insulin secretion (R^2 = 0.106, p = 0.049), insulin sensitivity (R^2 = 0.136, p = 0.029) and disposition index (R^2 = 0.201, p = 0.006). Second phase insulin secretion correlated with: (fasting glucose, R^2 = 0.165, p = 0.015; insulin, R^2 = 0.311, p = 0.001; BMI, R^2 = 0.323, p < 0.001; HDL cholesterol, R^2 = 0.236, p = 0.003; triglycerides, R^2 = 0.330, p < 0.001).

Conclusions: HbA1c independently correlates with FPIS, IS and DI. As the first quantifiable defects of glucose metabolism, the association with HbA1c suggests it may be a more valuable marker than fasting glucose and/or insulin to monitor for impending glycaemic abnormalities in transplant recipients at risk of diabetes.

THE PERCENTAGE INCREMENT OF 2H VS FASTING PLASMA GLUCOSE DURING OGTT PREDICTS THE DERANGEMENT OF B-CELL FUNCTION

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Aims: Normal glucose tolerance (NGT) range has fasting plasma glucose (FPG) < 100, 2h plasma glucose (2hPG) < 140 mg/dl after OGTT. Impaired glucose homeostasis is likely even when FPG < 100 mg/dl if PG% [(2hPG -

FPG) / FPG·100] > 40.5%. This study verifies whether, in the NGT range, the presence of PG% ≥ 40% implies alterations in β-cell function.

Methods: In 695 NGT subjects, measurements of glucose (FPG, 2hPG) and insulin (FPI and 2hPI) during OGTT were used to calculate the estimated insulin sensitivity index (EISI), and first phase and second phase (1stPH and 2ndPH) insulin secretion. Considering a series of PG% cut-offs (10, 20, 30, 40 and 50%), we compared the β-cell function indexes in subjects with a value below versus subjects with a value equal to or higher than each specific PG% cut-off.

Results: With rising PG% cut-off values (10, 20, 30, 40 and 50%), we measured a significant fall of EISI coupled to a rise in 1fsPH, while 2ndPH was never significant.

Conclusions: These data suggest that in the NGT range there are significant alterations in insulin sensitivity and secretion. With increasing PG% values, the increment in 1fsPH rose significantly to compensate the progressive fall in insulin sensitivity, a compensation necessary for each subject to remain within the NGT range. When the compensation (i.e. insulin secretion) falters, as evidenced by epidemiological studies, a progression towards glucose intolerance or type 2 diabetes is likely.

IS GENERAL PRACTICE A FEASIBLE SETTING FOR PREVENTION OF TYPE 2 DIABETES? THE APHRODITE STUDY

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Aim: Primary care seems a proper setting for 'real life' prevention of T2D in the Netherlands; Dutch GP's are freely accessible and close to the community. The APHRODITE study therefore aims to research both the feasibility and effects of a theoretically effective lifestyle intervention program in the setting of general practice.

Methods: Fifty GPs sent diabetes risk questionnaires to patients between 40 and 70 years old (n=15,825). Out of 9,875 responders (62%), 1,594 high-risk individuals were identified and invited for an interview and an OGTT. At baseline, 940 participants were included in the study.

During three-monthly sessions with the GP or the nurse practitioner (NP) a personalized intervention plan is developed and applied. Lifestyle information on diet and physical activity is provided both individually and in groups.

Results: Next to screening and baseline results, results at 6 months will be shown on glucose levels, T2D risk score, BMI, dietary and physical activity patterns and quality-of-life parameters. Furthermore, factors influencing implementation of the program (eg. views of GPs, NPs and patients, participation rates) will be presented.

Discussion: Preliminary results suggest that prevention of T2D by lifestyle intervention is feasible in Dutch primary care. The APHRODITE study is innovative as it combines active selection for high-risk individuals with the central role of the GP in Dutch health care. Furthermore, it focuses on both high-risk individuals with and without impaired glucose regulation.

AWARENESS OF PREDIABETES IN CANADA

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Aim: To explore awareness among Canadian family physicians and the general public concerning prediabetes and related diabetes prevention strategies.

Methods: The Public Health Agency of Canada (PHAC) is using a combination of focus groups and surveys in order to compare attitudes, knowledge and awareness of this issue among Canadian family physicians and the general public.

Results: Among family physicians, PHAC's 2007 focus groups (n=40 GPs) found low levels of awareness about the prevalence of prediabetes, the role of OGTT for detection, and proven intervention strategies for prevention. Most physicians believed an IGT finding would be unlikely to influence their care plan or patient prognosis, and many were unaware of current evidence about the proven benefits of lifestyle modification from the U.S. Diabetes Prevention Program and Finland's Diabetes Prevention Study. These preliminary qualitative results will be confirmed and expanded in an upcoming physician survey being planned by PHAC for fall 2008. PHAC is also planning to include the general population as part of the upcoming prediabetes awareness survey. It expects to find low levels of awareness, similar to the recent American NHIS results - which found that only 1 in 6 persons actually affected with prediabetes was aware of their condition.

Conclusions: Awareness about prediabetes and related preventive strategies is low among Canadian family physicians and the general public.

METHYLPREDNISOLONE REDUCES SERUM RAGE IN MULTIPLE SCLEROSIS PATIENTS DURING RELAPSE

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Introduction: The receptor for advanced glycation end products (RAGE) belongs to the immunoglobulin superfamily. Its blockage decreases autoimmune reaction in the central nervous system and suppresses Experimental Autoimmune Encephalomyelitis, the animal model for multiple sclerosis. The aim of our study was to evaluate the effect of standard steroid treatment on the level of serum RAGE in relation to insulin resistance indexes.

Material and methods: Fourty one patients with relapting-remitting multiple sclerosis (RR-MS) were included in the study during relapse. The blood samples were withdrawn before and one day after standard methylprednisolone (MP) treatment. Control group consisted of 15 healthy volunteers. Serum RAGE was estimated by means of ELISA (R&D). Serum insulin levels were estimated by ELISA (Biosource), and glucose concentrations with the use of the enzymatic method. Insulin resistance indexes HOMA and QUICKI were calculated.

Results: Serum RAGE after methylprednisolone was reduced (652pg/ml, p=0.0235), comparing to controls (957pg/ml) and values before steroid administration (995pg/ml, p=0.0018). There was no difference in glucose level after MP (101mg/dl) comparing to values before treatment (98mg/dl, p=0.3745). We observed increase in insulin level after MP (34.3mIU/ml and 11.9mIU/ml, p< 0.000001). HOMA increased (median 2.1; interquartile range:1.7-4.3; median: 1.45; interquartile range: 1.15-4.95; p=0.0016) and QUICKI decreased (median 0.06, interquartile range: 0.04-0.08; median: 0.08, interquartile range: 0.06-0.10, p< 0.000001) after MP administration. No correlations between serum RAGE and glucose, insulin, HOMA or QUICKI index before and after MP were found.

Conclusion: The decrease in serum RAGE concentration after standard methylprednisolone treatment of relapse of MS is independent from its influence on insulin resistance.

THE EFFECT OF A TARGETED, INTENSIVE RECRUITMENT STRATEGY ON PARTICIPATION IN SCREENING FOR PREDIABETES AND DIABETES MELLITUS AMONG PERSONS OF SOUTH ASIAN DESCENT

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Background: Screening may be indicated among populations at high risk for prediabetes or diabetes mellitus (DM), e.g. migrants of South Asian (SA) descent. However, little is known about the optimal strategy to promote participation in these populations. We investigated the effect of a targeted, intensive versus standard recruitment strategy on the participation in screening among SA-Surinamese men and women.

Methods: 878 SA-Surinamese (≥18 years, without known DM) were selected from general practice registers in The Hague, the Netherlands, and randomly assigned to the intensive (written invitation for an oral glucose tolerance test followed by a telephone call, reminder and home visit) or standard (written invitation and two reminders) group. Participation and characteristics were compared between groups using standard methods.

Results: In total, 29.2% in the intensive group and 21.6% in the standard group planned an appointment for screening. While a larger proportion of cancellations in the intensive group attenuated the overall differences, the participation among younger persons and among men remained significantly higher in the intensive group.

Compared to the standard group, participants in the intensive group were higher educated. The prevalence of prediabetes (37.8 vs. 39.0%) and DM (13.3% vs. 7.7%), family history of DM, body mass index and blood pressure were similar across groups.

Conclusion: Particularly among young and male participants, intensive recruitment results in a higher number of persons at risk identified. In practice, this has to be weighed against the extra effort required in order to make an appropriate choice for the recruitment strategy employed.

MILD DYSGLYCAEMIA ASSOCIATES WITH METABOLIC ABNORMALITIES AND ADVERSE CORONARY RISK PROFILE IN HYPERTENSIVE PATIENTS

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Background: The relationship between impaired fasting glucose (IFG,fasting plasma glucose, FPG, 100-125 mg/dL) and cardio-metabolic risk factors and coronary heart disease (CHD) risk profile is scarcely known in essential hypertension, an insulin resistant stae and a risk factor for new-onset type 2 diabetes.

Methods: 982 non-diabetic (FPG< 126 mg/dl), hypertensive referrals (age:56±12 yrs, M/F:57/43%) with either normal (FPG< 100mg/dL, n=650, NFPG) or IFG (n=333), these latter stratified by mildly (M, 100-109 mg/dL, n=196) or severely (S, 110-125 mg/dL, n=135) IFG. Evaluation variables were obesity (BMI>30 Kg/m^2, OB), triglycerides(TRIG)>200 mg/dL, HDL-C< 40 mg/dl, high white blood cell (WBC) count (>7.7x10^3, an index of subclinical inflammation) and high CHD risk (10/yr risk>20% by the Framingham Risk Score).

Results: As compared with NFPG, IFG patients were older (58±11 vs 54±11 yrs, p< 0.001), more frequently males (40% vs 26%, p< 0.001) and presenting with OB (30% vs 21%, p=0.002), TRIG>200 mg/dL (21% vs 12%, p=0.0004), HDL< 40 mg/dl (25% vs 17%, p=0.004), high WBC (32% vs 22%, p=0.003) and high CHD risk (17% vs 11%, p=0.003). BP, LDL cholesterol, prevalence of pts on-treatment (38% vs 42%) did not differ. OB (31% vs 29%), HIGH- TRIG>200 mg/dL (21% vs 20%), HDL< 40 mg/dl (28% vs 20%), high WBC (35% vs 29%), high CHD risk (20% vs 15%) were comparable between M and S IFG.

Conclusions: Cardio-metabolic risk factors and adverse CHD risk profile is clearly more frequent in dysglycaemic hypertensive patients, a pattern evident even in presence of only mild increments in FPG.

EVALUATION OF EFFECTIVENESS OF THE EUROPEAN PROJECT FOR THE PREVENTION OF TYPE 2 DIABETES (DM2) (DE-PLAN) ON RISK FACTORS FOR CARDIOVASCULAR DISEASES (CVD)

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Objectives: Recent studies have proved that the prevention of DM2 and its complications is possible using lifestyle intervention.The objective of DE-PLAN project is to improve ability to screen prevent DM2 and CVD in high risk persons in Europe.The purpose of this study was to investigate and evaluate the effectiveness of lifestyle intervention to reduce estimated CVD risk.

Methods: As part of this multicentric,multinational study 116 subjects,aged 45-74,both genders, no diabetes history, were randomly included.All subjects first fulfilled FINISHDIABETESRISK SCORE (FDRS) questionnaire.The following risk factors for CVD: BMI (kg/m^2),Waist circumference (W,cm),fasting plasma glucose (FPG,glucose oxidase),total,HDL,LDL cholesterol,triglycerides (spectrophotometry),systolic and diastolic blood pressure (SBP,DBP,mmHg) were investigated before and one year intervention program consisting of application of diet (saturated fat < 10E%, total fat < 30E%, fiber ≤15g/1000Kcal) and exercise (≥30min/24h).Statistical tests:ANOVA,Wilcoxon,χ^2.

Results: FDRS decreased after one year in all intervals (before and after,mean±SD, 14.8±3.4 and 13.3±3.4),BMI decreased in different intervals of FDRS (30.8±4.9 and 30.1±5.1),W (108.8±7.6 and 107.7±2.9),FPG (5.8±1.1 and 5.6±0.8) (p< 0.001).The decrease of SBP (139.9±21.4 and 137.7±18.9),DBP (87.5±13.2 and 85.0±10.3),total cholesterol (6.2±1.2 and 6.0±1.1),LDL (4.9±1.2 and 3.1±0.7), triglycerides (2.7±1 and 2.2±1) and increase of HDL (1.3±0.5and 1.5±0.6) were statistically non significant (p>0.05).

Conclusions: FDRS may be used for the screening of DM2 and CVD.The significant decrease of FDRS,BMI,W,FPG proved the ability of one year intervention program for the prevention of DM2 and CVD.The changes of lipids, even non significant, have similar meanings.It is possible to use these results to make new, optimal guidelines for the prevention of DM2 and CVD.

LONG-TERM EFFECTS OF LIFESTYLE MODIFICATION ON CENTRAL ARTERY STIFFNESS AND ENDOTHELIAL FUNCTION, AND SUBSEQUENT DRUG TREATMENT IN INDIVIDUALS WITH METABOLIC SYNDROME COMPONENTS

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Objective: To assess

1) the long-term effects of lifestyle modification, and

2) the effects of telmisartan on carotid artery stiffness (cAS) and endothelial function in individuals with metabolic syndrome (MS) components.

Methods: This is a follow-up of the SNAC (Staged Nutrition and Activity Counseling) study that examined the effects of lifestyle modification prescribed by family physicians on cardiovascular structures and function in people at increased risk for cardiovascular disease. Twenty-four subjects (58.5±8.4 yrs, 12F) were assessed following (mean of 26.3 months) discontinuation of the 1-year SNAC study. cAS and brachial artery flow-mediated dilation (FMD) were assessed by Doppler ultrasound. MS components and exercise capacity (VO_2max) were also assessed. Subsequently, 17 subjects (58.0±7.9 yrs, 7F) were reassessed following the 24-week telmisartan treatment.

Results: The reduced cAS observed at 1-year was still maintained at the follow-up, whereas the improved FMD at 1-year returned to the pre-intervention level ($p< 0.05$). Similarly, the reductions in triglycerides and fasting glucose seen at 1-year were maintained at the follow-up ($p< 0.05$). Following the 24-week telmisartan treatment, cAS and FMD significantly improved ($p< 0.05$). While BP was significantly reduced (ΔSBP 13.6±16.3 mmHg, ΔDBP 7.9±5.6 mmHg, $p< 0.05$), other MS components and VO_2max remained unchanged throughout the drug treatment.

Conclusions: These results show that 1) our lifestyle modification strategy can maintain a reduction in cAS as well as triglycerides and fasting glucose even after the active intervention, and 2) the telmisartan treatment may be another option to reduce cAS and improve endothelial function in this population.

COMPARISON OF CARDIOVASCULAR DISEASE RISK IN PREDIABETIC VERSUS NORMOGLYCAEMIC INDIVIDUALS IN A DEVELOPING COUNTRY

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Background and aim: Cardiovascular disease (CVD) mortality is increased in diabetics. Prediabetes is also associated with increased CVD mortality. This paper compares the CVD risk of prediabetic to normoglycaemic individuals in a developing country.

Methods: An epidemiological survey of a semi-rural community was conducted. Subjects aged 55 years and above were selected by attendance at a free health screening service in the community.A standardized questionnaire was applied by interview. Blood pressure (BP) was measured using a standardised mercury sphygmomanometer. Fasting plasma glucose (FPG) and serum lipids were also measured.

Normoglycaemia, prediabetes and diabetes was defined as FPG as < 6.1, 6.1-< 7, and ≥ 7 mmol/l respectively.

The Framingham Risk Score (FRS) based on total cholesterol was used as a measure of CVD risk. Separate charts were used for men and women.

Results: 1417 subjects participated. The response rate was 56%. A follow-up survey of the non-responders did not show any differences from the initial responders in any systematic way.

The mean age of the subjects was 65.4 years±SD 8. 53% were men. The mean FPG was 6.8±3.6 mmol/l.

The prevalence of normoglycaemia, prediabetes and diabetes was 64.6%, 16% and 19.4% respectively.

The FRS of prediabetic men was significantly higher than normoglycaemics (9.9 versus 9.4 respectively, p=0.034) However this difference was not significant in the women (11.4 versus 10.8 respectively, p=0.89).

Conclusion: CVD risk in men with prediabetes is increased compared to normoglycaemics. However this was not seen in women. Further studies are needed to confirm and explain these findings.

IMPACT OF A STRUCTURED CORPORATE WELLNESS PROGRAM (CWP) ON THE METABOLIC SYNDROME IN HONG KONG

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Objective: The Quality Work Life Health Challenge is a pioneer corporate wellness program initiated by a major public utility company in Hong Kong to promote a healthier weight among staff and to minimize metabolic risk factors through lifestyle intervention.

Methods: Health assessment of the staff was based on the International Diabetes Federation (IDF) criteria with Asian waist circumference reference on metabolic syndrome (MES). Central obese subjects are defined as having MES if they have 2 or more of the following conditions: low HDL-C, high TG, high BP and abnormal blood sugar. Staff from different geographical regions of the company was invited to health carnivals for health screening. Those with adverse metabolic risks were invited to join a 16-week CWP. The program includes 10 dietary counseling sessions conducted by registered dietitians and 4 exercise sessions.

Results: 49 staff (46 male and 3 female, mean age 48.2 ±10.0 years old , mean baseline WC 98.1±10 cm) have completed the program. There were significant improvements (mean±S.D, P< 0.001 for all) in body weight (-7.1 ±4.9kg), waist circumference (-9.8±7.0cm), body fat percentage (-3.3±2.4%), blood pressure (SBP : -21.8±16.1 mmHg; DBP: -6.4±9.8mmHg), FPG (-0.49±1.11 mmol/l) and lipid profile including TC (-0.82±0.88 mmol/l), TG (-0.72±0.82 mmol/l) and LDL-C (-0.74±0.77 mmol/l), without therapeutic intervention. MES dropped from 57.1% at baseline to 18.4%. Healtier diet and increased exercise were also acheived.

Conclusion: This ongoing structured CWP can significantly reduced the metabolic risks of the staff and potential medical costs to the company through lifestyle intervention.

HEAVY TOBACCO SMOKING IS RELATED TO INCREASED CASUAL PLASMA GLUCOSE IN PEOPLE WITHOUT PREVIOUSLY KNOWN DIABETES

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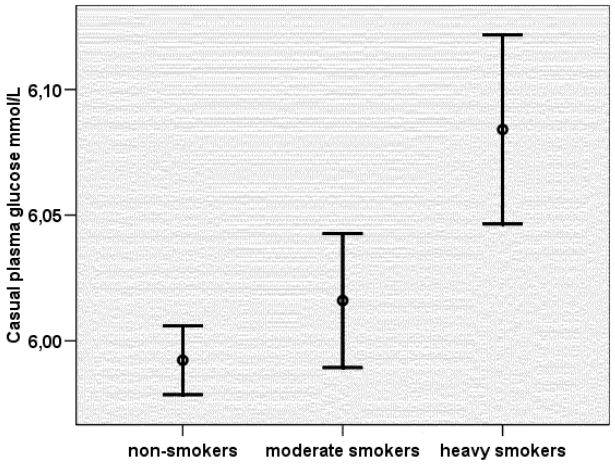
Smoking and dysglykemi/diabetes are important risk factors for all-cause mortality and cardiovascular events. Patients diagnosed with diabetes often give up smoking. We examined casual plasma glucose (PG) in smokers and non-smokers among non-diabetics.

Study population: A population-based cohort (n=33077; men 47.9%) were subjected to a health survey 1990-1999 in the county of Västmanland, Sweden. 45.8% were 40 and 54.2% 50 years old. The cohort comprised 50% of persons invited to the survey. The patients were classified as 1) non-smokers; 2) moderate smokers (daily smoking 1-14 gram) and 3) heavy smokers (daily smoking≥15 gram).

Results: 70% were non-smokers, 18% moderate and 12% heavy smokers. PG (median, interquartile range) for all participants was 5.9 (5.4-6.5) mmol/L; for non-smokers 5.9 (5.4-6.4), moderate smokers 5.9 (5.4-6.5) heavy smokers 6.0 (5.4-6.5).Difference between non-smokers and heavy

smoker was significant (p< 0.001). Mean and 95% CI for plasma glucose are shown below.



[Smoking and plasma glucose]

The relative mortality risk for heavy smokers versus non-smokers (median follow-up time 13.7 years) was 3.12. Inclusion of plasma glucose and smoking in a Cox regression model reduced this figure to 3.09.

Conclusion: Casual plasma glucose is slightly increased among non-diabetic heavy smokers. This increase does not substantially contribute to smoking related mortality.

PREVALENCE OF IMPAIRED FASTING GLUCOSE AND ITS RELATIONSHIP WITH CARDIOMETABOLIC RISK FACTORS AMONG CHINESE ADULTS

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Objective: To determinate the prevalence of IFG and evaluate its relationship between IFG and other risk factors for cardiovascular disease (CVD) in general Chinese population.

Method: 26703 individuals with a mean age of 50.71 were enrolled during the years 2005-2007. Detailed questionnaire, physical examination and blood samples were taken by trained observers using standardized procedures. IFG was defined as a fasting glucose of 100 to 125 mg/dl (5.6-7.0mmol/L) according to the American Diabetes Association (ADA) criterions. The age- and sex-specific prevalence of IFG and other associated CVD risk factors were calculated. Odds ratios for associations of IFG with CVD risk factors were obtained using logistic regression.

Results: The prevalence of IFG was 26.97% and was higher in male than in female (27.86% vs 26.32%).Adult with IFG had significantly higher levels of systolic blood pressure(SBP), diastolic blood pressure(DBP), total cholesterol, low-density lipoprotein cholesterol, and triglycerides, higher body mass index, and lower levels of high-density lipoprotein cholesterol than those with normal fasting glucose concentrations. Multivariate logistic regression analysis showed that high-density lipoprotein cholesterol was the strongest predictor of IFG among both males and females (odds ratio, 2.285; 95% CI, 1.981 to 2.636 and odds ratio, 2.386; 95% CI, 2.092 to 2.720, respectively, for every 1mol/L increase).

Conclusion: IFG occurs in 26.97% of Chinese and is associated with increased prevalence of other CVD risk factors. Furthermore, our findings also support the feasibility of treating modifiable risk factors in people with IFG.

COMPARISON OF COMMONLY USED MARKERS OF INSULIN RESISTANCE TO PREDICT THE DEVELOPMENT OF IMPAIRED FASTING GLUCOSE IN OVERWEIGHT SUBJECTS

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Aims: This prospective study in 211 overweight subjects (BMI>25 kg/m^2) compared the ability of several markers of insulin resistance (IR) to predict deterioration in blood glucose control over a 3-year period.

Methods: Data was collected at baseline, 18 and 36 months. The subjects were grouped according to fasting plasma glucose (FPG) status during the study and the potential of IR markers at baseline to predict the development of impaired fasting glucose (IFG, ≥5.6mmol/L) examined using ANOVA and ROC curve analyses. The markers assessed included FPG and insulin, the derived indices HOMA-IR, QUICKI and Mffm/I, plasma adiponectin concentration and triglyceride:HDL-cholesterol ratio (trig:HDL). Spearman's correlation analyses were used to examine the relationship between changes in FPG and baseline values of the IR markers.

Results: Fifty-one (24%) subjects developed IFG during the study. The strongest predictor of IFG was FPG, followed in ranking order by trig:HDL ratio, Mffm/I and plasma adiponectin concentration. Fasting insulin levels and the insulin-derived indices, HOMA-IR and QUICKI, did not predict the development of IFG, although these indices all changed significantly during the study. Correlation analysis showed subjects who were more insulin resistant at baseline had smaller increases in FPG over the study period.

Discussion: This study demonstrated FPG and non-insulin derived markers of IR are more sensitive than insulin-derived markers for identifying overweight subjects who develop IFG. Our data also showed time-related changes in FPG concentration were smallest in subjects who are more insulin resistant at the start of the study.

PREDIABETES AND DIASTOLIC DYSFUNCTION OF LEFT VENTRICLE IN ELDERLY WITH CHRONIC HEART FAILURE

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The aim of this pilot study was to investigate the influence of glicoregulation

disorders on degree of diastolic dysfunction in elderly with chronic heart failure (CHF).

Methodology: Study group was 53 patients with stable CHF elderly than 65years. Patients were divided in three groups according to standard criteria for prediabetes/diabetes mellitus (group I without glucose metabolism disorders, group II with prediabetes and group III with diabetes mellitus). Also, for all the patients echocardiography was performed and according to values of E wave, A wave, deceleration time and IVRT their diastolic dysfunction (DD) were determined as first, second and third degree.

Results: In whole study population there were 21 (39, 62%) patients in group I, 11 (20, 75%) patients in group II and 22 (41, 5%) patients in group III. In group I the majority of patients had first degree of DD, second and third degree was less frequent (52, 38% vs. 38, 10% vs. 9, 52%,

respectively). Also, in group III (diabetes mellitus) first degree of diastolic dysfunction was most frequent (54,72% vs. 39,6% vs. 5,66%, respectively). But, in the group with prediabetes, even 54, 55% patients had second degree of DD vs. 45, 4% with DD I degree.

Conclusion: This pilot study indicates that elderly patients with prediabetes mellitus and chronic heart failure are under the huge risk to develop diastolic dysfunction probably because of endothelial dysfunction caused by additional oxidative stress generated by fluctuation of glucose during the day.

IMPACT OF LIFESTYLE MODIFICATION ON THE CLINICAL AND BIOLOGICAL PROFILE OF NEWLY DIAGNOSED PATIENTS WITH METABOLIC SYNDROME

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Background and aims: The aim of the study was to analyze the Metsd (ATP III criteria) features in a group of patients at the time of diagnosis and after 6 months and the effects of the therapeutic intervention.

Materials and methods: We analyzed at baseline and after 6 months 50 subjects (27 f /23 m) with the following characteristics: **Characteristic**Baseline-mean (±SD)/At 6 Months mean (±SD) **Age (years)**56.88 (±11.81)/56.88 (±11.81) **Glycemia (mg/dl)**129.82 (±19.92)/115.12 (±22.58) **BMI(kg/m^2)**30.83 (±3.66)/29.33 (±3.61) **Waist circumference (cm)**104.28 (±11.28)/99.31 (±10.14)**Total Cholesterol (mg/dl)**234.14 (±56.28)/192.24 (±41.77)**Triglyceride (mg/dl)**255.78 (±224.66)/143.64 (±55.77) **HDL cholesterol (mg/dl)**43.78 (±13.29)/49.62 (±10.68) **HbA1c (%)**6.18 (±0.85)/6.30 (±1.05) **Uric acid (mg/dl)**5.29 (±1.64)/4.55 (±1.16).

Results and discussions: The majority of subjects (23) fulfilled 3 Metsd criteria, while only 8 patients fulfilled all the 5 criteria, especially those with T2DM (5). The most frequent component of Metsd was glycemia, upper waist circumference, hypertrigliceridemia, high blood pressure and low HDL cholesterol. The associated diseases revealed high blood pressure, newly discovered with T2DM, fasting glycemia, hyperuricemia, hypercholesterolemia.The comparative analysis after 6 months of therapeutic intervention shows significant improvement of the followings parameters: BMI, waist circumference, total cholesterol, glycemia ($p< 0.0001$); TG ($p=0.0001$); HDL cholesterol ($p=0.002$); uric acid ($p=0.005$). The mean value of HbA1c increased (NS); and 12 patients needed oral antidiabetic drugs after this period. At the 6 months reevaluation 4 pacients developed T2DM.

Conclusion: These data propose the multifactorial and intensive approach for patients with Metsd from the diagnosis in order to improve the therapeutic efficiency and shows significant improvement of Metsd components.

COGNITIVE FUNCTIONING, EMOTIONAL STATE AND QUALITY OF LIFE IN OBESE AND NOT-OBESE PREDIABETIC PERSONS

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Objective: To compare peculiarities of cognitive functioning, emotional state and quality of life in obese and not-obese prediabetic males and females.

Methods: 78 not obese (BMI< 30) (33 males, 45 females, age 54.2±8.9 years). 75 obese (BMI>=30) (34 males, 42 females, age 56.7±8.4 years) prediabetic persons (impaired fasting glycemia and impaired glucose tolerance in plasma). Cognitive functioning evaluated by Trail Making Test (TMT) and Wais-R Digit Span Test (DST) of Wechsler Adult Inteligence Scale, emotional state - by Profile of Mood State (POMS), quality of life (QoL) - by WHO Brief Quality of Life Questionnair.

Results: In males no significant differences were detected in cognitive functioning, emotional state and quality of life between obese and not-obese groups. In females cognitive functions were worse in obese prediabetic persons compared to not-obese: psychomotoric speed - TMT B score (84.6±35.6 vs. 72.5±25.7, $p=0.04$), memory-attention - DST Forward score (6.2±2.1 vs. 7.6±2.1, $p=0.005$) and DST Raw score (11.1±3.4 vs. 12.8±3.3, $p=0.026$). There were no significant differences in emotional state and quality of life between obese and not-obese females.Significant correlations in obese prediabetic persons: between TMT A score and QoL ($r=-0.255$, $p=0.035$); in not-obese prediabetic persons: between weight and QoL ($r=0.233$, $p=0.043$), weight and depression-dejection ($r=-0.246$, $p=0.040$).

In conclusion, obese prediabetic females, but not males have worse cognitive functioning, but not emotional state and quality of life. Some aspects of emotional state and quality of life in obese and not-obese prediabetic persons could be related to physical activity and weight.

PREDICTORS OF DIABETES TYPE II IN NORMOGLYCEMIC AND PREDIABETIC SUBJECTS

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Aims: In the 24-year follow-up of the Population Study of Women in Gothenburg potential independent predictors for diabetes type II were tested in normoglycemic and prediabetic women at baseline 1968/69.

Methods: Normal and impaired fasting plasma glucose defined by ADA (*Diabetes Care,* 2003) was used, < 5.6 mmol/L and ≥5.6 to < 6.9 mmol/L. The cardiometabolic risk factors tested were waist circumference (WC), serum triglycerides (s-TG), urate and leptin concentrations, hypertension (BP≥130/≥85), diabetes heredity, age, smoking, mental stress, alcohol intake and physical activity. Values giving the clearest increase in relative risk for contracting diabetes type II was used as limits for dichotomized variables analyzed in a Cox regression model.

Results: 5.5% of normoglycemic and 18% of prediabetic women contracted diabetes type II, however representing 73% and 27% respectively of all events during the 24-year follow-up.For normoglycemic women significant independent predictors in a Cox multivariate regression model were s-leptin, heredity and also WC, s-TG at limits lower than limits in the metabolic syndrome. Two or more of these risk factors resulted in increased risk (HR 7.7, $p< 0.001$) identifying 69% (sensivity 69%, specificity 70%) that developed diabetes type II.For prediabetic women, similarly WC, s-TG, s-urate and s-leptin were predictors. Exceeding calculated limits in both WC and s-TG resulted in marked increased risk (HR 11.0, $p< 0.001$) and 80 % had values above actual limits in one or both.

Conclusions: WC, s-TG at limits lower than limits in metabolic syndrome and s-leptin discern those with greatest risk in both normoglycemic and prediabetic women.

METABOLIC SYNDROME IS RAPIDLY INCREASED IN SUBJECTS WITH IMPAIRED FASTING GLUCOSE AND DIABETES IN KOREA: THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 1998-2005

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This study aimed to investigate whether the metabolic syndrome (MetS) is increasing recently in Korean adults. The data of 5,635 adults aged 30 and over in 1998, 3,702 in 2001, and 4,606 in 2005 among the KNHANES were analyzed.

Subjects with three or more of the following five criteria were defined as having MetS: abdominal obesity by waist circumference (men/women ≥90/85 cm), high BP (≥130/85 mmHg) or on antihypertensive medication, elevated fasting glucose (≥5.6 mmol/l) or on antidiabetic medication, high TG (≥1.7 mmol/l), and low HDL-C (men/women < 1.0/1.3 mmol/l).

The prevalence of MetS among adults aged 30 or over were 29.7% (29.5% men, 29.8% women) in 1998, 32.6% (32.2% men, 32.8% women) in 2001, and 29.5% (33.1% men, 26.1% women) in 2005. Estimated number of subjects with MetS was about 8.3 millions (4.6 million men, 3.7 million women) in 2005. The prevalence of MetS was slightly increased in men (Odds ratio, 1.17 (95% CI, 1.03-1.33), but decreased in women (OR, 0.75 (95% CI, 0.67-0.85) although the overall prevalence of MetS was not changed during 7 years.

The prevalence of MetS among subjects without glucose intolerance was not changed (15.2% in 1998, 16.6% in 2001, and 16.9% in 2005, p=0.06), but the prevalence of MetS among subjects with impaired fasting glucose or diabetes was rapidly increased (52.5% in 1998, 56.5% in 2001, 68.8% in 2005, p< 0.001).

We concluded that the prevalence of MetS in Korean adults was rapidly increasing in subjects with impaired fasting glucose or diabetes.

EFFECTS OF LIFESTYLE MODIFICATION WITH COMBINED AEROBIC AND RESISTANCE EXERCISE ON URINARY ALBUMIN EXCRETION IN THE POPULATION WITH METABOLIC SYNDROME

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Aim: Metabolic syndrome (MetS) is not only a risk factor for cardiovascular disease, but also for the development of albuminuria and chronic kidney disease. The effects and mechanisms of lifestyle modification including exercise on renal functions in MetS are not fully understood, so we investigated which diagnostic parameters are affected by aerobic and resistance exercises combined together (ARE).

Methods: Fifty-nine volunteers (20 men and 39 women; 15 with MetS [based on the Japanese criteria], 7 with obesity [BMI>25], 21 with hypertension, and 16 normal individuals) were enrolled in a 12-week lifestyle modification program with moderate ARE. Body weight, BMI, waist circumference, blood pressure (BP), glucose and lipid-related profiles, serum creatinine (Cre) and urinary albumin-Cre ratio (ACR) were measured before and after the program.

Results: The baseline ACR ranged from 2.28 to 72.14mg/gCre. Estimated glomerular filtration rate (eGFR) was calculated using the estimation formula modified for Japanese GFR. The ACR significantly decreased (13.4±15.1→8.6±7.3mg/gCre, P< 0.05,) just like body weight, BMI, BP, LDL-cholesterol and fasting plasma glucose, without major changes in eGFR(68.5±15.7→69.4±15.9ml/min/1.73m²) in all groups after the program. Though being the highest among all, ACR in MetS significantly dropped without change in eGFR after the program, like in the normal group. No regression was observed on renal functions in all groups. Yet, the multiple linear regression analysis revealed no parameters to be independent variables for the ACR reduction.

Conclusions: Lifestyle modification with ARE is effective in reducing albuminuria and maintaining GFR, especially in MetS, with the independent variables yet to be elucidated.

PREVALENCE OF METABOLIC RISK FACTORS IN PREDIABETICS OF OMAN FAMILY STUDY

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Aims: To examine the prevalence of metabolic risk factors among prediabetics of Oman Family Study.

Methods: We sampled 1198 individuals in Oman Family Study which is composed of 5, highly consanguineous pedigrees of Omani Arabs. There were 205 prediabetics (17%), 75 diabetics (6%) and 918 normoglycaemics (77%). The prevalence of metabolic risk factors in prediabetics and their sub-groups were compared with normoglycemics.

Results: Of 205 prediabetics, 70 (34%) had impaired fasting glucose [IFG]; 102 (50%) had impaired glucose tolerance [IGT] and 33 (16%) had both. Compared to normoglycemics, prediabetics were relatively older (mean 30 vs. 44 years), had a higher BMI (24 vs. 26 Kg/m^2), waist circumference (79 vs. 86 cm), % body fat (22% vs. 27%), blood pressure (123/81 vs. 127/84 mmHg), fasting insulin (5 vs. 7 mIU/L), insulin 2-hr (21 vs. 35 mIU/L), HOMA-IR (1.21 vs. 1.87), leptin (24.7 vs. 34.0 ng/ml), and TG (0.98 vs. 1.29 mmol/L). All differences were statistically significant (P < 0.05). No differences were found in HDL-C concentration (1.08 vs. 1.03 mmol/L). Percent body fat was higher in the IGT group compared to IFG group (28% vs. 24%; P< 0.021). Higher leptin (38.4 vs. 26.0 ng/ml, P< 0.006) and 2-hr insulin levels (42 vs. 23 mIU/L; P< 0.000), were also observed.

Conclusions: Metabolic risk factors were more prevalent in prediabetics, who are, therefore, more likely to progress to diabetes. Individuals with IGT appear more obese and insulin resistant ; while those with IFG appear lean and less insulin resistant.

THE RELATIONS BETWEEN IMPAIRED GLUCOSE TOLERANCE, ABPM PROFILE AND CAROTID INTIMA MEDIA THICKNESS IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME - STUDY ON 72 CASES

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Objectives: To study the correlation between impaired glucose tolerance (IGT) and carotid intima media thickness measured at the bifurcation of the common carotid artery (CIMT), arterial pressure assessed with ambulatory blood pressure monitoring (ABPM) in patients with metabolic syndrome (MS).

Methods: 72 patients (p) with MS, mean age 52 years, 29 men (41%) and 43 women (59%) were divided in Gr I-43 p without IGT and Gr II-29 p with IGT. Patients were diagnosed with MS and IGT according to the ATP III and ADA 2005 criteria. Statistical analysis used two- tallied test-t for comparison of means between teo groups.

Results: we observe statistically significant relations between IGT and increased mean values of CIMT, pulse pressure (PP), body mass index (BMI) and triglycerides levels.

	Group I		Group II		P value
	mean	std.dev.	mean	std.dev.	
Carotid Intima Media Thickness (mm)	1.38	0.33	1.56	0.22	0.013
Pulse Pressure (mmHg)	46.93	11.14	53.41	10.81	0.017
Body Mass Index (kg/m^2)	29.89	3.85	32.28	5.18	0.028
Triglyceride (mg/dl)	208.51	66.51	243.52	62.08	0.028

Conclusions: Patients with metabolic syndrome and impaired glucose tolerance compared with those without impaired glucose tolerance had statistically significant enhanced pulse pressure and increased carotid intima media thickness.

HIGH PREVALENCE OF UNDIAGNOSED DIABETES, AND PREDIABETES IN ELBASAN - THE SECOND LARGEST CITY IN ALBANIA

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Aims: To give data about undiagnosed diabetes and prediabetes in a large population, different from Tirana, the capital of Albania. To give a rate of known/unknown diabetes in our population.

Methods: Measurement of capillary blood glucose and anthropometric measures for persons older than 30 years. We collected information about general data, known diabetes, positive familiar anamnesis for diabetes, treatment for HTA and smoking. Diabetes is defined according to ADA criteria; fasting glycaemia≥126mg/dl or casual glycaemia≥200 mg/dl, (Prediabetes if IFG≥110 and< 126mg/dl, and IGT 120-200 mg/dl).

Results: From 2214 participants, we obtained all the data for 2003 of them. Males 1071 (53.5%), mean age 51.6±12.1 yrs, mean BMI 26.7±1.7 kg/m^2. Prevalence of undiagnosed Diabetes was **8.47**%, Prediabetes **14.58**%. The undiagnosed diabetes was more frequent in the age group 55-64 years old (12.8%) and >65 yrs 11.5%. Prediabetes was more frequent in the age group 45-55 yrs 14.8% but 10.1% in the age group 30-45 yrs. In our study 61 persons (3.04%) confirmed that they knew to have previous diabetes. The rate of known/unknown diabetes in our study was 1:3.

Conclusions: The prevalence of Diabetes, prediabetes and obesity is increasing rapidly in Albania and especially in younger age group. The risk factors for diabetes remain the same such as: overweight or obesity, sedentarity, familiar anamnesis. It is important to identify earlier the subject at high risk for Diabetes and raise the awareness of younger population about creating healthy lifestyle behaviors, as well as the frequency of controlling blood glucose level.

ASSOCIATION OF C-REACTIVE PROTEIN WITH MEASURES OF OBESITY, INSULIN SENSITIVITY AND GLUCOSE METABOLISM IN SEVERE OBESE WOMEN WITH NORMAL AND IMPAIRED GLUCOSE TOLERANCE

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Obesity is associated with low-grade inflammation, insulin resistance, type 2 diabetes, and cardiovascular diseases. The aim of the study was to investigate possible association between C-reactive protein (CRP) and adiposity measures as well as insulin sensitivity in 31 severe obese women (BMI >30kg/m2) with normal fasting glucose. In all women oral glucose tolerance test (OGTT) and euglycemic hyperinsulinemic clamp (120 min)) were performed. According OGTT impaired glucose tolerance were found in 10 of 31 women with normal fasting glucose. There was no correlation between CRP and BMI, waist circumference, fasting glucose, fasting insulin, M (insulin sensitivity from clamp study), AUCOGTT for insulin, AUCOGTT for glucose. When comparison in subgroup of women (with NGT-normal and IGT-impaired glucose tolerance) was done following results were obtained. There was no significant difference in CRP (NGT vs. IGT: 4.54±.98 vs. 6.08±1.10mg/L, p>0.05) as well as in BMI, waist, age, HOMA index, total cholesterol, HDL-C, LDL-C, fasting insulin, but there was significant difference in following parameters: M index (NGT vs. IGT: 5.31 ± 0.49 vs. 2.77 ± 0.37mg/kg/min, P< 0.05; index Total-cholesterol/HDL-C (NGT vs. IGT: 4.09 ± 0.19 vs. 5.26 ± 0.46; triglyceride (NGT vs. IGT: 1.43 ± 0.19 vs. 3.08 ± 0.61 mmol/L, P < 0.05; and between insulin response at 120 min of OGTT (NGT vs. IGT: 44.16 ± 7.15 vs. 85.49 ± 16.57 mU/L, p < 0.05). Our data suggest that impairment in insulin sensitivity and lipid changes precede change in inflammatory markers (CRP) during development of type 2 diabetes in obese women.

HEART RATE VARIABILITY IN PATIENTS WITH ELEVATED RISK FOR DEVELOPING DIABETES MELLITUS

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Background and aims: Autonomic dysfunction is associated with many cardiovascular risk factors, especially glucometabolic abnormalities.

The aim of this study was to estimate the relationship between Finnish Diabetes Risk Score (FINDRISC) and cardiovascular autonomic modulation.

Methods: We evaluated 88 subjects (52.4age ± 13.9years;40 males)divided into two groups according to FINDRISC. Group I included subjects with FINDRISC≥ 7 and subjects with FINDRISC< 7 consisted group II. Heart rate variability (HRV) was derived from 24h electrocardiogram and we analyzed the following time domain measures: standard deviation of all normal RR intervals (SDNN); standard deviation of the average normal RR intervals for all 5-minute segments (SDANN); average of the standard deviation of normal RR intervals for all 5-minute segments (ASDNN); percent of differences between adjacent normal RR intervals ≥ 50ms (pNN50).

Results: There were 58 subjects in group I (age 58.8±9.8 years; 29 males) and 30 subjects in group II (age 49,8 ±10.6 years; 11 males). Groups were similar in age and gender, mean (73.3 ±10.7 vs 77.2 ±9.4/min, p=0.101), minimal (51.9±14.6 vs 53.9±21.0/min, p=0.614) and maximal heart rate (129.4 ±30.1 vs 138.7 ±23.0/min, p=0.142).

SDNN was significantly lower in group I compared to group II (139.1±30.9 vs 158.5±41.9ms, p=0.017). Participants of both groups differed nearly significantly in SDANN (130.0 ± 37.5 vs 150.2 ±58.5ms, p=0.056)

ASDNN (59.0 ±21.6 vs 66.0 ±21.1ms, p=0.157) and PNN50 (8.7±10.9 vs 11.0 ±8.5%, p=0.329) were similar among the groups.

Conclusions: These finding suggest that even subjects with slightly elevated FINDRSC may be associated with impaired autonomic function.

EFFECT OF AGE ON ALL-CAUSE MORTALITY ASSOCIATED WITH PREDIABETES

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Objective: To determine the association between prediabetes and all-cause mortality by age group.

Method: Thai, third National Health Examination Survey (NHES III) 2004 data with information on several metabolic risk factors was linked to a death registry. Age-specific mortality rates per 1000 person-year were calculated. In each age group, Cox proportional hazard regression was used to examine the association of all-cause mortality with glycemic status [normoglycemia, prediabetes (FPG ≥ 100 - < 126 mg/dL) and diabetes], adjusted for other covariates.

Results: A total of 39,289 participants aged ≥15 years at baseline of NHES were included, yielding a total of 20,7264 person-days of follow-up. A total of 2,586 deaths were observed during the 5.4 years of follow-up. Age-specific mortality rates for people with prediabetes aged < 50, 50 - < 60, 50 - < 70, and ≥70 years were 3.64, 6.49, 14.0 and 25.17 per 1000 person-year respectively. Compared to those with normoglycemia in each age group, prediabetes was associated with all-cause mortality among participants aged < 50 yr (HR 1.56, 95%CI 1.04 - 2.33) and the strength of association became weaker in the older age group of 50-60 yr (1.23, 0.83 - 1.84), 60-70 yr (1.07, 0.88 - 1.29) and ≥70 yr (0.84, 0.71- 0.98). Physically active were significantly associated with lower risk of all-cause mortality among the age group of 60-69 yr and ≥70 yr.

Conclusion: Prediabetes in the middle age, compared to older persons, was more strongly associated with increased risk of all-cause mortality.

PREDIABETIC GLUCOSE DISTURBANCES AMONG PATIENTS WITH PERCUTANEOUS CORONARY INTERVENTIONS (PCI) AND CORRELATION WITH PREPROCEDURE GLYCEMIA

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Background and aims: Glucose disturbances are common in patients with coronary artery disease but usually remain undiagnosed. The aim was to estimate the newly diagnosed glucose abnormalities, especially prediabetes among patients who underwent PCI and to compare the preprocedure glycemia with glycemia during OGTT.

Materials and methods: We studied 50 patients without history of glucose abnormalities who underwent PCI at acute or elective admission and plasma glucose was measured on the day of the procedure. Glucose tolerance was defined according to ADA 2003 criteria during OGTT, performed 5-10 days after hospital discharge.

Results: 64% of subjects demonstrated glucose abnormalities, 38% of subjects had prediabetes-12% with IFG and 26% with IGT. Among patients with IGT, 53.8% were with normal fasting glycemia and 42.9% of all patients who met the fasting criterion 5.6-6.9mmol/l were with IGT. Prediabetic and normal glucose tolerance (NGT) individuals were at similar age (58.7±2.2 vs. 56.2±2.3, p=0.44). Preprocedure glycemia was significantly higher in prediabetic, compared to NGT subjects (6.64±0.49 vs 5.18±0.13mmol/l, p=0.007). We found positive correlation between preprocedure glycemia at acute admission with 0'(r 0.70, p=0.002) and 120'-glycemia (r=0.64, p=0.003) during OGTT. The positive correlation was seen in patients at elective admission too (r=0.69, p=0.0004, r=0.73, p 0.0001 respectively). There was no significant difference in FPG between isolated IGT (FPG< 5.6) and NGT subjects during OGTT (5.22±0.1 vs 5.07±0.1mmol/l p =0.39). We did not find significant differences in lipid parameters, BMI and waist circumference between groups.

Conclusion: Positive correlation between preprocedure and postchallange glycemia and substantial proportion of IGT patients who will be undiagnosed require routine OGTT.

PROINFLAMMATORY AND OXIDATIVE STRESS IS ASSOCIATED WITH INSULIN RESISTANCE IN PREDIABETIC INDONESIAN ADULT

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Elevated levels of proinflammatory proteins are predictive of both cardiovascular (CV) disease and type 2 diabetes. Previously, atherogenic changes in traditional CV risk factors in the prediabetic state were mainly seen in insulin-resistant subjects. Systemic oxidative stress is associated with insulin resistance in individuals at average or elevated risk of diabetes.

In this study we investigated the direct relationship of oxidative stress (F2-Isoprostane) and proinflammatory (TNF-α) with insulin resistance (HOMA-R) in prediabetic subjects.

We measured the plasma levels of 8-epi-prostaglandin F2α (PGF2α), TNF-α, in 66 prediabetic individuals and evaluated their relationship with HOMA-R. The plasma levels of 8-epi-prostaglandin F2α (PGF2α) were significantly correlated with TNF-α (r= 0.270, p< 0.05) but were not significantly correlated with HOMA-R. There was also a significant correlation between TNF-α with HOMA-R (r = 0.280, p< 0.05).

Although correlation does not prove causation, the results of this study suggest that oxidative stress is an important factor for enhanced pro inflammatory protein and triggers the development of insulin resistance in prediabetic subjects.

LIFESTYLE INTERVENTION IMPROVE CLINICAL FEATURES, ENDOCRINE, METABOLIC PROFILES AND INSULINORESISTANCE BETTER THAN METFORMIN AND PIOGLITAZONE TREATMENT IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Aims: The aim of this study was to assess the eficiency of a nonpharmacological treatment consisting in lifestyle intervention comparing with metformin and pioglitazone treatment in women with Polycystic Ovary Syndrome (PCOS).

Materials and methods: 67 insulino-resistant (based on HOMA index) with PCOS were recruited for this study. Serum LH, FSH, testosterone, free testosterone, IGF-I, insulin, glucose, cholesterol, triglicerides, LDL and HDL cholesterol were measured. 14 obese women with PCOS received

nonfarmacologic treatment, 28 women received metformin (500 mg tid) and 25 pioglitazone (15 mg daily) for 6 months. Patients were evaluated at baseline and at 6 months of treatment.

Results: After treatment 38 women had their menstrual pattern substantially improved. A significant decrease was observed in serum free testosterone, fasting insulin, fasting glucose, 2h-OGTT.

From clinical point of view no one of the three methods conduct to a significant improvement of the hyperandrogenism signs.

Regarding the testosteron levels, all the three methods conducted to the decrease (metformin and nonpharmacological therapy more efficient)

We founded a significant decrease of dehydroepiandrosterone sulfate, androstenedione and an increase of IGFBP1 values only at the nonpharmacological treated woman. The others endocrinologic parametters wasn't significant improved by no one of the treatment protocol.

All of the three methods conducted to the decrease of the basal insulinemia.

Conclusions: In insulin-resistant women with PCOS weight loss, metformin, pioglitazone treatment improved insulin-resistance and decreased androgen levels, with a significant improvement in fertility. Regarding the action on assessed endocrino methabolic parametters the nonpharmacologic treatment seems to be more efficient.

GLUCOSE TOLERANCE IN SUBJECTS AT RISK OF DEVELOPING TYPE 2 DIABETES

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Aim: The aim of the present study is to evaluate the prevalence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and newly-diagnosed diabetes (NDD) in subjects at risk of developing diabetes as well as to assess body fat mass in the different categories of glucose tolerance.

Material and methods: 1886 subjects (701 males and 1185 females), of mean age 50.3±14.3years and mean BMI 29.4±6.1kg/m^2, at risk of developing diabetes were enrolled. Glucose tolerance was studied during OGTT, applying 2006 WHO criteria. Plasma glucose was measured at 0 and 120 minute by a dehydrogenase method. Body fat mass and visceral fat area were assessed by bioelectrical impedance analysis (InBody 720, Biospace).

Results: 57.4% of subjects appeared to be with NGT, 13.1% - with IFG, 10.6% - with IGT (4.9% being with a combination of IFG and IGT) and 18.9 % - with newly-diagnosed diabetes. BMI was found to be significantly higher in IFG ($p< 0.0001$), IGT ($p< 0.001$) and NDD ($p< 0.0001$) as compared to NGT. The percentage of body fat and visceral fat area in NDD and the two prediabetic states also differed significantly from NGT. There were no statistically significant differences in the percentage of body fat and visceral fat area between IFG, IGT and NDD.

Conclusions: The prevalence of IFG, IGT and newly-diagnosed diabetes in individuals at risk of developing type 2 diabetes is rather high. The progression from NGT to prediabetes and diabetes correlates well with BMI, percentage of body fat mass and visceral fat.

THE INVESTIGATION OF THE SUBJECTS WITH IMPAIRED FASTING GLYCEMIA AS REGARDS INSULIN RESISTANCE

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Aims: Diabetes mellitus deteriorates without any subjective symptoms. Early detection and early treatment are important, particularly educating patients is essential. For subjects suspected as impaired glucose tolerance in the first medical checkup, we examined the patterns using OGTT.

Methods: FBS was examined for the 4205 subjects during the 12 months. Among the impaired hyperglycemic subjects (110mg/dl< FBS≤125), OGTT was performed on the 81 subjects who wished further examination.

Results: The result of OGTT was as follows. Sixteen subjects were normal, 53 subjects were in the impaired glucose tolerance state and 12 subjects were revealed to be DM. Sixty-three subjects showed low Insulinogenic Index. The time of peak concentration of blood insulin after glucose loading occurred within 30 minutes in 9 subjects, and between 60 and 120 minutes in 72 subjects. Other metabolic abnormalities were found among the 81 subjects, that is, 30 subjects had high BMI, 26 had high LDL, 28 had high TG, 28 had hypertension and 33 had fatty liver. As a whole, many subjects showed high insulin secretion. One individual indicated an extremely high IRI peak of 402 μu/l after oral glucose loading, the BS was 230 mg/dl at that time. No subjects suffered from small vascular complications nor large vascular diseases.

Conclusions: In the subjects with impaired fasting glycemia many have low insulin sensitivity and/or high insulin secretion. About one third of the 81 subjects had other abnormal metabolic elements. From these results we considered that the insulin resistance cannot be negligible in the initial time course of DM progression.

SALIVARY LYSOZYME AND THE PREVALENCE OF PREDIABETES AND DIABETES

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Objective: To assess the association between salivary lysozyme (SLZ), and the prevalence of prediabetes and diabetes

Background: Salivary lysozyme is a proteolytic enzyme that contains a domain with strong affinity to glucose and is expressed by oral leukocytes in response to infection or hyperglycemia. Because metabolic syndrome/diabetes is considered inflammatory disease involving hyperglycemia, we investigated the relationship between SLZ and the prevalence of prediabetes/diabetes.

Methods: Utilizing cross-sectional data from 250 CAD and 250 non-CAD patients, we assessed whether SLZ was associated with prediabetes/diabetes by logistic regression analyses controlling for age, sex, current smoking, past smoking, BMI, and CRP levels. A person was deemed prediabetic if s/he had any three of ATP III criteria, namely central obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low HDL levels. Diabetes was determined by medical records review. To test for possible

effect modification by CAD, we conducted stratified analyses by CAD status.

Results: The overall Odds Ratio (OR) associated with the highest quartile of SLZ ^{4th} was 1.71 (CI: 0.98 - 2.98), p= 0.06. Among non-CAD subjects the OR was 2.46 (CI: 0.92 - 6.61), p=0.07 while in the CAD group, SLZ did not provide any additional information with an OR of 1.02 (0.51 - 2.07), p=0.95.

Conclusion: Although marginally significant, SLZ may be associated with prediabetes/diabetes independent of CRP (P= 0.06). Among CAD patients this association was null suggesting that CAD and diabetes might share the same causal pathway. Thus salivary lysozyme may be associated with prediabetes/diabetes, an early stage in the continuum of atherogenesis.

WEIGHT REDUCTION AND HIGH DIETARY FIBER DIET COULD DELAY APPEARANCE OF T2DM IN OBESE SUBJECTS WITH IGT

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Numerous studies suggests that T2DM appearance in obese people with IGT is about 10% for 10 years. We have analyzed some of risk factors for T2DM in obese people after four years follow up period and appearance of T2DM.

Methods: Examined group (N=50) with IGT, BMI 34 ± 3.8kg /m2 was treated with 1800-2000kcal diet, 50-60% carbohydrates, 15-18% proteins, 22-23% predominantly unsaturated fats and 20-40g dietary fibers and control group (N=45) with IGT, BMI 33.8 ±2.8kg/m2 without calorie restriction and with 10-15g dietary fibers intake.

Results: After 4 years fasting glucose was significantly decreased ($p< 0.001$) in examined group, and NS in control group. BMI was decreased in examined group ($p< 0.001$) and significantly increased in control group ($p< 0.05$). Waist circumference decreased significantly ($p< 0.001$) in examined, but not in control group. Insulin resistance was calculated by HOMA IR decreased in examined group ($p< 0.001$) although in control group HOMA IR was NS. Triglycerides, LDL cholesterol and systolic blood pressure decreased in examined group (p=0.001) but not in control group. Diastolic blood pressure had no significant decrease in both groups. T2DM was appeared in 3 subjects (6.6%) in control group and no one in examined group after 4 years.

Conclusion: These results suggests that weight reduction with high dietary fiber diet had positive effect on fasting glucose, insulin resistance, waist circumference, hypertension and body mass index and could delay T2DM appearance at least during four years.

IMPROVEMENT OF METABOLIC RISK PROFILE WITH LIFESTYLE INTERVENTION DURING THE DIABETES PREVENTION PROGRAM DE-PLAN

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Diabetes and cardiovascular diseases share common risk factors and pathogenetic mechanisms. Life style intervention has been shown to be most effective method for diabetes prevention at population level.

Aim: The aim of this study was to evaluate the effect of the diabetes prevention program DE-PLAN (**D**iabetes in Europe - **P**revention using **L**ifestyle, Physical **A**ctivity and **N**utritional Intervention) on some macrovascular risk factors.

Patients and methods: In this prospective study were included 71 patients (15 men) at mean age±SD 50.9±12.4 years, pre-selected to have increased risk for development of diabetes with the questionnaire FINDRISC ≥ 14 points. They underwent laboratory exam with OGTT for exclusion of undiagnosed diabetes. The intervention program consisted of an initial complex of 4 group lectures of 1.5 h each (metabolic syndrome, obesity, hypertension, stress, unhealthy eating habits, physical inactivity, smoking, alcohol etc.), followed by individual and/or group sections throughout the study.

Results: The mean duration of the intervention phase of the project was 15.5±5.0 months. At the end of the study a significant improvement was mentioned in the studied parameters compared to the baseline: weight 87,3±19,5 vs. 93,4±17,5 kg; BMI 33,0±5,8 vs. 34,7±5,7 kg/m^2; waist circumference 102,5±14,6 vs. 107,4±14,1cm; HDL-C 1,56±0,39 vs. 1,39±0,38 mmol/l (all $p< 0.001$); total cholesterol 5,52±1,11 vs. 5,73±1,20; plasma glucose at 2 h in OGTT 5,91±2,02 vs. 6,3±2,1 mmol/l (both $p< 0.05$). Triglycerides and fasting plasma glucose did not change significantly.

Conclusions: Life style intervention is a valuable method to improve the metabolic profile of patients at high risk for diabetes.

THE SEVERITY AND MORTALITY OF CVD ARE INCREASED IN INDIVIDUALS WITH A FPG OF 5.6-6.1MMOL/L

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Objectives: To analysis the difference of cardiovascular disease (CVD) severity and mortalities of individuals with different fasting glucose, to provide hard end point evidence for the establishment of diagnostic criteria of IFG.

Methods: Our study including two groups of subjects: 1) 911 consecutive patients underwent coronary angiography in our hospital were selected . All the subjects were studied in view of the extent and severity of angiographic coronary artery disease and the cardiovascular risk factors with different FPG levels. 2) 1670 old subjects aged 60-90 who had health examination in our hospital. All the subjects were also classified into four groups according to their baseline FPG values . The CVD cumulative survival rates were calculated by Kaplan-Meier method and the log-rank test were used to compare the survival rates of the four groups.

Results: After adjustment of influencing factors, the number of diseased vessels in group of FPG 5.6- 6.1mmol/L were increasing significantly compared with group of FPG< 5.6 mmol/ L. The all-cause and CVD mortality in group of FPG 5.6- 6.1mmol/L were significantly higher than those in group of FPG < 5.6mmol/L. Compared with group of FPG < 5.6mmol/L, the CVD cumulative survival rats in group of FPG 5.6-6.1mmol/L was significantly decreased.

Conclusions: Our study indicate that the severity and mortality of CVD are both increased in individuals with a FPG of 5.6-6.1mmol/L, so lowering the criterion of IFG to 5.6mml/L will make an great effect of CVD prevention.

PREVENTION OF DIABETES MELLITUS AND CARDIO METABOLIC RISK SUPPORTED BY A TECHNOLOGICAL PLATFORM - THE PREDIRCAM PROJECT

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Diabetes, obesity, hyperlipidemia and metabolic syndrome means an interrelated and severe public health concern. Healthy life-style changes have shown to be more effective than just drug therapy in preventing the progression to diabetes for subjects at risk.

PREDIRCAM is an innovative technological platform which aims is to provide to both patients and healthcare professionals a comprehensive tool to improve the efficacy of behaviour modification by means of the intensive utilization of new technologies for monitoring and assessing cardiometabolic risk, as well as optimising the communication between subjects and health care providers on demand. PREDIRCAM covers, among others, two main technological components:

An advanced web-based application, which provides: a communication interface with different monitoring devices; an innovative application to facilitate the laborious task of recording and monitoring dietary intake; an ad hoc electronic clinical record; a communication system shared by healthcare professionals and patients and an advisory system, which provides positive feedback to the patients.

An integrated set of wearable physical activity monitors (e.g. heart rate, accelerometer, pedometer), which enables automated monitoring of physical activity and caloric consumption.

After a successful feasibility test, the effectiveness of the platform will be evaluated in a twelve month clinical trial. The protocol will include 96 obese (BMI>=30Kg/m^2) subjects, aged 40 to 65 years, depicting impaired fasting glucose or glucose intolerance. Surrogate indicators to evaluate potential changes in cardiovascular risk will include: weight, anthropometric parameters, abdominal adiposity quantification, cardiac function performance, OGTT, insulin secretion and sensitivity (HOMA, serum adiponectin, TNF-alpha, CRP), lipoprotein profile.

OGTT VERSUS METABOLIC SYNDROME TO DETECT CARDIOVASCULAR RISK IN SUBJECTS WITH FASTING PLASMA GLUCOSE (FPG) < 100 MG%

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Aims: Aim of our study was to compare, on the same population, the effectiveness of FPG and metabolic-syndrome (MS) with that of OGTT (oral-glucose-tolerance-test) in detecting cardiovascular (CV)-risk.

Methods: We recruited 791 subjects with FPG< 100mg%, 336 males and 445 females, average age 48.8 years, performing OGTT and applying MS-criteria to all.

Results: By ATPIII-2004 criteria, 178 (22.5%) had MS. After OGTT, 133 out of 178 (74.7%) were normo-gluco-tolerant (NGT), whereas 45 (25.3%) had either impaired glucose tolerance (IGT) or diabetes mellitus (DM). The MS was absent in 613 out of 791 (77.5%) subjects. Of these, 551 (89.9%) were NGT, whereas 62 (10.1%) were IGT/DM.The MS has a diagnostic-yield for CV risk of 178/791=22.5% when FPG < 100 mg%, vs (62+45)/791=13.5% of OGTT alone.However, 62 out of 107 subjects with altered OGTT, 8 of whom with DM, were not affected by MS. These patients were prevalently females (44), of age (54.11 years), BMI (28.8 Kg/m^2), waist circumference (93,3 cm), IRIO (11,4), HOMA (2,5), fibrinogen (361 mg/dl), microalbuminuria (34,6 mg/dl) and BP significantly higher than those measured in NGT (P< 0.05 for all).

Conclusions: Our study demonstrates that while MS is effective, FPG < 100 fails to detect a number of patients who are at high CV risk even though not affected by MS. These patients, 7.9% of the total, suffer from IGT/DM.OGTT could prove very useful even in subjects with FPG < 100 mg% when affected by a cluster of alterations including advanced age, female sex, insulin-resistance, high plasma fibrinogen, microalbuminuria and hypertension.

RISK FACTORS FOR VASCULAR COMPLICATIONS IN PRE-DIABETIC PATIENTS

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Aims: Pre-diabetes is characterised by hyperinsulinism and insulin resistance, both related to abdominal obesity, hypertension, lipid status disorders and vascular complications. Aims were to analyze vascular complications risk factors in patients with early glycoregulation disorders.

Material and methods: 45 patients aged over 45 (average age 52,6±9,6%) (64.4% females, 35,6% males) with early glycoregulation disorders, impaired fasting glucose (IFG) and glucose intolerance (IGT) were analyzed. Oral glucose tolerance test (OGTT) was used to evaluate the extent of disorder. Lipid status, analyzed by spectrophotometry, determined total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides (TG). Insulin sensitivity was determined by HOMA IR.

Results: IFG and IGT were found in 44,4% and 55,6% patients, respectively. Abdominal obesity (waist circumference (WC) of 99.6±13.2cm, body mass index (BMI) of 31.4±5.6kg/m2 were present. There were increased values of blood pressure (systolic 140.5±20.0mmHg, diastolic 88.4±14.1mmHg), cholesterol (total cholesterol 5.9±1.1mmol/l, LDL cholesterol 3.86±1.6mmol/l) and triglycerides (1.81±1.0mmol/l), and decreased values of HDL-cholestrerol (1,1±0,55mmol/l.). Average glycemia (5.,9±1.23mmol/l), basic insulinemia (18.7±15.1mU/l) and HOMA IR (4.,9±3.5µmol/mU/ml) were also increased.

Conclusion: Early glycoregulation disorders are related to vascular complications risks due to existing insulin resistance and metabolic syndrome with all its characteristics (abdominal obesity, hypertension, lipid disorders). Early diagnosis of glycoregulation disorders (pre-diabetes) and introduction of diet and physical activity affect risk factors and contribute to prevention of diabetes and chronical vascular complications.

GLYCEMIC PROFILE OF PREDIABETIC OUTPATIENTS AFTER NUTRITION INTERVENTION IN SÃO PAULO, BRAZIL

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Guidelines regarding nutrition therapy to prevent diabetes and its complications are imperative in developed and underdeveloped countries.

Objective: To evaluate glycemic profile in prediabetic outpatients after nutrition intervention.

Methods: Data were collected from poatients entering the Nutrition Ambulatory from the Nutrition Unit - Department of Preventive Medicine - Federal University of São Paulo between 2007 and 2008. Information was obtained through patients´s records containning the results of fasting blood glucose tests. There were selected only patients under the criteria of prediabets (American Diabetes Association, 2008) and that had at least 1

blood glucose test result 1 year prior to nutrition intervention and another one within 7 months after nutrition intervention. When entering the nutrition ambulatory patients received general nutrition guidelines and na individualized plan aimed at prediabetes treatment and prevention of commorbidities.

Results: From February/2007 till October/2008 373 patients entered the nutrition ambulatory and 9.65% (36) were diagnosed as prediabetics. Age range was 21 to 70 years and 23 women and 13 men had pré intervention fasting blood glucose (FBG) result anda t least 1 FBG result up to 7 months after intervention. It was observed that from the overall patients 75% (28) showed reduction in the glycemic profile after intervention and 56.14% reached normal levels of fasting glucose.

Conclusion: General and individualized nutritional intervention in prediabetic patients showed to be effevtive in the reduction and normalazation of glycemic profile preventing though complication due to prediabetic state development.

THE IMPORTANCE OF LIFESTYLE PREVENTION PROGRAM ASSOCIATED WITH AN ANTIDIABETIC DRUG ON DIABETIC CONTROL FOR UNCONTROLLED TYPE 2 DIABETES MELLITUS IN GENERAL PRACTICE

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Life style adaptation (LSA) is known to reduce hyperglycaemia on Type 2 diabetes Mellitus (T2DM) , however, few studies have assessed patient compliance to LSA and the combined effect of LSA with an antidiabetic drug.

1205 uncontrolled patients were treated with fixed-dose combination (FDC) of sulphonylurea and biguanide (Glucovance®). The physician was instructed to motivate the patient to improve life style (physical exercise, smoking cessation and diet) in addition to treatment with an oral antidiabetic.

We considered a patient as responding to therapy (or controlled for glycaemia) when FPG < 1.26 g/L and HbA_{1c} < 7%.

Only 21.7% of the patients partly followed LSA advice, however, 8.3% interrupted their LSA, and 70% did not change. Only 3.1% were totally compliant to LSA advice.

An overall RP of 36.6% [95% CI: 33.9, 39.4] was achieved. Further to the physician recommendation, A reduction (vs Improvement) of LSA was associated with an RP increase (vs decrease) of 9% [4%, 13%], p< .001, representing 25% of the drug effect.

Our study was the first to assess compliance and combined effect of LSA adaptation and antodiabetic drug. A clear additive effect of LSA was shown to increase or decrease the RP of 25% for patients improving or interrupting LSA, respectively. Unfortunately, compliance to LS adaptation was very poor, as only 11.4% patients improved their LS.

Our conclusion is that, even after first line, an adequate LS prevention should be promoted as it provides a clinically relevant additive effect in addition to the pharmacological treatment.

THE RELATINOSHIP BETWEEN THE HEMOGLOBIN LEVELS AND THE CARDIOVASCULAR RISK FACTORS IN PREDIABETES

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Introduction: Hemoglobin (Hb) is the scavenger of endothelial Nitric oxide (NO). An inverse correlation between Hb values and the endothelial functions was observed in patients with Type 2 diabetes. Searching this correlation in prediabetes is important because prediabetes is associated with an increased risk of cardiovascular disease and mortality. Therefore, we investigated the association between Hb and the cardiac risk factors and the soluble CD40 Ligand levels, a marker for endothelial dysfunction and inflammation, in patients with impaired glucose tolerance (IGT).

Methods: We enrolled 82 normotensive, non-obese and cardiovascular events free patients with impaired glucose tolerance (IGT) (M=46, age=45.95±6.7yrs). Plasma insulin, hsCRP, soluble CD40Ligand levels were measured. The parameters were compared according to the higher and lower median Hb values of the patients.

Results: The systolic (SBP) and diastolic blood pressures (DBP) and uric acid levels were significantly higher (p< 0.001, p=0.04, p=0,01 respectively) and the HDL cholesterol levels were significantly lower (p=0.02) in patients having Hb values above the median. No difference was found between the hsCRP (p=0.06) and the soluble CD40L levels (p=0.07). In the correlation analysis, Hb levels were positively associated with SBP(r=0.44, p< 0.001), DBP (r=0.26, p= 0.02), Soluble CD40L (r=0.35, p= 0.002) and uric acid (r=0.27, p=0.02) and negatively associated with HDL cholesterol levels (r=-0.32, p= 0.004).

Discussion: According to the results, higher Hb levels in IGT is associated with increased cardiovascular risk factors. Whether this finding will have any clinical implication in the increased cardiovascular risk of prediabetic patients warrants further investigation.

THE EFFECTS OF PRE-DISEASE RISK FACTORS WITHIN METABOLIC SYNDROME ON ALL-CAUSE AND CARDIOVASCULAR DISEASE MORTALITY

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The metabolic syndrome has been criticized for being "polluted with the inclusion of frank "diseases" with "pre-diseases". We assessed the effect of a single or multiple "pre-disease (s)" of metabolic syndrome on the overall and cardiovascular disease (CVD) mortality. They included pre-diabetes (fasting glucose: 110-125 mg/dL), pre-hypertension (systolic BP: 120-139 mmHg), overweight (BMI: 25-29.9) and borderline dyslipidemia (triglyceride: 150-199 mg/dL). The cohort consisted of 35,259 adults (age 40 years or older) with a medium follow-up of 15 years. Relative risks (RRs) for all-causes, CVD and "CVD plus diabetes" mortality were calculated with the Cox proportional hazards model. Prevalence of the pre-disease risk factors (40.2%) was nearly four times larger than the metabolic syndrome (10.6%). Individual pre-disease risk factor was associated with significant increases of 13% and 67% (pre-diabetes), 22% and 62% (pre-hypertension), 23% and 32% (overweight) and 17% and 46% (borderline hypertriglyceridemia) on all-cause and "CVD plus diabetes" mortality, respectively. Smoking had comparable risks as "pre-diseases", and, as such, should also be considered as the fifth "pre-disease".

Like metabolic syndrome, each "Pre-disease" is a major and significant risk factor for all cause and cardiovascular mortality, but unlike metabolic syndrome, the definition or clinical follow up of "Pre-disease" is simple and straightforward. Recognizing each of the four "pre-disease" as a clinical entity, a hitherto sub-clinical status but involving significantly increased mortality, can alert and justify early intervention through changing lifestyle and modifying biologic risk factors.

GENDER HAS SIGNIFICANT IMPACT ON OBESITY-RELATED METABOLIC ABNORMALITIES AND PHENOTYPIC TRAITS IN HEALTHY FIRST-DEGREE RELATIVES OF TYPE 2 DIABETES PATIENTS

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The aims of this study were to determine the impact of gender and family history of Type 2 diabetes (T2DM) on adipokines, beta-cell function (%B), insulin sensitivity (% S) and resistance (HOMA-R). Fasting adiponectin, leptin, leptin receptor (sOB-R), insulin, glucose, and full lipid profile were determined in 229 normoglycemic first-degree relatives (FDR) of 115 T2DM probands and 41 healthy nondiabetic control subjects without a family history of diabetes matched for age, sex, and BMI. Variables were compared between T2DM, FDR and controls and between males and females. Gender dimorphisms were noted with female patients having significantly higher mean insulin (21 vs 8 uIU/mL) and HOMA-R (10 vs 2.5) compared to male patients. 83% of female patients and 32 % of female FDR had HOMA-R > 2 compared to 33% of male patients and 24% of male FDR. Male patients and male FDR had significantly lower mean %B (45 and 113% respectively) compared to female patients (57 and 136% respectively). Female patients also had significantly higher leptin, HbA1c and significantly lower adiponectin and sOB-R than male patients. However, in the FDR and control subjects, gender dimorphism was noted with only leptin with females having significantly higher leptin than males. FDR of the T2DM probands had significantly higher insulin and leptin and lower sOB-R and adiponectin compared with control subjects. Our results suggest that some of the obesity-related metabolic parameters in T2DM are genetic/heritable but gender and environmental factors may influence the clinical and metabolic phenotypes.

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EARLY DETECTION OF DIABETES MELLITUS PROJECT (EDDP)

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Objectives: Assessment of the prevalence of pre diabetes and undiagnosed diabetes among the at risk (over 25 years old individuals) and its relation to some risk factors in Egypt.

Design: Clinic based cross sectional design based on analysis of data derived from the service statistics for participants in the screening tests for diabetes. WHO diagnostic criteria for diabetes and pre-diabetes have been used.

Subjects: The study included all the risk participants in the screening test services through out the period July 2003-June 2005, in six MOHP clinics prepared to provide early detection of Diabetes Mellitus services.

Results: The prevalence of pre diabetes was 8% according to the criteria of FPG level at 110-125 mg/dl, and the prevalence was 11% according to the criteria of 2-h PG 140-199 mg/dl. Using results of either FPG or 2-h PG or both criteria, the prevalence of pre diabetes was 12% and the prevalence of undiagnosed diabetes was 14%.The ratio of pre diabetics to diabetics is higher among the individuals 25-39 years of age compared to those above 39 years of age.

Conclusion: There is a probability of having diabetes prevalence in Egypt at a level higher than 14% among persons more than 25 years of age. The study is still ongoing, covering more than 60,000 high risk participants and an intervention arm using Metformin in pre diabetics has started one year earlier. The final results of the study will be revealed when complete coverage of the Egyptian governorates is achieved.

IMPACT OF CARBOHYDRATE DISORDERS ON LEFT VENTRICULAR MASS AT PATIENTS WITH ARTERIAL HYPERTENSION

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Aims: To investigate the relationship between carbohydrate disorders (CD) and left ventricular hypertrophy (LVH) evaluation at patients with arterial hypertension and metabolic syndrome.

Methods: 190 essential hypertensives (60% females, mean age 54,1±0,7), mean body mass index (BMI) 32,8±5,9 kg/m2, free of the major cardiovascular diseases underwent determination of anthropometric, biochemical parameters and measurement of 24-blood pressure. All subjects performed an echocardiographic study. Patients was divided into 4 groups: 1- without CD, 2- with insulin resistance, 3- with impaired glucose tolerance, 4- with diabetes type 2.

Results: Patients of gr.1 was demonstrated significantly less LV mass (LVM) - (226,5±7,2g) and LVM index - (57,9±2,1g/m2,7), than patients gr.2 - (263,1±9,4g), (64,4±2,4g/m2,7), 3- (259,7±7,8g), (65,6±1,8g/m2,7), 4 - (296,8±13,1g), (72,3±3,7g/m2,7) (all p < 0,001). LVH evaluation was: in gr.1 - 77% (concentric LVH - 19%), 2 - 86% (26%), 3- 95% (31%), 4 - 100% (37%). There were established significant correlation of LVM and LVMI with glucose level (for both r=0,32; p< 0,001) and relative LV wall thickness with HOMA index (r=0,20; p< 0,05 only at females). The independent association of LVM with potential predictors was confirmed by linear multiply regression analyses (beta for BMI = 0,48; p< 0,001 for glucose = 0,32; p=0,02).

Conclusion: Carbohydrate disorders seems to increase LVM over the contribution of blood pressure, sex, obesity, age at patients not only with diabetes, but although with prediabetes and may contribute to development of the most prognostic unfavorable concentric LVH, especially at females.

BLOOD PRESSURE PROFILE IN PATIENTS WITH PREDIABETES

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Some studies revealed that prediabetes may be combined with unfavorable BP which can increase cardiovascular risk. The aim of our study was assessment of BP profile in prediabetic patients with and without significant coronary artery disease.

Material and methods: The study was performed in 302 patients (177 male and 125 female, mean age 64±9) hospitalized to perform elective angiography. Study group was divided into 4 subgroups: < 55 years (n=43), 55-65 years (n=116), 65-75 years (n=113), ≥75 years (n=30). Two weeks after diagnostic coronary angiography, patients had performed 24 hour ABPM.

Results: Analysis of BP profile revealed not significant differences between 24 h, Day and night systolic, diastolic and HR in patients without CAD. Results of BP and HR analysis in patients with CAD are presented in the table.

< 55 y. 55-65 y. 65-75 y. ≥75 y.

24 h DBP 75±7□ 73±8□ 68±8 67±8

24 h HR 69±8□ 68±10□ 64±8 61±8

Day DBP 78±8# 76±8# 70±8 70±8

Day HR 72±9∫ 71±11∫ 66±9 64±8

Night DBP 69±8˚ 68±8˚ 64±9˚ 62±9

Night HR 63±8□ 63±9□ 60±7□ 57±7

□ vs. ≥ 75 y. p< 0,05; □ vs. ≥ 75 y. p< 0,05; # vs. ≥ 75 y. p< 0,05;

∫ vs. ≥ 75 y. p< 0,05; ˚ vs. ≥ 75 y. p< 0,05; □ vs. ≥ 75 y. p< 0,05

In patients with significant coronary artery disease higher values of DBP and heart rate are observed in younger patients with prediabetes. Similar relationship does not occur in prediabetic patients without significant CAD.

PREVALENCE OF PREDIABETES IN YOUNG ASPIRINGS TO AUTONOMOUS UNIVERSITY OF SAN LUIS POTOSI, MEXICO

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Background: The prediabetes is considered a previous condition that progress to overt diabetes, this state is characterized as fasting glucose blood levels grater than 100 mg/dL and lower than 126 mg/dL. Which are associated to others risk factors that contribute to development of chronic diseases.

Objective: To estimate the prevalence of prediabetes in young aspirings to Autonomous University of San Luis Potosi, México.

Material and methods: This study included 10,154 youth aspiring to Autonomous University of San Luis Potosi, México, who were ranged from 16 to 39 years, both sexes and healthy subjects. We measured age, gender, weight, height, BMI, hip circumference and fasting glucose in blood sample The statistical analysis was performed with SPSS version 16.0 software.

Results: The prevalence of prediabetes were 4.2% (1.7% W and 2.5% M) and 95.8% (52%W and 43.8% M), were healthy subjects, significant differences were found between gender, men displayed mayor prevalence (p< 0.001).

Conclusions: The prediabetes presence in early ages in this study, it might be considered as well as modifiable risk factor to develop chronic-metabolic diseases and it is required continuing check up and consider a change lifestyle.

PREDICTING DYSGLYCEMIA IN PRIMARY HEALTH CARE AMONG THE OMANI ADULT POPULATION BASED ON ANTHROPOMETRIC MEASUREMENTS

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Background and objective: In a recent cross-sectional, community-based study revealed that 36.1% of the study population are pre-diabetic as per ADA criteria. The objective of this study was to examine the relationship of Body mass index (BMI), Waist-to-hip ratio (WHR) and Waist circumference (WC) with the blood sugar level in the Omani adult population based on a community based survey.

Methods: Our study included 1274 Omani adults (476 males and 798 females). The anthropometric measurements together with estimation of fasting plasma glucose levels were carried out and ADA criteria was considered for prediabetes and diabetes.

Results: Mean age, BMI, WHR and WC increased significantly from normoglycemic to pre-diabetic and further to diabetic status in both the sexes (P< 0.001). Males have more than two times risk for developing pre diabetes with odds ratio (OR) 2.13 (95% CI: 1.60-2.84; p< 0.001) and diabetes with odds ratio 2.32 (95%. CI: 1.18-4.52; p< 0.01). Step-wise regression showed that higher BMI and abnormal WHR are significant predictor of becoming dysglycemic with adjusted OR being 2.07 (95%. CI: 1.32-3.26; P< 0.002) and 1.75 (95% CI: 1.23-2.50; P< 0.002) respectively. The risk of developing diabetes mellitus among the obese is very high with adjusted OR 4.74 (95% CI: 2.34 -9.61; P< 0.001).

Conclusion: In this study, higher body mass index and waist-to-hip ratio were found to be significant predictors of pre-diabetes while waist circumference was found to be a significant predictor of Diabetes mellitus.

PREDIABETES AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH AUTOIMMUNE THYROIDITIS

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Aims: To examine whether autoimmune thyroiditis (AIT) is associated with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes (DM) and other cardiovascular risks.

Patients and methods: We recorded thyroid function tests, BMI, HOMA-IR, IGI (Insulinogenic Index) and the levels of total cholesterol (TC), HDL, LDL-cholesterol, triglycerides, ApoB, ApoA1, lipoprotein(a), homocysteine, CRP, folic acid and vitamin B12, in 165 patients with AIT. Patients with AIT were treated with levothyroxine, in order to normalize FT3, FT4 and TSH levels. A 75-g OGTT was performed to measure plasma glucose, insulin, and C-peptide.

Results: After dividing the OGTT sample in 3 groups (IFG-16,6%, IGT-24,2% and diabetes DM-9,6%) we found that patients with IFG had significantly higher levels than IGT patients in homocysteine (9,50±2,09 µmol/L vs 7,24±1,33µmol/L;p=0,002) and HOMA-IR (3,86±2,76 vs 2,14±1,00; p=0,01). In the whole sample we observed significant correlations between TSH and insulin (r=0,20;p=0,02). In the IFG group we found significant correlations between FT3 and TC (r=-0,53;p=0,01), LDL (r=- 0,57;p=0,006) and ApoB (r=-0,53;p=0,03). In IGT group we detected correlations between insulin and CRP (r=0,61;p=0,002), and between homocysteine and anti-TPO antibodies (r=0,46;p=0,02).

Conclusions: In euthyroid patients with AIT we found significant correlations between TSH and insulin. FT3 was associated with TC, LDL and Apo B in patients with IFG. In patients with IGT we found correlations between insulin and CRP, and between homocysteine and anti-TPO antibodies. These findings suggest an increased cardiovascular risk associated to the low grade of chronic inflammation, in euthyroid patients with AIT and prediabetes.

COMPARISON OF INTERMEDIATE HYPERGLYCAEMIA IN OBESE PATIENTS ACCORDING TO ADA AND WHO DIAGNOSTIC CRITERIA

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Introduction: Fasting plasma glucose concentration is maintained within a very narrow range. The state, where abnormalities in glucose metabolism are present but elevation in glucose is below the cutoff point for establishing the diagnosis of diabetes (DM), is referred as pre-diabetes. It includes impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).

Aims: To compare the prevalence of intermediate hyperglycaemia categories in obese patients using American Diabetes Association (ADA) and World Health Organization (WHO) diagnostic criteria.

Design and methods: A total of 225 obese patients were evaluated in their first obesity medical appointment at São João Hospital: 206 women and 19 men. Anthropometric variables and plasma glucose levels at 0' and 120' were measured during oral glucose tolerance test (OGTT).

Results: Patients had mean age of 39.7±11.3 years and mean BMI of 43.7±6.6Kg/m^2. Mean waist circumference (WC) was 120.9±14.2cm and mean waist-to-hip ratio (WHR) was 0.92±0.09. The prevalence of IFG by ADA criteria was 22.2%, contrasting with 12.0% of IFG by WHO. On the other hand, the prevalence of IGT was 23.6%. Following ADA criteria, the proportion of patients with IFG who also had IGT was 30% and according to WHO criteria it was 25.9%. Considering only fasting plasma glucose, the percentage of patients with diabetes was 6.7%. This percentage raised to 13.3% when considering also the result of OGTT.

Conclusions: Fewer patients were classified as having IFG by ADA criteria than by WHO criteria. OGTT increased DM diagnostic sensitivity when compared to isolated fasting glucose.

IMPARED FASTING GLYCAEMIA AND INCIDENCE OF TYPE 2 DIABETES MELLITUS

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Impaired fasting glycaemia (IFG) refers to a condition in which the fasting blood glucose is elevated above what is considered normal levels but is not high enough to be classified as diabetes mellitus. It is considered a pre-diabetic state, associated with insulin resistance and increased risk of cardiovascular pathology. There is a 50% risk over 10 years of progressing to overt diabetes.

Aim: To evaluate the liason between impared plasma glicaemia and incidence of type 2 diabetes mellitus.

Material and methods: Standard 75 grams OGTT was performed on 1170 adult patients with suspition of high risk for type 2 diabetes mellitus. Assesment of glucose metabolism was conducted by plasma measuremens using glucose-oxidase method. The patients were divided by the last WHO criteria into 5 groups.

Results: Normal OGTT was revealed in 514 subjects (43,9%), isolated impared fasting glycaemia (IFG) was found in 166 subjects (14,2 %), isolated impared glucose tolerance (IGT) in 110 subjects (9,4%), IGF and IGT in 131 subjects (11,2%), and 249 subjects (21,3 %) were diagnosed as type 2 diabetes mellitus. Eighty two patients from diabetes diagnosed group revealed FPG under 6,9 mmol/l, which means that 7% of all subjects showed IFG and were diagnosed as type 2 diabetes.

Conclusion: Fasting plasma glucose itself is not a relevant indicator for impairment of glucose metabolism. OGTT should be performed any time when there is a minimal suspision of diabetes mellitus existence.

TYPE 2 DIABETES MELLITUS RISK FACTORS IN UNIVERSITY STUDENTS

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An increase has been detected in the incidence of type 2 Diabetes Mellitus in young populations associated to obesity and other risk factors.

Objective: To determine type 2 Diabetes Mellitus risk factors in students at the school of medicine from the University of Zulia.

Methods: 150 university students were studied in a transversal investigation.

Results: Anthropometrics parameters found were: BMI 24.54 ± 0.40 Kg/mt^2 and abdominal circumference of 80.62 ± 1.05 cm. 62 % of the population had a normal BMI; 22% overweight and 10% obesity according with classification. Biochemical variables for all patients were: basal glucose 88.24 ± 1.5 mg/dl, Post prandial glucose 88.72 ± 0.75 mg/dl., Total cholesterol 158.93 ± 2.79 mg/dl., Triacilglicerydes 75.34 ± 2.41 mg/dl., HDL-cholesterol 46.60 ± 0.99 mg/dl., LDL-cholesterol 98.20 ± 2.53 mg/dl., VLDL-cholesterol 15.07 ± 0.48 mg/dl., Basal insulin 14.78 ± 0.75 mg/dl and Post prandial insulin 36.56 ± 1.82 mg/dl., Homa-IR 1.8 ± 0.71 and Homa β cell 148.55 ± 4.01. Significant differences were found among normal individuals and with obesity in basal insulin ($p< 0.002$) post prandial insulin ($p< 0.02$) and Homa-IR ($p< 0.006$). Family history for DM2 revealed important differences in cholesterol ($p< 0.04$), triacilglicerydes ($p< 0.001$), LDL-cholesterol ($p< 0.04$) and VLDL-cholesterol ($p< 0.019$). Consumption of alcohol reveals differences between both groups related to Homa β cell ($p< 0.008$).

Conclusions: Diet disorders established differences among LDL cholesterol and IBM. A large amount of individuals have risk factors associated with obesity and insulinresistence for type 2 Diabetes Mellitus.

EFFECTIVENESS OF A SIMPLE LIFESTYLE INTERVENTION IN PRIMARY PREVENTION OF TYPE 2 DIABETES AMONG SEMI-URBAN SOUTH ASIAN POPULATION WITH IMPAIRED FASTING GLUCOSE

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Study design and method: The intervention study was conducted as a cluster randomized trial (n=190). The intervention group received the lifestyle intervention package though primary care doctors and family

health workers in a primary care setting while the control group received only a brief advice. Duration of the study was six-months.

Results: This study has shown effectiveness in reduction in fasting blood glucose ($p< 0.01$) and insulin sensitivity ($p< 0.03$) in the intervention group compared to the control group. There was also significant reduction in systolic blood pressure ($p=0.03$) and diastolic blood pressure ($p=0.01$) in the intervention group compared to the control group. A statistically significant weight reduction ($p= 0.03$) occurred in the intervention group compared to the control group. It is notable that all domains of physical activity , except leisure time activity, showed significant improvements ($p< 0.01$) in the intervention group compared to the control group. There was a significant reduction in added sugar ($p=0.03$) and fat consumption ($p< 0.01$) in the intervention group at follow up assessment

Conclusions: With the beneficial results observed in some of the primary and secondary outcome measures we could conclude that lifestyle intervention was effective in primary prevention of diabetes and reducing the existence of some modifiable risk factors among the high-risk IFG group.

Recommendation: Action towards the primary prevention of diabetes of high-risk IFG individuals encountered at primary care level needs incorporation into routine health care system in Sri Lanka and developing counties.

THE COMPUTER PLACE IN (PRE)DIABETES CONSULTATION

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Aim: To optimize the (pre)diabetes consultation in a time restricted location.

Materials and methods: The patient comes to „Medi's" Outpatient Clinic in Campina, Romania, he enters the nurse's cabinet, where data are recorded only in computer including blood results. Then he goes to the doctor's cabinet, who continues the consultation recording data only in computer. The diagnosis is automatically generated, medications are chosen from small lists, the medical discharge documents are automatically generated and printed, including personalized diet and receipts. One discharge letter goes to the patient medical file as a source document. The computer also generates the consultations registry and the monthly report to the Health Insurance Company.

Results: During 15/03/2008-30/09/2008 period, there were 2450 (pre)diabetes consultations, with a mean time of medical care (nurse+doctor) of 8 minutes/patient, which corresponds to 15 consultations/hour (4 minutes/patient x two cabinets). The patients are prospectively studied, with the automatically generation of the database.

Conclusions: It is possible to completely externalize the present and future birocracy, If all medical documents are signed and stamped before, there is no need for pen and stamping during the consultation. The gained time can be transferred to activities for education and research. The issue of very low access to doctor is solved and The National Diabetes Registry can be easily fed with information.

PREVENTING DIABETES THROUGH A PRIMARY SCHOOL-BASED INTERVENTION -THE HEALTHKICK PROGRAM

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Aim: To develop a school-based intervention aimed at increasing knowledge and promoting the adoption of healthy eating and physical activity behaviours for the prevention of diabetes in children, their parents and teachers in primary schools in the Western Cape (WC) province, South Africa.

Methods: A formative assessment was done at a random sample of 100 primary schools in 2007. Desired outcomes in knowledge, attitudes and behaviour in children and in the environment (including teachers and parents) were formulated based on the information gathered. Ten behaviours, including increasing the number of fruit and vegetables eaten daily and decreasing the consumption of high-fat and high-sugar snacks/foods were targeted for change. Sixteen schools were purposively selected from the 100 school sample and randomly assigned to an intervention (I) and control (C) group for a 4 year intervention trial. The intervention schools went through an action planning process and received a toolkit containing a resource guide and curriculum support material . Baseline data on nutrition and physical activity determinants were collected from 800 randomly selected Grade 4 children as well as 200 parents and 600 teachers in the I and C schools.

Results: Baseline data on children and parents showed poor dietary intake, poor nutrition knowledge and very little diabetes awareness.. Baseline data of the teachers showed that 32% were overweight, 47% obese, 55% had high blood pressure, and 80% smoked.

Conclusion: Results from a baseline study of a 4-year school-based intervention showed the need for an intervention that includes learners, parents and teachers.

A STUDY OF CARDIOVASCULAR RISK FACTORS IN ELDERLY PREDIABETICS

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Background: Prediabetes is the intermediate metabolic state between normal and diabetic glucose homeostasis. It comprises of Impaired Fasting Glucose(IFG) and Impaired Glucose Tolerance(IGT). Both IFG and IGT have been associated with cardiovascular disease(CVD) due to presence of cardiovascular risk factors.

Aim of the study: To study the prevalence of prediabetes in elderly age group(60 years and above) and to study cardiovascular risk factors in prediabetic group.

Methodology: Study was conducted on 200 patients of age group 60 years and above attending OPD. They were screened for prediabetes as per ADA guidelines 2006. Such prediabetic study group (32 cases) was investigated for cardiovascular risk factors(obesity, hypertension, microalbuminuria, CRP, retinopathy, dyslipidemia) along with age matched controls. Standard statistical tests were applied for analyzing data.

Results: Prevalence of prediabetes in elderly population is found to be 16%. Prevalence of IFG is 5% and prevalence of IGT is 11%. There is a significant association of obesity, dyslipidemias, microalbuminuria, hypertension and retinopathy with the prediabetic state while CRP do not have significant association. Risk factors are more associated with IGT as compared to IFG.

Conclusion: Prediabetes is widely prevalent in the elderly population. Prevalence of IGT is higher as compared to IFG. Similarly, cardiovascular risk factors are widely prevalent in the prediabetic population. Dyslipidemia, obesity, microalbuminuria, hypertension and retinopathy share the significant association as risk factors while the role of CRP is less evident. Early identification, of prediabetic state followed by primordial and primary prevention of cardiovascular disease should be the focus of intervention.

A POLYPHENOL APPLE EXTRACT REDUCES GLUCOSE IAUC FOR FEMALES WITH BMI>20KG/M²

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Obesity and type 2 diabetes are major public health problems in Western society. A diet too high in simple carbohydrates encourages weight gain and, ultimately, the onset of diabetes.

A balanced diet is the first step in preventing the onset of these disorders. However, ingredients limiting glucose absorption may be beneficial. This type of ingredient could also help to prevent metabolic disorders by limiting the absorption of food in the intestine.

Apples have been considered for their positive impact on health. Among the numerous compounds contained on apple one of them, a polyphenol called phloridzin, specific of the *Rosaceae* family, is well known to inhibit glucose transport.

The aim of this monocentric, double-blind, cross-over intervention study is to compare the glycaemic response upon intake of 50 g of sucrose after ingestion of the investigational product or the placebo. 18 healthy volunteers tested 3 times the placebo, 3 times a low dose and 3 times a high dose of test product.

The primary evaluation endpoint is the incremental area under the curve (IAUC) for glucose.

The high dose of Polyphenolic apple extract significantly reduces the incremental area under the curve for blood glucose levels over 2 hours versus placebo for females with a BMI greater than 20 kg/m² (11.6% reduction). This reduction of blood glucose should be linked to a reduction of insulin and could therefore reduce lipolysis inhibition.

ETHNICITY AS A DETERMINANT OF THE UTILITY OF TRIGLYCERIDE-RELATED MARKERS FOR IDENTIFYING INSULIN RESISTANT PREDIABETIC BLACKS

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Objectives: To determine if the triglyceride (TG) to HDL cholesterol ratio (TG/HDL) is a useful screening measure for insulin resistance in Hispanic blacks and non-Hispanic blacks of Caribbean origin.

Methods: Serum lipids, glucose and insulin were determined and compared for 144 Hispanic blacks and 655 non-Hispanic Blacks in the US Virgin Islands (USVI). Insulin resistance was estimated by the HOMA_IR. The utility of the TG/HDL cut-point of >2.0 that is suggested for discriminating insulin resistance in blacks was assessed using area under the receiver operating characteristics (AUROC) curve analyses.

Results: Hispanic blacks had significantly higher levels of TG and insulin resistance and a lower level of HDL than non-Hispanic blacks. The AUROC curve for the ability of the TG/HDL to discriminate insulin resistance was 0.71 (95% CI =0.62 -- 0.79) for Hispanic blacks and 0.64 ((95% CI =0.59 -- 0.69) for non-Hispanic blacks.

Conclusions: The TG/HDL ratio does not appear to be a useful screening measure for insulin resistance in non-Hispanic Afro-Caribbean persons, but may have utility for Afro-Caribbean persons with Hispanic ethnicity.

IMPACT OF IMPAIRED GLUCOSE TOLERANCE AS POWERFUL RISK ON JAPANESE ACUTE CORONARY SYNDROME

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Background: Impaired glucose tolerance (IGT) with postprandial hyperglucosemia is the powerful cardiovascular risk factor. However, the proportion that IGT accounts for in massive subjects of acute coronary syndrome (ACS) is not fully investigated in Japan. HbA1C is a convenient index of IGT that correlates with 5.3 to 5.7% of HbA1C.

Patients and methods: One hundred thirty five consecutive patients (89 men, mean age 67±12) presented with first-ever ACS (Group 1) and 422 ambulatory type-2 diabetic patients (Group 2) were evaluated. HbA1C, LDL-C, HDL-C, and triglyceride were measured at the admission in Group 1. Distributions of HbA1C were assessed in Group 1 and 2.

Results: The prevalence of HbA1C between 5.3 and 6.4 was significantly higher in Group 1 (56.0% vs 24.2%, p< 0.01). The percentage of HbA1C of < 5.3%, 5.3% to 5.7%, 5.8% to 6.4%, 6.5% to 6.9%, 7.0% to 7.9%, and < 7.9% were 11.8, 35.9, 20.4, 7.5, 8.6, 16.1% in Group 1 and 14.5, 9.5, 14.7, 14.2, 22.0, 25.1% in Group 2 respectively. Mean levels of LDL-C, HDL-C, and triglyceride were 123±36, 45±11, 156±112 mg/dl in Group 1. The ratio of HDL-C > 40 mg/dl and triglyceride < 150 mg/dl was only 28% in Group 1.

Conclusions: In Japanese patients of ACS, we observed a high prevalence of IGT and mild diabetic state with the impaired lipid profile similar to metabolic syndrome at the sideration.

PREVALENCE OF CHANGES IN UNDIAGNOSED GLUCOSE INTOLERANCE ACCORDING TO AGE AND GENDER IN JAPANESE MIDDLE AGED WORKING PEOPLE

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Aims: Undiagnosed diabetes and impaired fasting glucose have important health consequences. This study sought to examine the prevalence of undiagnosed glucose intolerance in Japanese Middle Aged Working People.

Methods: We carried out 75g oral glucose tolerance tests in 1142 consecutively enrolled middle-aged subjects (age range 40-55 yr; 914 men, mean 50.7 yr; 228 women, mean 49.4 yr) who had not been diagnosed with either impaired fasting glucose, impaired glucose tolerance or diabetes.

Results: Fasting glucose levels increased with age in both men and women, with the levels being higher in men than women at every age. Glucose intolerance was more common in men compared with women (Fasting glucose 100.1±19.7 vs. 92.9±9.6, p< 0.01; 1-hour 170.7±52.1 vs. 139.7±11.6, p< 0.01; 2-hour 136.0±50.1 vs. 119.8±31.5mg/dl, p< 0.01). The prevalence of IGT and DM was also higher in men than in women (IGT: 24.1 vs. 16.7, p< 0.01; DM 10.7 vs. 1.4%, p< 0.01). Blood pressure and triglyceride levels were higher in men than in women (124.0±18.5/76.9±11.6 vs. 114.8±19.4/70.6±12.5mmHg, p< 0.01; 148.1±109.4 vs. 88.2±44.0mg/dl, p< 0.01), while HDL cholesterol levels were lower in men (58.8±16.0 vs. 72.6±17.4mg/dl, p< 0.01).

Conclusions: Coronary heart disease occurred at a younger age in men, with the incidence of the disease being similar in men and women who were ten years older. These features of undiagnosed glucose intolerance in working age people may contribute to the gender difference in the incidence of coronary artery disease in Japan.

HOW TO IMPROVE SCREENING OF PRE-DIABETIC GLUCOSE ABNORMALITIES AND ARTERIAL HYPERTENSION AMONG PATIENTS SUFFERING FROM OBESITY?

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Aims: To improve searching of pre-diabetic glucose abnormalities and arterial hypertension among obese people.

Patients and methods: The study comprised individuals (n=312) with an average age 43,5±16,1 years old. Data on anthropometric parameters, such as body mass index, waist circumference, blood pressure, fasting glucose, total and high-density lipoprotein cholesterol, triglycerides were collected through clinical, biochemical measurements. Besides that insulin resistance index Homa and Caro, making body fat monitor, estimate of food behavior type and degrees of depression were determined during this study.

Results: Fasting and post-prandial insulin resistance was revealed among all the participants. Pre-diabetic glucose abnormalities were revealed in 57% individuals for the first time. They included diabetes mellitus (18%), impaired glucose tolerance (34%),h impaired fasting glucose (3,8%). Arterial hypertension suffered from 38,1%. Moderate hypertriglyceridemia, low high density lipoprotein were revealed in 66% patients. Food behavior abnormalities and depression were common in 94,6%.

Conclusion: Although the obese patients considered themselves healthy the frequency of diabetes, pre-diabetes, dyslipidaemia, insulin resistance and arterial hypertension among them is high. They should have a medical cheek up to find out the factors of cardiovascular risk.

WEIGHT REDUCING NATIONAL PROGRAM IN SLOVENIA

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Aims: Evaluation of preliminary outcomes of national weight management program on results from one-centre, as Slovenian family practitioners are obliged to perform 5-year screening examination of population (women aged 45-70 years, men aged 35-65 years) for evaluation of cardiovascular risk factors, including obesity.

Methods: Overweight subjects were referred to national reducing weight program after examination by family practitioners. 52 subjects participated in 12-week lifestyle weight loss program consisting of group-based workshops and group physical activity. Weight and waist circumference changes, during and 3 months after program, were analyzed with paired-samples t-test.

Results: Women (N=41, age 56±12 years, BMI 32.5±4.6 kg/m^2, waist circumference 101±13 cm) and men (N=11, age 58±11 years, BMI 32.8±4.8 kg/m^2, waist circumference 113±11 cm) who participated in weight reduction program had drop-out frequency rate of 26.9% at 12 weeks. Participants who completed program had higher coefficient of variation of body weight than drop-outs ($P<0.001$). Weight and waist circumference decreased at program completion for 3.4±2.6 kg and 5.3±6.0 cm, respectively. Three months after program completion, weight and waist circumference decrease were maintained or even further decreased by 87.5% of participants. Weight loss during first week of program was associated with weight loss during program ($r=0.561$, $P<0.001$), weight loss 3 months after program ($r=0.504$, $P=0.047$) and reduction of waist circumference in period from program completion until 3 months after ($r=0.643$, $P=0.007$).

Conclusions: Low drop-out rate during treatment period demonstrates that participants found program acceptable. In addition, weight loss and reduction of waist circumference were maintained during following 3-months.

INOS PROTECTS THE LIVER IN A MODEL OF CHRONIC INJURY AND INFLAMMATION

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The role of iNOS in liver damage progression and in liver diseases is not clear. Recently it has been suggested that nitric oxide (NO) may activate different metabolic pathway in the liver via the PPARγ-coactivator 1α (PGC1 α). Therefore, we hypothesized that under condition of liver damage and inflammation iNOS may preserve the metabolic status of the liver.

Methods: Wild type C57BL and C57BL iNOS(-/-) mice were supplemented with a choline deficient ethionine supplementation (CDE) diet. Mice were also treated with 5 mg/kg LPS via an i.p. injection to upregulate iNOS protein and to potentiate liver inflammation. The effect on liver damage and metabolic status was evaluated.

Results: CDE diet resulted with a significant steatosis of the liver. Following 14 days of diet almost all hepatocytes have demonstrated microvesicular steatosis. Following CDE diet animals had a decrease in the expression of gluconegenic genes PEPCK and G6Pase compared to animal supplemented with control diet and lower blood glucose levels. These effects were much exacerbated by LPS treatment. Comparison between WT and iNOS(-/-) animals under these conditions demonstrated a protective role of iNOS to support the expression of gluconeogenic genes, blood glucose level, liver tissue structure and survival.

In conclusion: Under conditions of steatosis and chronic injury the capacity of the liver to support glucose metabolism is impaired, this effects is much potentiated by LPS-induced inflammation. Up-regulation of iNOS under such conditions was found to be a protective and adaptive mechanism of the liver to preserve its tissue function.

PLASMA BILE ACIDS ARE ASSOCIATED WITH INSULIN SENSITIVITY, BUT NOT GLYCEMIC STATUS, IN ADULTS

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Introduction: Recent studies, both *in vitro* and *in vivo* in rodents, indicate a novel role for bile acids (BAs) in modulating metabolic homeostasis. BA treatment has been shown to improve insulin sensitivity as well to increase energy expenditure in mice. However, such a metabolic function of BAs remains to be determined in humans.

Aim: We investigated the relationship between plasma BAs concentration, insulin sensitivity and basal energy expenditure in humans.

Methods: Insulin sensitivity was calculated according to homeostasis model assessment (HOMA) as well as by the determination of the glucose infusion rate (GIR) during hyperinsulinemic-euglycemic clamps in 14 healthy, 20 type 2 diabetic, and 22 non-diabetic obese subjects. Energy expenditure was measured by indirect calorimetry. Plasma cholic acid (CA), chenodeoxycholic acid (CDCA) and deoxycholic acid (DCA) concentrations were analyzed by gas chromatograph-mass spectrometry. Regression analyses were used to estimate the correlation between plasma BAs and metabolic parameters.

Results: In univariable analysis, a positive association was found between HOMA and plasma CDCA ($p=0.001$), CA ($p=0.009$) and DCA concentrations ($p< 0.0001$). A negative association between GIR and CDCA ($p=0.003$), CA ($p=0.001$) and DCA ($p=0.04$) was also identified. Basal metabolic rate was positively correlated with CDCA ($p=0.01$) and CA ($p=0.05$). In multivariable analysis, HOMA remained positively associated

with CDCA (p=0.003), CA (p=0.05) and DCA (p=0.003). In contrast, neither HbA1C nor energy expenditure were correlated with plasma BAs levels.

Conclusion: Plasma BAs concentrations were negatively correlated with insulin sensitivity in humans, supporting the hypothesis for a role of BAs in glucose homeostasis.

HCV CORE-INDUCED NONOBESE HEPATIC STEATOSIS IS ASSOCIATED WITH HYPOLEPTINEMIA AND IS AMELIORATED BY LEPTIN ADMINISTRATION

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Background/ aim: Obese hepatic steatosis is commonly associated with central fat accumulation and hyperleptinemia; however, the connection between nonobese hepatic steatosis and leptin is unclear. We sought to uncover the connection using an animal model.

Methods: Double transgenic mice (DTM), in which hepatic over-expression of HCV core is regulated by tetracycline transactivator (tTA), were given permissive chow following 1 month of a doxycycline-rich diet since their births. Nonobese hepatic steatosis was exhibited in the 2-month-old DTM but diminished with time. The levels of leptin and adiponectin, and various metabolic features, were subsequently assessed in 2-, 3-, and 4-month-old DTM (i.e., HCV core-tTA) and single transgenic mice (STM; i.e., tTA). The total fat mass and body fat distribution of the mice were evaluated by dual-energy X-ray absorptiometry and magnetic resonance imaging. Microarray analyses and quantitative real-time polymerase chain reaction were conducted using RNA from the visceral fat of paired DTM and STM. Leptin was administered intraperitoneally to the 2-month-old DTM.

Results: After adjusting for fat mass, the protein and RNA expression of leptin was lower in the 2-month-old DTM than in the STM, and the DTM had hypoadiponectinemia; nevertheless, these differences diminished with time. Leptin treatment significantly ameliorated hepatic steatosis in the 2-month-old DTM.

Conclusions: HCV core-induced nonobese hepatic steatosis is associated with down-regulation of the leptin gene in visceral fat and subsequent hypoadipocytokinemia; however, these effects may be ameliorated by leptin treatment.

INCREASED LIVER OXIDATIVE STRESS AND ALTERATIONS IN POLYUNSATURATED FATTY ACID METABOLISM PRECEDE DEVELOPMENT OF NONALCOHOLIC STEATOHEPATITIS IN SREBP1A TRANSGENIC SPONTANEOUSLY HYPERTENSIVE

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The relationship between hepatic steatosis, non-alcoholic steatohepatitis (NASH), insulin resistance, oxidative stress and fatty acid (FA) composition is not fully understood. We developed an experimental model of hepatic steatosis and NASH, the transgenic spontaneously hypertensive rat (SHR) that overexpresses a dominant positive form of the human SREBF1 gene. These rats develop hepatic steatosis that progresses towards NASH in older animals. We investigated the role of oxidative stress and changes in FA composition in the pathogenesis of NASH in this model. We determined antioxidant enzyme activities and lipid peroxidation product levels as oxidative stress markers as well as FA composition in plasma phospholipids in young (10 week old) SHR transgenic and SHR control rats that were fed a high fructose diet for 2 weeks. At the age of 10 weeks, transgenic SHR exhibited simple hepatic steatosis which was associated with significantly increased hepatic levels of oxidative stress markers. The activities of superoxide dismutase (SOD) , seleno-dependent glutathione peroxidase (GSH-Px) and glutathione levels were significantly reduced and plasma levels of a- and g-tocopherol were more than 4 times lower in transgenic rats when compared to SHR controls. Transgenic rats exhibited increased plasma levels of saturated FA, decreased levels of n-3 and n-6 polyunsaturated FA (PUFA) and increased n-6/n-3 PUFA ratio when compared to controls. These findings demonstrate that in the SREBP-1a transgenic SHR, hepatic steatosis is associated with disordered antioxidant status of the liver, PUFA depletion, and an increased PUFA n-6/n-3 ratio.

DYSFUNCTION OF A GLYCEROL TRANSPORTER, AQUAPORIN-9 (AQP9), IN LIVER STEATOSIS

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Aims: Hepatocytes express AQP9, a basolateral membrane channel permeable to water, glycerol and other small neutral solutes. Although liver AQP9 is downregulated by insulin and hypothesized to mediate glycerol uptake from the bloodstream for gluconeogenesis, its relevance in carbohydrate and fat pathophysiology remains elusive so far. Here, we evaluate whether liver AQP9 acts as real hepatocyte glycerol transporter and has relevance in liver steatosis.

Methods: Glycerol permeability (Pgly) of hepatocyte basolateral plasma membrane was assessed by stopped flow light scattering while the expression and subcellular localization of AQP9 were defined by real time PCR, immunoblotting and immunocytochemistry.

Results: Increased AQP9 expression was seen in the livers of fasted (vs fed) mice and was paralleled with a comparable increase in basolateral membrane Pgly, suggesting a major role for AQP9 in liver glycerol uptake. Of note, both Pgly and AQP9 protein levels in the fatty liver of ob/ob mice were significantly lower than those of control wild-type mice. Similar AQP9 dysregulation was observed in liver biopsies by morbidly obese patients with insulin resistance or type 2 diabetes mellitus (T2DM) undergoing bariatric surgery.

Conclusions: Besides indicating major relevance for AQP9 in glycerol influx into hepatocyte these findings suggest a compensatory mechanism aimed to avoid further accumulation of triglycerides within the steatotic hepatocyte. A deeper understanding of the regulation of liver AQP9 may be useful to devise novel therapeutic targets aimed at control of metabolic syndrome and closely related disorders such as liver steatosis.

ASSESSMENT OF ADIPONECTIN, LEPTIN AND INSULIN LEVELS IN PATIENTS WITH NON ALCOHOLIC STEATOHEPATITIS (NASH) AND GALBLADDER DISMOTILITY

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Background: The high prevalence of gallstones in patients with NASH might be due to the fact that both conditions belong to the metabolic syndrome, insulin resistance being the common pathogenic mechanism. Our aim was to investigate the citokines' profile and gallbladder motility in patients with NASH.

Methods: 28 patients with NASH (confirmed histologically) - 12 men and 16 women, mean age 46.36 ± 7.56) were included. The control group included 10 patients with no chronic liver disease or gallbladder disease (4

men and 10 women, mean age 51.47± 8.03). Fasting gallbladder volume (FV) was measured and gallbladder emptying [RV-minimal residual volume, FE= (FV-RV)/FV*100 (ejection fraction)] was monitored by ultrasound, for 90 minutes, after a test meal (14 g fat, 425 kcal). Serum levels of adiponectin, insulin and leptin were assessed in both groups.

Results: The patients with NASH had an increased FV, RV and EF comparative with controls ($p< 0.05$). Mean FV was significantly increased in diabetic NASH patients, as compared with NASH patients without diabetes (p=0.0048). There were no significant differences regarding levels of adiponectin (62.62ng/ml in NASH patients vs 75.12 in control group, p=0.54), leptin (136.58 pg/ml vs 176.95, p=0.54) and insulin (13.99 mU/ml vs 12.31, p=0.46).

Conclusions: The present study, to our knowledge the first report in the literature, found a significantly decreased gallbladder motility in patients with NASH. This could be a contributive factor to cholesterol gallstone formation in NASH. There are necessary further studies in order to assess the cytokines contribution to this process.

MECHANISMS UNDERLYING HEPATIC IRON ACCUMULATION IN A DIETARY EXPERIMENTAL MODEL OF NONALCOHOLIC FATTY LIVER DISEASE

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Increased hepatic iron stores are frequently observed in the metabolic syndrome, and associated with hepatic and vascular damage. Aim was to investigate the effect of high fat diet (HFD) on iron metabolism in rats. Six-weeks male Sprague-Dawley rats were fed for 12 weeks with standard chow (control, n=6), or HFD (n=6), or HFD+s.c. iron administration (250mg, n=6), HFD resulted in mild steatosis and increased glucose and insulin resistance vs. controls. Dietary iron intake was lower in HFD treated rats vs. controls (.74±.3 vs 8.5±1.5 mcg/week, $p< .0001$), but hepatic iron concentration (16±9 controls, 33±10 HFD, 122±40 mcg/100mg HFD+iron,p=.01), H and L ferritins mRNA and proteins were higher in HFD vs. controls, whereas serum iron was not influenced by diet. mRNA of hepcidin, the hormone regulating iron absorption, was higher in HFD vs. controls (p=.01), but hepcidin/ferritin ratio and mRNA levels of the hepcidin regulators were not affected. Expression of the iron exporter ferroportin-1, was decreased relative to iron stores by HFD (p=.01). mRNA and protein levels of transferrin recepetor-1 (TfR-1), the physiological mediator of iron uptake from plasma usually downregulated by iron, were upregulated by HFD (2.6-fold, $p< .05$), and normalized by iron supplementation.

Conclusions: HFD affects the expression of iron genes and favors hepatic iron accumulation. HFD decreased the expression of ferroportin-1 relative to iron, was not associated with impairment in hepcidin transcription and with that of its main regulators, but with up-regulation of TfR-1 reversed by iron supplementation. TfR-1 up-regulation may contribute to early phases of iron accumulation associated with HFD.

DETERIORATION OF GLUCOSE TOLERANCE AND INSULIN SENSITIVITY ARE ACCOMPANIED BY GRADUAL ELEVATION OF HEPATIC AMINOTRANSFERASES

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We examined whether elevation of aminotransferases occurs in parallel to the development of insulin resistance (IR) and glucose intolerance. Associations of aminotransferases and HOMA-IR were investigated in 223 individuals stratified by glucose tolerance status: normal, impaired fasting glycemia, impaired glucose tolerance (IGT) and diabetes. Correlations ($p< 0.01$) between alanine aminotransferase (ALT) and waist-to-hip ratio (r=0.255), fasting (r=0.249) and post-challenge plasma glucose (r=0.297) and HOMA-IR (r=0.272) were detected. Aspartate aminotransferase (AST) was correlated ($p< 0.05$) to waist-to-hip ratio (r=0.147) and fasting (r=0.149) and post-challenge plasma glucose (r=0.231). ALT was higher in diabetes.

	Normal glucose tolerance (n=136)	Impaired fasting glycemia (n=34)	Impaired glucose tolerance (n=24)	Diabetes (n=34)
Men (%)	28.7	44.1	37.5	48.3
Age (years)	49.8 ± 16.1 ab	53.8 ± 13.5	62.7 ± 10.4 a	58.4 ± 12.5 b
Abdominal circumference (cm)	95.0 ± 13.6 a	100.4 ± 12.7	100.6 ± 12.0	102.0 ± 8.5 a
Waist-to-hip ratio	0.91 ± 0.08 ab	0.94 ± 0.08	0.96 ± 0.09 a	0.97 ± 0.07 b
Body mass index (kg/m2)	28.5 ± 5.9	30.3 ± 6.3	29.8 ± 5.4	30.4 ± 3.7
Fasting plasma glucose (mg/dL)	86.6 ± 8.3 abc	106.1 ± 6.1 a	106.3 ± 10.2 b	125.1 ± 38.8 c
Post-challenge glucose (mg/dL)	98.4 ± 18.7 ab	109.8 ± 21.0	157.2 ± 15.7 a	216.7 ± 62.6 b
ALT (U/L)	14.0 ± 8.6 a	16.6 ± 3.8 b	17.5 ± 13.2 c	27.1 ± 20.8 abc
AST (U/L)	16.4 ± 6.0 a	17.1 ± 6.7 b	17.3 ± 6.0	22.1 ± 13.5 ab

Same letters indicate statistical difference ($p< 0.05$).

Aminotransferases elevate in parallel with central fat accumulation and insulin sensitivity deterioration. ALT is more specific for the liver than AST, and showed stronger correlations with IR. Higher ALT levels in individuals with diabetes are in agreement with higher prevalence of NASH in diabetic compared to general populations.

EXPRESSION OF RETINOID X RECEPTOR GAMMA ISOFORM IS REGULATED BY FASTING-FEEDING CYCLE IN LIVER

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Aims: Glucose metabolism is balanced by glycolysis and gluconeogenesis with precise control in liver. Recently, it is emphasized that nuclear receptors play important roles in regulating the gene expression of glucose metabolism, for example, LXR, PPAR, FXR, and so forth. These nuclear receptors heterodimerize with retinoid X receptor (RXR) to bind to their specific regulatory elements on the promoters. We performed following study to investigate the interaction between nuclear receptors in liver.

Methods: Mice were fasted and then refed, and total RNA from liver were prepared in the time course. To investigate the role of RXRg, we performed RT-PCR, luciferase assay, overexpression, EMSA, and so forth.

Results: In the present study, we found RXRg is rapidly induced after feeding in mouse liver, indicating that RXRg play a role in controlling glucose or lipid metabolism in fasting-feeding cycle. In addition, RXRg expression was upregulated by glucose in primary hepatocytes. Liver expresses RXRg2 whereas skeletal muscle expresses both RXRg1 and RXRg2. Interestingly, RXRg2 expression was not suppressed in fasted liver of ob/ob mouse, which was similar to glucokinase expression. This suggests that glucokinase could be regulated by RXRg2 concerting with other nuclear receptors such as LXRa or PPARg. EMSA showed that RXRg could also heterodimerize with LXRa. Luciferase assay showed that RXRg1/RXRg2, as well as RXRa, activated the reporter gene in concert with PPARg or LXRa.

Conclusions: These results suggest that, in the fasting-feeding cycle, nuclear receptors in different combination might be important for the tight control of glucose metabolism.

NON ALCOHOLIC FATTY LIVER DISEASES AND SUB CLINICAL CORONARY ATHEROSCLEROSIS

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Background: NAFLD is increasingly associated with metabolic syndrome. The independent role of NAFLD in cardiovascular risk remains unclear.

The **aim** of the present study is to evaluate the relationship between NAFLD and coronary atherosclerosis in patients with major cardiovascular risk factors, with or without metabolic syndrome.

Methods: 29 patients (age 53±7) with NAFLD and 32 gender/age matched individuals without NAFLD were recruited. Coronary artery disease was defined as stenosis of >50% in at least one major coronary artery. We measured degree of fatty infiltration by ultrasound, coronary plaques and stenosis by coronary computed tomography angiography and biomarkers of insulin resistance, lipotoxicity, systemic inflammation, and markers of oxidant-antioxidant status.

Results: NAFLD patients showed higher prevalence of coronary plaques (67% vs. 34%, P< 0.001), in particular soft plaques (52% vs 25%, P< 0.001), higher prevalence of non obstructive coronary stenosis (34% vs 14%, P< 0.008), higher insulin resistance (HOMA 3.8±3.6 vs. 2.6±3.2, P< 0.005), and higher triglyceride levels (208± 87 vs. 148±70, P< 0.005) than controls. Patients with severe fatty infiltration had higher prevalence of multiple coronary plaques than mild fatty liver (64% Vs 38%, p< 0.004). Multiple regression analysis showed that fatty liver is a strong predictor of coronary atherosclerosis (OR 2.0, P< 0.04) independently by metabolic syndrome and by biomarkers of insulin resistance, lipotoxicity, lipid peroxidation and inflammation.

Conclusions: NAFLD patients have higher prevalence of coronary soft plaques independently by metabolic syndrome diagnosis. This might optimize the cardiovascular risk stratification.

NON-INVASIVE ASSESSMENT OF HISTOLOGICAL INFLAMMATION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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Background: Nonalcoholic steatoepatitis (NASH) represents the most severe form of NAFLD.The progression of NASH to most severe form of liver disease is due to increase inflammation and serum transaminases don't reflect the severity of liver disease. Serum Hyaluronic acid (HA), tissue inhibitor of metalloproteinase 1 (TIMP1), are reliable markers of liver fibrosis and are linked to the proinflammatory status.

Aim: build a mathematical model able to detect moderate-severe inflammation in biopsy proven NAFLD using the means of serum TIMP1 and HA.

Patients and methods: 46 histological proven NASH. Serum HA and TIMP1 were assessed by commercial ELISA kits. Difference among groups were assessed by ANOVA. Demographic, clinical, and laboratory findings were analyzed by univariate and multivariate analiysis.The ROC curve was used to identify the cut-off point of the mathematical model and to assess the sensitivity and specificity.

Results: Moderate-severe histological inflammation was present in 21,7% of our population. Serum levels of HA and TIMP1 were statistical different in patients with different stages of histological inflammation. In the logistic regression among clinical parameters , only BMI was able to predict the moderate-severe inflammation. On the ground of these results we built a mathematical model including BMI, TIMP1 and HA. The result of this model with a cut-off of 116,2522 showed good sensibility 83,3% and specificity: 87,5% with a Negative Predictive Value of 87,1% for moderate-severe inflammation.

Conclusions: Our model we could exclude with a good accuracy the presence of moderate-severe inflammation avoiding the need of liver biopsy in a substantial proportion of patients.

HEPATIC INSULIN RESISTANCE AND FATTY LIVER: RELATIONSHIP WITH EARLY MARKER OF ATHEROSCLEROSIS AND METABOLIC SYNDROME COMPONENTS

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Introduction: Fatty liver (FL) is recognized as the hepatic manifestation of the metabolic syndrome (MS) and closely related with cardiovascular risk. Systemic insulin-resistance appears to be the common factor. However, pure hepatic insulin-resistance may lead to severe atherosclerosis in mice and might play a crucial role in MS.

Aim: To assess the relative importance of hepatic insulin-resistance (H-IR) in FL and to determine the relationship with carotid artery intima-media thickness (IMT) and MS components.

Patients and methods: In 132 consecutive non-diabetic subjects with liver steatosis we measured: H-IR by oral glucose tolerance test as proposed by DeFronzo, FL score and IMT as assessed by ultrasonography. Components of MS as defined by ATP-III, HOMA-IR and liver enzymes were also measured.

Results: FL was mild in 49 subjects, moderate in 66 and severe in 17. H-IR was progressively increased with the severity of FL (p< 0.0001). Among components of MS, H-IR was related with waist circumference (r=0.30; p=0.001), HDL levels (r=-0.26; p< 0.01) and fasting plasma glucose

(r=0.20; p< 0.02). In addition, H-IR correlated significantly with alanine-aminotransferase (r=0.30; p< 0.001) and HOMA-IR (r=0.60; p< 0.001). IMT was increased with the severity of FL (p< 0.01) and significantly related with H-IR (r=0.40; p< 0.001). Multivariate linear regression analysis found that H-IR was closely associated with IMT independently by age, gender, body mass index and HOMA-IR (p< 0.001).

Conclusion: These results show that H-IR is strongly associated with progressive liver fat infiltration and MS components and may be a crucial link with cardiovascular risk.

NAFLD IS THE MOST COMMON FORM OF CHRONIC LIVER DISEASE IN PSORIASIS AND IT IS ASSOCIATED TO PSORIATIC ARTHRITIS

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Background: The primary end point of the study was to assess the prevalence of NAFLD in psoriatic patients in an tertiary hospital based setting and to define the clinical features of NAFLD in patients with psoriasis comparing the results with a matched cohort of histologically proven NAFLD.

Methods: All consecutive patients with psoriasis attending the Outpatient Dermatologic Unit were screened for the presence of liver disease. The diagnosis of fatty liver was performed on the basis of the ultrasound report. In order to define the severity of NAFLD we used the mean of NAFLD Fibrosis Score in the psoriatics with NAFLD and in a matched cohort of NAFLD subjects without psoriasis.

Results: We enrolled 142 patients with psoriasis. The prevalence of fatty liver was 66,2%. Subjects with NAFLD and psoriasis had higher prevalence of psoriatic arthritis which remained independently correlated to NAFLD in the binary logistic regression analysis (OR: 7,329; 95%CI=1,04-51,81; p=0.046). In the second part of the study, on the basis of NAFLD Fibrosis Score, the prevalence of advanced fibrosis (F>3) was recorded in 7,4% of NAFLD patients and in 13% of psoriatics with NAFLD (p< 0,05).

Conclusion: Fatty liver and NAFLD are common in psoriasis (66.2% and 59,1%). NAFLD seems to be the more prevalent cause of liver disease in psoriasis and is strongly associated to PsA. The NAFLD fibrosis score suggests a major prevalence of severe fibrosis in subjects with psoriasis and NAFLD. Screenig for fatty liver should be recommended in patients with psoriasi.

THE EFFECT OF PROBIOTICS ON LEVEL OF ENDOTOXIN IN PATIENTS WITH LIVER DISEASE - POTENTIAL THERAPY OF NON ALCOHOLIC STEATOHEPATITIS?

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The aim: Nonalcoholic steatohepatitis (NASH) is important part of metabolic syndrome. One of the etiological factors is increase of intestinal bacterial overgrowth, increase bacterial translocation with increase of endotoxin what can increase fibrogenesis. Probiotics are living microorganisms that have favorable effects on these mechanisms. The aim of our study was to determine the effect of probiotics in patients with damage of liver functions.

Patients and methods: Forty five patients (26 male, 19 female, av. age 53,1 /35 - 69 years/) with liver cirrhosis were randomized to the treatment with E. coli Nissle (Mutaflor) (24 patients) or placebo (21 patients) for 42 days. Microbiologic quantitative analysis of stool and level of endotoxin were investigated before and in the 42nd day of the treatment.

Results: Microbiological findings was improved in the treatment group (2,0 ± 0,7 vs. 1,4 ± 0,6 /p < 0,001/), in the placebo group there were no changes (2,2 ± 0,7 vs. 2,3 ± 0,5 /n.s./).

Level of endotoxin decreased in treatment group (0,015 ± 0,006 vs. 0,009 ± 0,007 /p=0,07/), there were no changes in the placebo group (0,013 ± 0,007 v.s 0,014 ± 0,006 /n.s./.

Conclusion: Probiotics seems to be effective in the restoration of physiological flora in the gut in patients with liver injury and can decrease the level of endotoxin. As these changes plays role in the etiology of NASH, therapy with probiotics can be useful in patients with NASH in the future.

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RELATIONSHIP BETWEEN INSULIN RESISTANCE AND DISEASE PROGRESSION IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS

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Object: The elevation of serum copper concentration is frequently observed in patients with type 2 DM as well as cholestatic liver diseases. Serum zinc level inversely correlates with the severity of hepatic fibrosis in patients with chronic liver disease. The purpose of this study is to examine whether the changes in serum copper and zinc levels affect insulin resistance in patients with primary biliary cirrhosis (PBC) or not.

Methods: Five patients with PBC at early stage (Sheuer's stage 1 and 2) and four patients with PBC at late stage (Sheuer's stage 3 and 4) were enrolled. None of the enrolled patients had concurrent type 2 DM. Peripheral platelet count, serum zinc and copper concentrations in the enrolled patients were measured. Insulin resistance was evaluated by HOMA-IR.

Results: Mean serum zinc level and peripheral platelet count at late stage were significantly lower than those at early stage (47±15 vs, 67±7μg/dl, p=0.0268, 7.9±3.6 vs, 21.0±4.9×10^4/μl, p=0.0275), while there was no apparent difference in serum copper level between the groups. The linear regression analysis revealed significant correlation between serum zinc level and peripheral platelet count (R^2=0.451, p=0.0335), and inverse correlation between peripheral platelet count and the value of HOMA-IR (R^2=0.470, p=0.0416). PBC patients at late stage showed definitely higher values of HOMA-IR than those at early stage (2.18±0.46 vs, 0.91±0.31, p=0.0143).

Conclusions: These findings suggest that insulin resistance emerges at late stage of PBC, and that insulin resistance is associated with the degree of hepatic fibrosis which derives from zinc deficiency.

ASYMPTOMATIC DIABETIC PATIENTS WITH ABNORMAL LFTS

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Objective: Patients with diabetes mellitus often have abnormal liver function tests without any symptoms.Our aim in this study was to evaluate the frequency and cause of abnormal LFTS in diabetic patients.

Methods: 150 patients were enrolled from diabetic clinic who had been diagnosed with diabetes, [creatinine,fasting glucose,random glucose, GTT were recorded]. The following demographic data were recorded from each patient: age, sex, duration of diabetes, BMI, waist circumference, lipid profile, HbA1C, BP[blood pressure]. All patients had liver function tests performed and of these patients with abnormal LFTS, underwent full hepatitis screening including ultrasound of hepatobiliary system. I f the cause for the abnormal LFTS, was still elusive the patients underwent a liver biopsy and was seen by hepatologist.

Results: 54% of patients had abnormal LFTS, of which 61% had hepatitic picture and 28% a mixed hepatitic and cholestatic picture.The remainder 11% hd cholestatic picture.

The majority of patients with abnormal LFTS had non-alcoholic fatty liver disease[NAFLD] 94%, and 4% had non-alcholic steatohepatitis [NASH]. 0.7% had autoimmune liver disease,0.2 had viral hepatitis,and 0.1 haemachromatosis and 1% cholelithiasis. In the cohort of patients with NAFLD or NASH,there was poor glycaemic control,obesity,abnormal lipid profile and hypertension.

Conclusion: Abnormal LFTS in diabetic patients dictate further investigations with treatment of underlying cause. Patients with NAFLD or NASH often have more than one components of the metabolic syndrome and the later patients are usually poorly controlled.

ASTRAGALUS MEMBRANACEUS IMPROVED PREDIABETES CONDITIONS AND NONALCOHOLIC FATTY LIVER DISEASE IN RATS

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Hyperglycemia, hyperlipidemia, cardiovascular dysregulation are major features of metabolic syndrome which are also risk factors for the onset of diabetes. In addition, nonalcoholic fatty liver disease (NAFLD) also frequently occurs in prediabetes. Astragalus Membranaceus (AM), a widely used Traditional Chinese Medicine, has been demonstrated possessing active components to improve diabetic hyperglycemia or diabetic relative complications, such as cardiomyopathy, arthrosclerosis, peripheral neuropathy, and nephropathy as well as to ameliorate chemically induced liver injury. However, it remained to be evaluated whether AM could be employed at the prediabetes stage. In the current investigation, we would like to evaluate whether AM could improve prediabetes conditions in rats received both high-fat diet manipulation coupling with a single STZ (50 mg/kg, i.p.) injection. Two months of daily administration of water extract of AM (500 mg/kg, i.p.) was then carried out. During the administration, amelioration of elevated serum glucose, insulin, triglyceride and cholesterol level as well as the body weight were observed in AM treated animals although glucose utility was not improved by AM treated group concluded from intravenous glucose tolerance test (IVGTT). Based on liver pathological examinations and Oil Red O staining, results were demonstrated that fat accumulation was reduced by AM administration. Besides, reduction of liver glycogen content (PAS staining) was recovered in AM treated animals. Therefore, it was concluded that Astragalus Membranaceus administration could be beneficial for prediabetes population and potentially applied for NAFLD therapy.

THE ASSOCIATION BETWEEN FREE T4 AND FATTY LIVER IN EUTHYROID WOMEN

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Aims: In the previous study, we demonstrated Free T4 was negatively associated with BMI in euthyroid women. However, there is still uncertain whether thyroid function within normal range is associated with fatty liver and liver function abnormalities. So we sought to evaluate thyroid function (free T4, TSH) and its possible relationship with fatty liver in euthyroid women.

Methods: A total of 1034 euthyroid, non heavy alcoholics women who visited Daegu Catholic Uni. Medical Centre for primary health screening from January 1, 2006, to December 31, 2006 participated in this cross-sectional study. Women who were not euthyroid, heavy alcoholics(>70g/week in women according to DSM-IV) and had viral hepatitis were excluded.

Hepatic ultrasonography scanning was performed in all participants by a single experienced radiologist. TSH, free T4, BP, fasting glucose, serum liver enzyme (AST, ALT, GGT, T-bilirubin), lipid profiles [total-cholesterol, triglyceride (TG), HDL-C, LDL-C]and fatty liver were evaluated.

Results: Euthyroid women with fatty liver had lower free T4 levels than euthyroid women without fatty liver. Free T4 was negatively correlated with serum AST, but, was positively correlated with serum total bilirubin. Free T4 was not correlated with serum ALT and GGT. After adjustment for age, BMI, fasting glucose, and triglyceride, free T4, but not TSH, was significantly negatively correlated with fatty liver.

Conclusions: We demonstrated a negative association between free T4 and fatty liver in euthyroid women. This finding suggests low free T4 is associated with NAFLD in euthyroid subjects.

INSULIN RESISTANCE AND NON-ALCOHOLIC FATTY LIVER DISEASE. ASSOCIATION WITH CARDIOMETABOLIC RISK FACTORS

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The increased prevalence of metabolic syndrome (MS) is associated to high risk of cardiovascular disease. Non-alcoholic fatty liver disease (NAFLD), characterised by an exaggerated triglyceride (TG) depot, is related to obesity and insulin-resistance (IR), and it is considered the hepatic manifestation of MS.

Aim: To evaluate the influence of IR on the prevalence of NAFLD and its relation with cardiometabolic factors.

Methods: Non diabetic-MS patients without treatment (n=165) were divided above (A, n=85) and below (B, n=80) HOMA-IR median: 3.30. Hepatic ultrasonography was performed and steatosis was classified as low, moderate or severe. Adiponectin and free fatty acids (FFA) were measured in serum samples. VLDL was isolated at d< 1.006 g/ml and its chemical composition determined.

Results: Prevalence of severe steatosis was higher in group A (68%) than in B (26%) p< 0.01. Relative Risk (RR) was 3.4; CI: 2.1-5.6. BMI and MS components were increased in A p< 0.01. FFA and apoB-VLDL were

higher in A than in B (0.67±0.32 vs 0.50±0.16 mM and 5.0±3.2 vs 2.7±1.18 mg% respectively, p< 0.05), and associated between them (r=0.36 p< 0.04). Patients from group A presented decreased levels of adiponectin (7.4±3.8 vs 9.6±6.3µg/ml, p< 0.04) which were directly associated to FFA (r=-0.40; p< 0.03) and to apoB-VLDL (r=-0.5, p< 0.02).

Conclusions: Patients with higher IR presented elevated RR to develop severe NAFLD. Increased FFA flux to the liver would promote overproduction of VLDL, indicated by higher apoB-VLDL, and TG accumulation in the liver, favoured by lower adiponectin levels.

IS THERE ANY CORRELATION BETWEEN THE LIVER FIBROSIS AND THE CARDIOVASCULAR RISK AT THE DIABETIC PATIENTS WITH METABOLIC SYNDROME?

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Introduction: Patients with metabolic syndrome can develop non-alcoholic fatty liver disease (NAFDL), which can progress from steatosis to fibrosis. The cardiovascular disease risk is high in diabetic patients. Our aim was to study if there is any correlation between the liver fibrosis and the cardiovascular risk at the diabetic patients with metabolic syndrome.

Methods: We studied 47 diabetic patients with metabolic syndrome hospitalized in the Diabetes Department from the Sibiu Clinical County Hospital, Romania, during August-October 2008. At them, we have calculated the cardiovascular risks using the UKPDS risk engine. The liver fibrosis was non-invasively assessed using the Forns index, which depends on age, gamma-glutamil transpeptidase, cholesterol and HDL-cholesterol; a value < 4.2 excludes liver fibrosis and a value > 6.9 is a predictor for significant fibrosis. The results were statistically analyzed using the Pearson index of correlation (r).

Results: The medium age was 59.23 ± 12.65 years and the medium diabetes duration was 10.65 ± 6.16 years. 12.76% of the patients had type 1 and 87.24% had type 2 diabetes. A tight linear correlation was found between the liver fibrosis index and the 10 years risk of developing coronary heart disease (r =0.4568), fatal coronary heart disease (r =0.3502), stroke (r=0.3072) and fatal stroke (0.5913).

Conclusions: Our findings suggest that liver fibrosis in diabetic patients with metabolic syndrome is well correlated with the risk of developing cardiovascular diseases. The clinical impact of NAFLD on cardiovascular risk deserves particular attention because of the growing number of patients with NAFLD.

METABOLIC SYNDROME AND LIVER STEATOSIS

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An association was reported between liver steatosis and the metabolic syndrome in obese patient. The main feature of this syndrome is hyperinsulinemia with insulin resistance which may induce an altered lipid profile, hypertension and predispose to vascular diseases.

Aim: The aim of this study was to evaluate the prevalence of liver steatosis in Tunisian patients with metabolic syndrome.

Patients and methods: Forty five patients (32 women, 13 men) mean aged 50 years (range 27-75 years) had the metabolic syndrome as defined by International Diabetes federation 2005. Liver analysis, abdominal echography, viral serology B and C are done. We measured waist circumference, fasting serum lipid and glucose levels. Patients with other liver disorders are excluded.

Results: Hepatic steatosis is found in eighteen patients (42%). Laboratory results showed a liver cytolysis in 5% of cases. One of these patients was in a stage of hepatic cirrhosis confirmed by a liver biopsy. All patients with steatosis had diabetes, higher triglyceridemia (2.4 *vs* 1.8 mmol/l), waist circumference (99.8 *vs* 85.4 cm) and lower high density lipoprotein cholesterol levels (0.8 *vs* 1.2 mmol/L) than patients without steatosis.

Conclusion: Hepatic steatosis is frequently associated with a metabolic syndrome. A fibrosis may appear after several years particularly if the obesity is severe. It is therefore justified to propose a hepatic biopsy in an obese patient when transaminase levels exceed twice the normal value. Treatment is aimed at correcting the metabolic disorders.

METABOLIC SYNDROME AND NONALCOHOLIC STEATO-HEPATITIS IN OBESE SUBJECTS

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Aim: To determine the prevalence of Nonalcoholic Steato-Hepatitis (NASH) and Metabolic Syndrome (MS) on obese subjects.

Methods: The study was performed on 118 consecutive subjects (37 males, 81 females, median age 44, and range 26 - 68 years); mean body mass index (BMI) 38.8 ± 3.7 kg/m^2. Serology was negative for viral and autoimmune hepatitis; alcohol consumption was less than 20g/day in all subjects. No evidence of metabolic liver disease was found on any subject. The diagnosis of NASH was based on ultrasonography and serum ALT (> 2xN). MS was defined by ATP III, as a combination of 5 risk factors [waist circumference >102cm (M) or >88 cm (F), fasting glucose ≥110mg/dL, triglycerides ≥150mg/dL, HDL-cholesterol < 40mg/dL (M) or < 50mg/dL (F) and blood pressure ≥140/90mmHg]. Three or more of these criteria identified MS. Insulin resistance (IR) was calculated according to homeostatic model assessment (HOMA), when HOMA was >3.

Results: NASH was found on 57 (48%) of our subjects and MS on 71 (60%) of them. Presence of NASH and MS increased with BMI. Predictive value for NASH were calculated by BMI >35kg/m^2, ALT level >2.5N and triglycerides >171mg/dL; while for MS, BMI >40kg/m^2, triglycerides >179mg/dL and fasting glucose >121mg/dL. IR was significantly associated with NASH (HOMA 12.11±3.4) and MS (HOMA 2.3±3.3).

Conclusions: Our findings suggest that NASH and MS are highly prevalente in obese subjects.

IR is significantly associated with NASH and MS, due to the important role of these conditions in its pathogenesis.

THE ROLE OF DIABETES MELLITUS AND OBESITY ON SURVIVAL IN PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC) IN A GEOGRAPHICAL ROMANIAN REGION: POTENTIAL ROLE OF LEPTIN

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Background and aim: Recent data suggest a strong link between chronic inflammation, angiogenesis, and the development of cancer. Few data are known about the effects of adipokines in HCC. Our aim was to assess the influence of diabetes and obesity on survival in patients with HCC and the

correlations between serum leptin, in HCC and VEGF, as a marker of angiogenesis.

Methods: 91 consecutive patients (36 women and 55 men, mean age 68.5 ± 11.25 years) with HCC were included. Leptin were assessed in the serum of 60 patients with HCC and 30 pacients with liver cirrhosis. The expression of VEGF and microvessel density (MVD) in 12 HCC were also analysed. The result of serum leptin was further correlated with VEGF expression, intratumour MVD and clinicopathological characteristics.

Results: Mean survival was 10.9 +/- 9.1 months; there was no significant difference regarding age distribution, gender ratio, diabetes mellitus and obesity (p>0.05). Obesity and diabetes were not significantly correlated with survival (p=0,83 and p=0,73, respectively). Serum leptin values were increased in 60.3% of patients with HCC and were significantly correlated with intratumour MVD, (p< 0.05), but not with VEGF expression. No marked correlation was seen between leptin expression and clinicopathological characteristics.

Conclusion: Diabetes and obesity were not significantly correlated with survival. High leptin expression was associated with an increased intratumour MVD and thus may be associated with HCC development. Further studies are needed in order to assess the role of leptin in the development of hepatocarcinogenesis.

EFFECTIVENESS AND SAFETY OF ROSIGLITAZONE IN THE TREATMENT OF TYPE-2 DIABETES WITH NON-ALCOHOLIC FATTY LIVER: A ONE-YEAR CONTROLLED STUDY

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Aims: Insulin-sensitizing rosiglitazone (R) is well known to be effective in type-2 diabetes but interest is arising about its benefits on non-alcoholic fatty liver (NAFLD) linked to diabetes and/or metabolic syndrome.

Methods: Sixty-six type-2 diabetics in poor glycaemic control on either sulphonylurea (S) or metformin (M) were randomized to add R 8 mg or M/S to previous therapy: two groups (36:30) matched for age (62.6 vs 62.8 yr), BMI (29.8 vs 29.5 kg/mq), mean blood pressure (MBP)(106.3 vs 105.8 mmHg), HbA1c (9.3 vs 8.8%), AST and ALT. Features were evaluated at baseline and after 1-yr treatment; NAFLD was assessed and graded (score 0-3: absent, mild, moderate, severe) with ultrasonography by two blind experienced operators.

Results: Highly significant decrease in HbA1c-level in both groups (R: -1.10±1.2 p<

0.0001; S+M: -1.07±1.4 p< 0.0004); slight but significant weight gain (+1.7±3.6 kg p=0.014) and significant decrease of MBP (-6.8±12.0 p=0.005), AST (19.0±6.2 vs 24.7±12.0 p=0.017) and ALT-level (23.0±7.9 vs 36.8±16.8 p< 0.0001) in R-group, AST (p=0.009) and ALT (p=0.0005) being highly different within the groups. US-findings of NAFLD were detected in 49 non-heavy alcohol drinkers, 28 in R-group and 21 in S+M-one. After R a new blind ultrasonography assessed improvement in 17, no change in 8 and worsening in 3 (p=0.004); no significant change after S+M. R-treatment was well-tolerated and safe.

Conclusions: R plus either S or M improves glycaemic control such as S+M combination but only R is able to lower blood pressure and to improve NAFLD-imaging due to its effect on insulin-resistance.

SERUM FERRITIN LEVELS ARE SIGNIFICANTLY RELATED WITH THE PRESENCE OF NAFLD AND HYPERINSULINEMIA

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Background: Previous studies provide results regarding the relationship of an association between the serum ferritin level and the metabolic syndrome.

There are few evidences related to NAFLD.

Aim: To asses the mediating NAFLD role in the association between serum ferritin and the metabolic syndrome.

Methods: A cross-sectional study was performed. Exclusion criteria were any known etiology for secondary NAFLD. Participants underwent an abdominal ultrasound (US), biochemical tests, and anthropometric evaluations.

Results: Sixty-four subjects were included in the analysis. Serum ferritin was higher in the NAFLD group (p< 0.001). After adjusting for age and gender, we found significantly changes between increased ferritin levels and the following variables : hyperglycemia,abdominal obesity, hypertriglyceridemia, hyperinsulinemia, HOMA, and the metabolic syndrome itself, while for NAFLD, only abdominal obesity and hyperinsulinemia were significantly associated with serum ferritin level. The interaction between NAFLD and hyperinsulinemia, according to the multivariate analysis, was a strong predictor of serum ferritin (*P*=0.005).

Conclusions: The association between serum ferritin and the metabolic syndrome is mediated by NAFLD. The interaction between NAFLD and hyperinsulinemia is a major determinant of serum ferritin levels.

CORRELATIONS BETWEEN THE ACTIVITY LEVEL/GRADING OF VIRAL HEPATITIS AND ALTERATIONS IN LIPID AND GLUCOSE METABOLISMS

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Background and aims: Viral hepatitis may induce important alterations in glucose and lipid metabolisms.The study aims to uncover the answer to two major questions. Are there any possible correlations between the severity of the hepatic lesions and lipid and lipoprotein plasma levels? To what extent is the liver involvement linked to the impaired glucose tolerance?

Materials and methods: The present investigation included 53 patients (30 female, 23 male, mean age 45.5 years) who underwent a complete clinical examination and the following laboratory tests: liver function tests, markers for viral hepatitis, protein electrophoresis; we have also investigated glucose and lipid metabolisms by means of fasting glucose level, urinary glucose, oral glucose tolerance test, total cholesterol level, HDL and LDL fractions and triglyceride level.

Results: In the group we have studied, 30 patients (57%) were positive for B viral hepatitis, 19 patients (36%) had type C viral hepatitis and 4 patients (7%) had positive markers for both B and C hepatitis viruses. We also found an IGT in 7 persons; 14 participants presented with high cholesterol level, 5 participants had high triglycerides and in 19 participants we found an insolated decrease of HDL cholesterol while 11 others had low total cholesterol level.

Conclusions: The alterations in glucose metabolism have been correlated with a poor prognosis of any type of viral hepatitis.

Plasma levels of lipid fractions do not correlate with the activity / grading of chronic hepatitis.

Low cholesterol level appears to be linked to severe hepatic lesions.

CORRELATION BETWEEN THE METABOLIC SYNDROME AND FATTY LIVER AMONG CHILDREN AND ADOLESCENTS

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Introduction: Metabolic syndrome and nonalcoholic fatty liver disease (NAFLD) are common in overweight youths. We aimed to study the correlation of metabolic syndrome and NAFLD in a population-based sample of children and adolescents.

Methods: The study population was selected from school students in Isfahan,the second large city of Iran. In addition to anthropometric measurements and liver sonography, blood pressure, fasting blood sugar, lipid profile, and liver function tests were examined.

Results: The study comprised 1110 children aged 6-18 years, and consisting of 438 (39.5%) normal weight, 377(34%) overweight and 295(26.6%) of obese individuals. Overweight and obese children were much more likely to have elevated alanine aminotransferase (ALT), aspartate aminotransferase(AST) and alkaline phosphatase (ALP) levels than normal weight peers. High serum triglycerides concentrations were significantly associated with elevated ALT, AST and ALP.Having metabolic syndrome increased the chance of elevated ALT levels and sonographic fatty liver. The unadjusted odds ratios for elevated ALT were 1.06 (95% CI : 0.05, 2.19), 1.61 (95% CI : 0.79, 3.27), and 3.69 (95% CI : 1.61, 8.45) for individuals with 1, 2, and ≥ 3 risk factors. The adjusted odds ratios for elevated ALT were significant for the subjects with ≥ 3 risk factors [3.69 (95% CI : 1.61, 8.45)].

Conclusion: Metabolic syndrome was correlated with fatty liver among children.Overweight and abdominal obesity were the most important predictors of fatty liver, .Preventive measures for chronic diseases should be taken into account from early life.

NONALCOHOLIC FATTY LIVER DISEASE - A RISK FACTOR FOR MICROALBUMINURIA IN TYPE 2 DIABETIC PATIENTS

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Background: In diabetic patients studies have suggested that nonalcoholic fatty liver disease-NAFLD may increase the risk of microalbuminuria and thus that of chronic kidney disease(CKD). The pathogenetic link between these conditions could be proinflammatory cytokines secreted by the liver.

The aim of our study was to assess the presence of microalbuminuria in diabetic subjects with nonalcoholic fatty liver disease (NAFLD) compared with diabetic patients without NAFLD and to correlate this with inflammatory markers such as high sensitive C- reactive protein (hsCRP).

Material and methods: The study was conducted on 75 diabetic subjects with ultrasonographical NAFLD, in which alcohol consumption and other causes of chronic liver disease have been excluded. We excluded smokers, hypertensive and known renal disease. The control group consisted of 70 diabetic patients, matched for age and gender, without ultrasonographical evidence of NAFLD.

In all subjects we measured height, weight, BMI, fasting glucose, HbA1c, total cholesterol, LDL and HDLcholesterol, triglycerides, serum transaminases, hsC-reactive protein and microalbuminuria. A p-value< 0,05 was considered statistically significant.

Results: Microalbuminuria was significantly more frequent in subjects with NAFLD than in controls(12,7%vs 7,8%,p< 0,05). Microalbuminuria was positively correlated with waist to hip ratio, HbA1c, triglycerides, hsCRP and negatively correlated with HDL in subjects with NAFLD.

Conclusion: NAFLD is positively correlated with microalbuminuria-marker of early stage CKD, in diabetic patients. This seems to be related to higher levels of proinflammatory factors released by the liver, such as hsCRP. Diabetic patients with NAFLD had significantly higher levels of HbA1c, witnessing a poorer glycemic control.

EFFICACY OF TREATMENT BY SYMBIOTIC PREPARATION BIFTOP FOR STEATOGEPATOSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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The investigation is directed at the determination of the efficiency of the correction of steatogepatosis symptoms for patients with type 2 diabetes mellitus by symbiotic biftop. Steatogepatosis development is connected with diabetes mellitus, the degree of abdominal obesity since free fatty acids production increases in the result of intensified lipolysis of visceral fat that promotes the development of lipotoxicity and dyslipidaemia.

All the patients have been defined carbohydrate metabolism, blood lipid spectrum before the treatment and after two weeks of conducted therapy.Investigating patients were divided into 2 groups: the fist control group patients (n=22) received only standard therapy and second group of patients (n=30) was added biftop to the standard therapy twice per day. The following indices dynamics was observed in comparison with the initial data: the level of TC for patients who received biftop fell by 12,8 % (Δ0,25±0,05) while for the control group only by 8,0% (Δ0,55±0,12); triglycerides - reduced by 28,6%(Δ0,65±0,03), and patients who received standard therapy only by 10,0% (Δ0,12±0,02); HDL rose in dynamics by Δ0,13±0,03 and for the control group it rose only by Δ0,05±0,01. It was achieved the fall of the level of LDL for the second group of patients by Δ0,37±0,10, and for the control group only by 0,04±0,02(p< 0.05 for all the indices).

The expediency of using basic therapy including symbiotic (biftop) has been proved for the complex therapy of patients with diabetes mellitus type 2 with steatogepatosis for better compensation of compensation of carbohydrate andfat metabolism.

THE RELATIONSHIPS BETWEEN BILE ACIDS AND HYPERTENSIVE HEART IN HYPERTENSION WITH AND WITHOUT DISORDER OF LIVER FUNCTION STATE

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Objective: The intercommunication between changes of level of bilious acids in plasma, indices of lipid exchange and function of the liver in atherogenesis was related.Aim. To study the influence of bile acids (BA) signs on echocardiography (ECG) parameters in patients(pts) with hypertension stage II(H) and associated with chronic hepatitis(CH) and liver cirrhosis(LC).

Design and methods: 272 pts and 20 healthy persons have been studied. The pts were divided into three groups(gr): 1 gr - 185 pts with H; 2 gr - 49 pts with H associated with CH; 3 gr - 38 pts with H associated with LC. Left ventricular myocardial mass(LVMM), LVMM index(LVMMi), relative LV wall thickness(RLVWT), end systolic diameter(ESD), end diastolic diameter(EDD), stroke volume(SV) and ejection fraction(EF) were examined by using M-mode ECG. The levels of free and conjugate BA were determined by chromatography method.

Results: The direct correlation was found between the concentration of BA in serum and ESV, EDV, SV, LVMM, LVMMi in pts with H(r=+0,54;+0,58;+0,61;+0,49;+0,48;p< 0,05-accordingly) and correlation indices increased in pts with H associated with CH(r=+0,57;+0,63;+0,65;+0,52;+0,48; p< 0,05) and LC (r=+0,58;+0,65;+0,68;+0,57;+0,45;p< 0,05). The negative correlation was revealed between the concentration of BA in serum and EF in pts with H(r=-0,62;p< 0,01), in pts of 2 gr(r=-0,64;p< 0,01) and of 3 gr(r=-0,66;p< 0,01).

Conclusions: Obtained data reflect indicate on relationships between level of BA and echocardiography parameters of hypertensive heart. Increasing concentration of BA in serum has a negative influence not only on liver, but on myocardium in patients with H associated with CH and LC especially.

RELATIONSHIP BETWEEN ULTRASOUND FINDINGS OF FATTY LIVER CAUSED BY NON-ALCOHOLIC FATTY LIVER DISEASE, AND OBESITY AS DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME

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Introduction: Fatty liver (FL) is common incidental finding on ultrasound (US) examination. Non-alcoholic fatty liver disease (NAFLD) is consider as associate characteristic of metabolic syndrome (MS).

Methods: US examination of patients, by the same operator (autor), in 3 month period(total 362) was done and subgroup of those with US finding of FL was made. After excluding alcohol intake as cause of FL(CAGE protocol) and advanced examination biochemic (fasting glucosae, AST, ALT, GGT, bilirubin, Fe, cholesterol, HDL, LDL, trigliceride), and virusology(in the presence of elevated levels of AST and ALT), the diagnose of NAFLD was established (total 102). Waist circumference(WC), body high and body weight was measured to them, and BMI was calculated.

Results: Obesity 1) refered to BMI(>30) had 43(42,3%) of man and 48(49%) of woman, 2) refered to NCEP ATP III criteria had 34(65,38%) of man and 46(88,46%) of woman, and 3) refered to IDF criteria had 50 (88%) of man and 50 (92%) of woman with US findings of FL.

Conclusion: US findings of FL caused by NAFLD,in higher percentage correlate with visceral obesity(which represent diagnostic criterium for MS) then with obesity measured by BMI, so finding of FL on US is indication for further examination of other components of MS and eventual presence of cardiovascular disease.

VIRAL AND METABOLIC FACTORS OF STEATOGENESIS AT PATIENTS WITH CHRONIC HEPATITIS C

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Liver steatosis (LS) as a sign of metabolic syndrome (MS) has an incidence of 30-40% among the patients infected by hepatitis C virus (HCV).

Methods: 49 patients with CHC were observed. Exclusion criterion was the alcoholic genesis of LS. Expression intensity of MS components and LS stages were investigated and compared before and after the antiviral therapy (AVT) course and compared with a type of viral response to AVT.

Results: It was shown that a rate of LS at patients with CHC is 38.8%. 7 patients from 19 those with LS had other clinical signs of MS. Analysis of hereditary anamnesis and CHC course allowed to testify that at 36.8% patients the LS might be caused to genetic determinants whereas in 63.2% patients it could be considered as being HCV-induced. All 19 patients were treated with pegylated interferon and ribavirin. Among them, a sustained virological response (SVR) was achieved 68.4% patients, including 5 patients with 3a genotype (83.3%). Only patient with CHC caused 3a genotype HCV, which did not reach SVR, had all signs of MS present. Upon comparison of SVR rate in patients with CHC of non-3a genotype, a combination of LS and MS led to significantly decreased SVR rate (25% patients) than the LS alone (77.7% patients).

Conclusions: The majority of LS cases in patients with CHC is due to HCV-induced but not hereditary-based mechanisms of MS formation. The negative effect of MS on the efficiency of AVT is most pronounced in patients with non-3a genotypes of HCV.

STEATOSIS AND STEATOHEPATITIS - DIFFERENT MANIFESTATION OF THE SAME DISEASE?

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Objectives: Non-alcoholic fatty liver disease is an organ manifestation of the metabolic syndrome. It encompasses simple steatosis (NAFL) and steatohepatitis (NASH). The latter one may progress to liver cirrhosis.

Aim: Comparison of glucose and lipid parameters between patients with NAFL and NASH to see whether these conditions have the same underlying pathomechanism.

Methods: 65 patients with steatosis found in ultrasound examination were included. A diagnosis of NAFL and NASH was established on liver biopsy. Excessive alcohol consumption, chronic HCV and HBV infections as well as Wilson´s disease were excluded. BMI, fasting glucose, fasting insulin level, HOMA-IR, lipid parameters, liver enzymes (ALT, AST, GGTP), leptin and adiponectin were determined in every case and mean values were compared between the two groups. Statistical analysis was performed.

Results: NAFL was found in 49 and NASH in 16 patients. BMI, lipid parameters and aminotransferases were comparable in both groups, whereas GGTP level was significantly higher in NASH (106.5 v. 217.8, p< .02). Patients with NAFL had significantly higher fasting insulin level (34.14 v. 17.07, p< .01) but insignificantly higher HOMA-IR index (8.11 v. 4.76, NS). In contrast, fasting glucose was significantly lower in NAFL patients (91.0 v. 110.3, p< .02) and it was abnormal in 4.9% of patients v. 41.7% in the NASH group. Adiponectin was comparable and leptin was significantly higher in the NASH group (42.3 v. 24.8, p< .02).

Conclusions: Insulin resistance is caused by hiperinsulinemia in NAFL and by hiperglycemia in NASH. NAFL and NASH can develop via a different mechanism.

KERATINOCYTE-DERIVED CHEMOKINE IN OBESITY: EXPRESSION AND ROLE IN ADIPOSE MACROPHAGE INFILTRATION AND GLUCOSE HOMEOSTASIS

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Aims: Obese adipose tissue (AT) is associated with chronic inflammation and we hypothesized that the keratinocyte-derived chemokine (KC), the mouse ortholog of human IL-8, plays a role in obesity-mediated AT inflammation and the subsequent manifestation of insulin resistance (IR).

Methods and results: KC expression is increased in the AT and plasma of genetic (ob/ob) and high fat diet-induced obese (DIO) mice. Obesity-induced KC expression occurs primarily in stromal vascular cells and not in adipocytes, and is high in preadipocytes and decreases during adipogenesis. KC does not affect adipogenesis but increases adipocyte expression of inflammatory factors. Importantly, we show that the KC receptor CXCR2 plays an important role in AT macrophage recruitment and development of IR in a DIO model in chimeric mice lacking CXCR2 in their bone marrow.

Conclusions: These studies suggest that KC and its receptor CXCR2 are potential targets for the development of new therapeutic approaches for treatment of obesity-related insulin resistance, type II diabetes and related cardiovascular diseases.

METFORMIN IN YOUNG OBESE PRESENTING WITH INSULIN RESISTANCE

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To assess Metformin could be helpful in young obese presenting with insulinoresistance (IR), 407 overweight/obese children and adolescents were invesitigated (mean age 12 years). 61 (15% - mean age 11,6 years) had a fasting insulin (FI) >20µU/ml. Body Mass Index (BMI) was ranging 21 to 51 kg/m2 (mean: 30,2). In excess BMI/percentile 50 for age and gender was 126% to 271% (mean: 173,5%). Diabetes 2 was documented in 44 families (first and/or second degree parents). OGTT was performed in 55 patients. It was normal in 30. In 25 abnormal high insulin response was found (insulin >150µU/ml at any time and/or >75µU/ml at 120 minutes) reflecting insulin resistance (IR) (Reaven, J Clin Endocrinol Metabol 1996). Three had glucose intolerance (GI). In 22 Metformin was prescribed (GI patients included): progressively 1X500mg to 3X500mg/day.Treatment and follow up was immediately discontinued in 7. In the 15 others, Metformin was taken 3 to 21 months. Efficacy regarding controls in FI, OGTT and clinical evolution is presented and discussed. In adults, lifestyle positive changements and BMI reduction are better contributors than the Metformin regarding pre-diabetes (Diabetes Prevention Program Research Group, N Engl J Med 2002). However adolescence is an age at risk for insulin sensitivity: Metformin could be transitory helpful in young obese presenting with IR.

IRON STATUS, SERUM AND URINARY HEPCIDIN LEVELS AND METABOLIC CONTROL IN OBESE PRE-MENOPAUSAL WOMEN

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The hypoferremia of obesity is characterized as a functional and inflammation driven phenomenon. Hepcidin, a key iron-regulatory hormone, controls systemic iron metabolism by regulating the iron transporter ferroportin and is influenced by inflammation, circulating and stored iron, and erythropoiesis. Hepcidin levels increase with inflammation resulting in a down-regulation of ferroportin and decreased iron bioavailability. Produced mainly in the liver, hepcidin mRNA and protein were found in human adipose explants with increased levels in obese. However, systemic hepcidin levels and its influence on iron status in obesity have yet to be investigated.

Objective: Evaluate the association of obesity and inflammation with iron status and hepcidin levels in obese(BMI> 37) and lean hemoglobin matched females(BMI< 25).
Methods: Pre-menopausal women (n=55) provided fasted blood, first-void urine, anthropometric, demographic, dietary and physical activity (PA) measures. Assays included serum and urinary hepcidin, as well as iron status, metabolic and inflammatory markers. Basic comparisons, correlations, multivariable linear modeling predicting hepcidin and stratified analysis by iron and BMI were examined.

Results: Obese women had higher serum($p \leq .0001$) and urinary($p=.0003$) hepcidin compared to lean women despite similarities in iron profile, diet, PA, and demographics. The strongest predictors of serum hepcidin included waist circumference, sTFR, and CRP(adj.r^2=.55). In stratified analysis, obese women with low iron had higher HOMA-IR (p=.003), waist circumference(p=.020), and marginally higher CRP compared to iron-normal obese.

Conclusion: Central adiposity and inflammation are associated with higher levels of hepcidin which can decrease iron bioavailability. Metabolic control in obesity may play a role in maintaining normal iron status.

ACE GENE POLYMORPHISMS, ANTHROPOMETRICAL AND BIOCHEMICAL PARAMETERS IN GROWING-SLIM FEMALES

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Introduction: Many genes have been implicated in determination of diabetes and obesity, but our knowledges about the genes responsible for individual differences in weight loss after physical intervention are poor. One of the candidate genes is a gene for angiotensine converting enzyme (ACE) ant its insertion/deletion (I/D) polymorphism.

Aim: The aim of the study was to analyze ACE I/D variant in 93 unrelated non-diabetic females. There were 17 II homozygotes and 74 D allele carriers.

Material and methods: DNA was isolated from frozen EDTA blood and I/D polymorphism was analyzed using two steps PCR. Before and after 9 weeks of training programme, biochemical (plasma lipid levels) and anthropometrical measurements were performed. The participants were advised (and supervised) to sustain a heart rate of 115-145 beats (according to age) per minute within 60 minutes of exercise 3 times per week.

Results: The changes between anthropometrical and lipid parameters did not differ between females with different ACE genotypes. Nevertheless, in D allele carriers, plasma levels of TG decreased after 9-weeks physical training, but II homozygotes have higher plasma levels of TG after intervention (p= 0.02).

Conclusion: ACE I/D variant has no effect on anthropometrical and most biochemical parameters changes after physical training. But, in contrast to the D allele carriers, I/I homozygotes have after training higher plasma TG levels and their energy supply for muscle performance could be so improved.

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THE EPIDEMIOLOGY OF OBESITY AND METABOLIC SYNDROME IN INDIA

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Aim: To assess the burden of overweight and its association with cardiovascular risk factors in urban India.

Methods: Data was obtained from a series of cross sectional surveys done in 2007-2008 in Chennai, representative of the general population. The study subjects were categorized as normal, overweight and obese based on BMI for analyzing the parameters.

Results: The overall age adjusted prevalence of overweight on 2021 subjects aged ≥18 years was 28.5% (CI = 26.2-30.8) and Obesity was 10.7 % (CI= 9.3-12.2). Prevalence of overweight and obesity was higher among females in all age groups. .Hyperglycemia, hypercholesterolemia, hypertriglyceridemia, hypertension and diabetes were significantly higher with increasing BMI (p< 0.05). The effect of increasing BMI from overweight to obesity showed significant increase especially in diastolic blood pressure (2.4, p = 0.017) and cholesterol (2.9, p = 0.003). The percentage increase in prevalence of central obesity for women is 62.1% since 1995, whereas it was only 13.9% for men. Prevalence of metabolic syndrome increased according to increasing BMI. It was 21.7% , 48.6% and 60.0% among group I (BMI18.8-24.9kg/m 2) , group II(BMI 25.0 - 29.9 kg/m 2) and group III (BMI > = 30 kg/m 2) respectively. Variables showing strong association with metabolic syndrome were overweight and obesity, Increasing age, hypercholesterolemia and family history of hypertension.

Conclusion: Obesity and metabolic syndrome showed very high prevalence. Female gender is at high risk for obesity and cardiovascular diseases in future. There is an urgent need for intervention strategies through multi - disciplinary approach.

THE RELATIONSHIP BETWEEN VISCERAL OBESITY IN PATIENTS WITH METABOLIC SYNDROME AND SERUM CONCENTRATIONS OF CRP, IL-6 AND VISFATIN

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Objective: To investigate the relationship between serum concentrations of C-reactive protein (CRP), Visfatin, and interleukin 6 (IL-6), with obesity and visceral adiposity in patients with metabolic syndrome (MetS).

Design and method: A total of 37 patients with MetS and 37 age matched controls were included (mean age 46.35 ± 1.6 years). Metabolic syndrome was defined by the criteria of the international diabetes federation 2005. Anthropometric and biochemical profiles, including high-sensitivity C-reactive protein (Hs-CRP), interleukin-6 and visfatin were measured. Data were compared between groups by using t-test. Pearson´s correlation was used to evaluate the relationship between continuous variables. P values less than 0.05 was considered as statistically significant.

Results: In patients with MetS, CRP and IL-6 were significantly correlated with BMI, waist circumference and and waist-hip ratio.Visfatin level was significantly (P< 0.05) lower in metabolic syndrome patients compared with controls (log visfatin: 1.74 ± 0.27ng/ml vs. 1.86 ± 0.13 ng/ml, MetS vs. control group respectively). There was no correlation between visfatin levels and any anthropometric parameters in patients with metabolic syndrome or control group.

Conclusions/ interpretation: Serum visfatin was deacreased in patients with MetS. Therefore it seems that Visfatin can not be considered as a new proinflammatory adipocytokine in metabolic syndrome. But the positive associations of obesity and visceral adiposity with elevated cytokine levels suggest the importance of reducing obesity and visceral adiposity to prevent the risk of coronary disease.

Keywords: Metabolic Syndrome; Obesity; Visceral adiposity; CRP; Visfatin; IL-6.

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND BLOOD PRESSURE IN OBESE SUBJECTS

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Aims: The renin-angiotensin-aldosterone system has been proposed to play a major role in obesity-related hypertension. Although obesity is closely related to hypertension, not all obese subjects have hypertension. The aim of this study was to investigate the relationship between the renin-angiotensin-aldosterone-system and blood pressure (BP) in obese subjects.

Methods: In a cross-sectional study design, we studied 112 obese men, defined as body mass index > 30 kg/m^2, free of major cardiovascular disease and not taking any medications. BP was measured accurately by 24-hr ambulatory BP measurements. Blood was drawn in the supine position, and plasma angiotensinogen, aldosterone, renin, angiotensin I, and angiotensin II were determined. A 24-hr urine collect was used to measured 24-hr sodium excretion.

Results: In total, 57 men were hypertensive, defined as 24-hr mean BP ≥130/80 mmHg, and 55 men were normotensive, defined as 24-hr mean BP < 130/80 mm Hg. Compared with the normotensive group, the hypertensive group had significantly higher mean (±SD) levels of angiotensinogen (897±183 vs. 980±214 nmol/L; P= 0,032) and aldosterone (97.5 ±42.3 vs. 129.3±71.2 pmol/L; P=0.008), whereas there were no significant differences in the other variables measured. In a multiple linear regression analysis, including age, body mass index, waist to hip ratio, angiotensinogen, aldosterone, and 24-hr sodium excretion, both angiotensinogen and aldosterone were significantly associated with 24-hr systolic BP with regression coefficients (95% confidence intervals) of 0.017 (0.002-0.032; P=0.027) and 0.055 (0.004-0.106; P=0.034), respectively.

Conclusions: In the obese male population, angiotensinogen and aldosterone were significantly associated with BP.

NON-PHARMACOLOGICAL INTERVENTION FOR WEIGHT GAIN MANAGEMENT IN SEVERE MENTAL DISORDERS: RESULTS FROM A LARGE MULTICENTRIC STUDY

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Background: A high prevalence of metabolic abnormalities has been observed in patients with severe mental disorders and schizophrenia. Obesity interventions studies in this population are scarce.

Objective: Evaluate the effectiveness of a non-pharmacological intervention in controlling body weight and metabolic parameters.

Method: An open, multicentric, longitudinal study was conducted on 57 mental health services in 34 cities in Brazil. Patients included in this study received a 12-week 1-hour group intervention. Topics such healthy nutrition, lifestyle, physical activity and self-esteem were discussed with patients and their relatives. Weight, high, waist circumference and blood pressured were measured before and after the intervention. A total of 656 patients participated in the intervention. All of them were in use of some antipsychotic and/or mood stabilizers and had some concern about weight gain.

Results: 512 patients completed the intervention. A significant weight loss (0.5 ± 3.4kg, p< 0.000) and a significant BMI reduction (0.2±1.4kg/m^2, p< 0.007) were observed. There was a marked increase in physical activity after the intervention, at the baseline 55.2% of the patients were enrolled in

some kind of exercise program, after the intervention, 72.8% were regularly practicing physical activity.

Conclusion: To our knowledge, the Brazilian Wellness Program is the largest national, multicentric, naturalistic study of a non-pharmacological intervention for severe mental disorder patients showing positive outcomes on weight gain management, reducing diastolic blood pressure and increasing physical activity. Efficacy and effectiveness studies are being conducted to further inform the implementation of the wellness intervention as public mental health policy.

THE EFFECT OF REDUCTION DIET OF OVERWEIGHT, LEVELS GLUCOSAE AND INSULINAEMIA IN OBESE PATIENTS

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Introduction: Insulin resistance is a state of impaired insulin action. The main cause is central obesity. Excess abdominal adipose tissue releases increased amounts of tumor necrosis factor α and free fatty acids, which directly affect insulin signaling, diminish glucose uptake in the muscle, drive exaggerated triglyceride synthesis and induce gluconeogenesis in the liver. They represent strong risk factors for diabetes mellitus type 2 in obese individuals.

Objective: The purpose of the study was to establish the effect of reduction diet on overweight, glucose concentrations and insulin secretion in obese patients.

Methods: We included 30 obese patients, over 54 years, who were treated on the Department for Internal Disease in Kosovska Mitrovica. They were treated with reduction diet, 1800 kcal /day and increased physical activity. After six months of treatment blood biochemistry was tested again and BMI was also determined.

Results: The study included 30 obese patients, 23 women (69%) and 7 men (21%). Reduction diet and increased physical activity significantly lowered BMI (BMI - 31.02 kg /m^2-28.7 kg/m^2), waist circumference of mean value 98±0.55 -93.12 cm, for women and 106± 0,89-10±0,95 cm for men. During the therapy the glycaemia decreased (7,25 -5.45 mmol/l), as well as insulinaemia mean value 27,14 -23, 69 ml U/I.

Conclusion: Dietary modification and life style changes, may be the first therapeutic option in prevention of the diabetes mellitus type 2. Reduction diet produces beneficial changes in glycaemia control, and moderates weight, lipids and insulinaemia.

Keywords: Diet, obesity, insulinaemia.

THE INVESTIGATION OF THE RELATION BETWEEN THE SIZE AROUND WAIST AND THE AREA OF VISCERAL FAT. ARE THERE SOME FALES NEGATIVE SUBJECTS?

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Aims: In Japan, the area of visceral fat is essential to diagnose Metabolic Syndrome (MS). We examined the relation between the size around waist and the area of visceral fat measured by CT scanning, and investigated the rate of false negative subjects.

Methods: In Katsura Health Care Center, we examined FBS for the 9911 subjects during the 24 months. Among the impaired hyperglycemic subjects

(110mg/dl< FBS≦125), OGTTs were performed for the 154 subjects and

abdominal CT scannings were performed for the 102 subjects (male female ratio was 75/27) who had wished further examinations.

Results: In 75 male subjects, 53 subjects (70.7%) had measured not less than 85cm around the waist, 59 subjects (78.7%) had the visceral fat area of 100cm^2 or over. In 27 female subjects, 4 subjects (14.9%) had measured not less than 90cm around the waist, 13 subjects (48.1%) had the visceral fat area of 100cm^2 or over. By the measurement around the waist, 11 males (19.3%) and 10 females (76.9%) were estimated not having visceral fat obesity, though these subjects were judged having visceral fat obesity by CT scanning. Ten males of that 11 males (91.0%) and 7 females of that 10 females (70.0%) were diagnosed as MS falsely in the negative.

Conclusions: The measurement around the waist was considered not to have good correlation with the visceral fat area especially in females, and to have the potentialities to cause the overlooking the progressions of MS.

COMPARISON OF THE EFFECTS OF ABDOMINAL AND OVERALL OBESITY ON INSULIN RESISTANCE ACCORDING TO SEX

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Background: Although both overall obesity and abdominal obesity have been identified as causal factors for diabetes and are known to act as independent parameters, the relative usefulness of each measure in the prediction of type 2 diabetes remains controversial. This research compares the predictive value of the abdominal obesity indicator, WC, and the overall obesity indicator, BMI, among men and women in regard to type 2 diabetes.

Methods: This study used data collected from 4,400 households selected by a stratified multistage probability sampling method during the 2001 Korea National Health and Nutrition Examination Survey (KNHANES). The final study sample included 5,500 subjects over 30 years of age who had completed the health examination required for the analysis of the health interview and health behavior surveys.

Results: Both men and women showed significant differences in FBG or HBA1C levels based on abdominal obesity irrespective of BMI. However, the presence of overall obesity among men with abdominal obesity was not significantly correlated with FBG or HBA1C levels while the presence of overall obesity among women with abdominal obesity was significantly different in regard to FBG or HBA1C levels.

Conclusions: Both WC and BMI emerged as measures of risk factors for diabetes and hyperglycemia among women while only WC emerged as a risk factor for diabetes among men.

Keywords: Abdominal obesity, Obesity, Insulin resistance, Sex difference.

BODY COMPOSITION AND VITAMIN D LEVELS IN WOMEN WITH TURNER´S SYNDROME

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Introduction: Turner´ syndrome (TS) results from partial or complete X chromosome monosomy. TS women have an increased risk of obesity. Previous studies have demonstrated that hypovitaminosis D is associated with obesity in women with normal karyotype.

Aim: The aim of our study was to investigate the relationship between 25-hydroxyvitamin D (25OHVD) and body composition in TS women.

Method: A retrospective audit of TS women attending the TS Long term Care clinic was conducted. Data collected included clinical, body composition (assessed by dual X-ray absorptiometry (DXA) scan) and serum 25OHVD (within 3 months of DXA scan). Females aged < 15 years or body mass index (BMI)< 20 were excluded.

Results: 14/38 women, aged 15-59, were eligible for analysis. Group median BMI and percent fat mass were 25.7 (range 20-37.5) and 37.3% (range 20.7-49.8%) respectively. Although 6/14 women had normal BMI (20-25), fat mass greater than 30% was observed in 10/14 women. As two different 25OHVD assays were used, women were classified as 25OHVD replete (level in normal range) or 25OHVD deficient (level below lower limit normal range). There was no significant difference between the 2 groups in regard to age, BMI, fat mass or total body mass.

Conclusion: This study demonstrated that fat mass is increased in women with TS and suggests that DXA percent fat mass may be superior to BMI in evaluating fat status. In this study fat mass was not associated with vitamin D status which may reflect the small sample size or be associated with the TS phenotype.

INFLUENCE OF LEPTIN ON DEVELOPMENT OF LEFT VENTRICULAR REMODELING IN HYPERTENSIVE PATIENTS WITH OBESITY

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Aim: The aim of the study was to investigate plasma leptin levels in hypertensive patients with obesity depend on left ventricular (LV) remodeling type.

Methods: 106 persons (46 male, 60 female) of 49±12.5 years old age were examined. Observed persons were divided into three groups: 71 (67%) patients with arterial hypertension (AH) accompanied by obesity (basic group); 15 (14%) patients with AH without obesity (comparison group); 20 (19%) healthy person (control group). Anthropometric parameters, plasma leptin levels by ELISA were measured and echocardiography was performed.

Results: Plasma leptin level in basic group patients (21.78±1059 ng/ml) were statistically higher as compared with comparison group patients (18.47±1.09 ng/ml; $p< 0.05$) that confirms possible role of this hormone in the pathogenesis of AH and obesity. Concentric LV hypertrophy and normal LV geometry prevailed in hypertensive patients with obesity. Close correlations between interventricular septum thickness and plasma leptin levels ($r=0.51$; $p< 0.05$), body mass index ($r=0.50$; $p< 0.05$) were found in basic group hypertensives with obesity. Also relationships between LV myocardium mass index and plasma leptin levels ($r=0.30$; $p< 0.05$), body mass index ($r=0.27$; $p< 0.05$) were revealed in basic group. Obtained data can confirm hypothesis about leptin role in the development of LV myocardium alterations in AH.

Conclusion: Our results suggest that elevated plasma leptin concentration is associated with increased myocardium wall thickness depend on body mass index in hypertensive patients.

ALTERATIONS IN PARAMETERS INDICATING INCREASED CARDIOMETABOLIC RISKS WITH BODY MASS INDEX

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Aims: We aimed to determine the alterations of some parameters with the body mass index (BMI), and to find out which parameters are much sensitive for identification and management of cardiometabolic risks.

Methods: A total of 792 female patients were taken into this study. Anthropometric measurements and body composition analyses were performed and fasting blood samples were taken for some biochemical parameters. Patients were grouped as normal, overweight, obese and morbidly obese according to their BMI.

Results: Mean age of participants were 38,07± 12,87 (15-80) year. Waist circumference (WC), WHR, waist to height ratio, body fat percent, fasting blood glucose (FBG), insulin, triglyceride, triglyceride to LDL-C ratio, ferritin, fibrinogen, HbA1c, uric acid levels and HOMA_IR increased but HDL-C levels decreased significantly while BMI increasing. According to IDF metabolic syndrom definition criteria WC was only acceptable level (71.88±5.44 cm) at normal BMI (18.5-24.9 kg/m^2) group. Body fat percent was also higher (31.42 ±5.13) in overweight group (BMI= 25.0-29.9 kg/m^2) than it was expected as to referance values. Fasting blood glucose levels of all groups were lower than either IDF or NCEP ATPIII criterias for MetS. But HOMA-IR levels showed significant increase in obese (BMI: 30.0-39.9 kg/m2) and morbidly obese (BMI ³ 40.0 kg/m2) group with higher levels than 4.0 (4.11±3.01 and 5.50±3.67 respectively). While HDL-C levels of normal and overweight groups met IDF and ATPIII criterias (54.81±9.58 and 55.15±16.84 mg/dl respectively) other groups did not.

Conclusions: Findings of this study revealed that cardiometabolic risks increase markedly at BMIs higher than 30.0kg/m^2.

THE EFFECT OF MULTIDISCIPLINARY TREATMENT ON OBESITY IN RELATION TO THE METABOLIC SYNDROME IN THE PAEDIATRIC AGE GROUP

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Childhood obesity is associated with increased prevalence of hypertension, dyslipidemia and impaired glucose metabolism. The clustering of these risk factors is called the Metabolic Syndrome (MS). Diagnosis of MS in children may give an indication of those most at risk for developing diabetes and cardiovascular disease. The best accepted treatment in children with obesity is lifestyle intervention.

We evaluated the effect of our three months family-based multidisciplinary cognitive behavioural treatment on BMI-SDS and waist circumference (WC) in relation to MS as defined by the International Diabetes Federation for the paediatric age group.

After stratification on gender and ethnicity 25 children were enrolled by randomisation to the intervention group (age 13.0±1.9yr; 14M/11F; BMI-SDS 2.9±0.9; WC 90.2±10.1cm) and 22 to the control group (age 13.0±2.1yr; 9M/13F; BMI-SDS 3.0±0.6; WC 88.1±7.1cm).

At baseline there was no significant difference between groups for gender, ethnicity, puberty stage, age, BMI-SDS and WC. However prevalence of MS in the intervention group (8/25) was significant higher ($p=0.05$) vs. control group (2/22). After treatment there was a significant time effect on BMI-SDS (2.6±0.9; $p=0.00$) and WC (87.5±10.4cm; $p=0.03$) in the intervention group but not for MS (10/25). In the control group there was no significant time effect on BMI-SDS (3.0±0.8) and WC (89.7±10.7cm), however prevalence of MS had significantly increased (7/22; $p=0.02$).

Our intervention significantly improved (central) obesity. This improvement showed at leased a stabilisation of prevalence of MS. While prevalence of MS significantly increased during this period in the control group with stable measures of obesity.

THE EFFECTS OF RIMONABANT ON INSULIN SENSITIVITY AND PLASMA LIPID LEVELS IN COMPARISON WITH A HYPOCALORIC DIET

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Aim: To investigate the direct (weight loss independent) metabolic effects of an endocannabinoid CB1 blocker, Rimonabant, on insulin sensitivity and plasma lipids levels in obese subjects.

Method: In a randomised clinical trial 14 obese (BMI=33.0±1.9kg/m2, BW=86.6±6.7kg) Caucasian post-menopausal women, aged 57.8±4.7 years, were randomised to 2 treatment groups. Rimonabant group received rimonabant (20mg/d) for 13 weeks with energy intake matched to their energy requirements. Diet group achieved the same body weight loss by hypocaloric dietary intervention. Body weight, insulin sensitivity (euglycaemic-hyperinsulinaemic clamp), plasma NEFA, triglycerides and cholesterol were measured at baseline and at the end of the treatments. Energy intake was monitored by daily diet diary and was maintained in Rimonabant group.

Results: Mean body weight loss in Rimonabant group was 2.6±1.4kg (2.9±1.6% of baseline body weight, p=0.003), and in Diet group was 3.1±2.8kg (3.7±3.3%, p=0.027). This was not significantly different between two groups. Although insulin sensitivity (glucose infusion rate at steady state) increased in both Rimonabant group (5.9±16.4%) and Diet group (13.2±23.4%), this did not achieve statistical significance. NEFA levels decreased by 22.0±13.2% in Rimonabant group (0.60±0.23 vs.0.46±0.18 mmol/l, p=0.005), with no significant change in the diet group (0.65±0.23 vs.0.66±0.21mmol/l, p=0.889) (no statistical difference between two treatments). Plasma triglycerides and cholesterol did not change significantly in either group.

Conclusion: Rimonabant treatment for 13 weeks (without any reduction in energy intake) reduced body weight and NEFA levels, with no significant change in insulin sensitivity, plasma triglycerides and cholesterol levels. This effect was not significantly different from the dietary intervention.

PRE AND 6 DAY POS FASTING GLUCOSE, INSULIN AND C-PEPTIDE LEVELS IN OBESE DIABETIC PATEINTS UNDERTAKING ROUX-EN-Y GASTRIC BYPASS SURGERY

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Aim: To monitor changes in fasting glucose, insulin and C-peptide levels in obese diabetic patients undertaking gastric bypass and to look for potential parameters to help predict those who will resolve their diabetes.

Methods: Venous blood samples were taken at the day of operation and six days post operation from 127 diabetics undertaking gastric bypass surgery (GBS) at the Wakefield Hospital and were analysed for for fasting insulin, glucose and C-peptides levels at Canterbury Health Laboratories.

Results: 70% of the obese diabetic patients resolved their diabetes (FPG < 6 and HbA1c < 6) , 15% produced an intermediate response (6 ≤ FPG ≤ 7 or 6 ≤ HbA1c ≤ 7) and 15% did not resolve their diabetes (FPG > 7 or HbA1c > 7) . All patients experienced a reduction in glucose and insulin levels. C-peptide levels fell significantly in most patients along with insulin levels suggestng that reduction in the level of insulin production contributed to the reduction in the level of serum insulin. However, a small but significant number of patients either produced the same level of C-peptide as before the operation or had significantly increased levels of C-peptide despite significant falls in circulating insulin levels, suggesting improved insulin turnover.

Discussion: A small but significant number of patients had either increased or constant c-peptide levels post operatively compared to levels seen preoperatively while their insulin levels fell sharply, suggesting that improved insulin turnover may play a part in the rapid improvement in glycaemic control seen post GBS.

ASSOCIATION BETWEEN SOCIOECONOMIC FACTORS AND OBESITY IN IRAN

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The present study was conducted to determine the relationship between socio-economic factors and obesity within a population from Iran. Male and female subjects (n=4977) aged 15-65 years, were recruited from the Great Khorasan province of Iran using a cluster-stratified sampling method. Demographic and socioeconomic data were collected by questionnaire. Of the study population, 29.1% were overweight and 13.8% were obese. Being overweight and obese was significantly more prevalent among women than men and urban- compared to rural-dwellers. A high prevalence of overweight and obesity was seen among individuals who were divorced or widowed and among housewives, or individuals with poor education. Urbanization, age, illiteracy, female gender and divorced, or widowed status were significant predictors of obesity ($p < 0.001$). The association of obesity with urban-dwelling which is consistent with previous reports was also found to be the most important determinant of obesity. The prevalence of obesity in urban residents of Iran is high, particularly among poorly educated women. A community-based approach using multiple strategies including appropriate education will be required to address this problem.

INFLUENCE OF SOCIOECONOMIC STATUS ON OVERALL AND ABDOMINAL OBESITIES AND THE RISKS FOR CARDIOMETABOLIC SYNDROME AMONG FEMALE NURSES IN KANO, NORTHWEST, NIGERIA

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Socioeconomic status (SES) has been linked with overweight and obesity among men, women, and children in developing societies. The objective of this survey was to determine the effect of socioeconomic status on overall and abdominal obesities and the danger it poses on the risks for cardiometabolic syndrome among female nurses.

Two hundred and fifty-three nurses participated in this study. The participants' SES (i.e. low middle and high) were determined using standardized questionnaire, following which their overall and abdominal obesity levels were measured (BMI and waist circumference for the two obesity measures respectively). Participants were subsequently classified into risk and non-risk groups of cardiometabolic syndrome based on the obesity measures using the WHO criteria.

The outcomes indicate a significant difference on overall obesity ($F=18.689$, $P < 0.001$) and abdominal obesity ($F=43.692$, $P < 0.001$) across SES, with obesity measures increasing with increase in SES. Similarly, positive and significant correlations were found between middle and high SESs and the risk for cardiometabolic syndrome based on overall and abdominal obesities ($P < 0.05$), with an insignificant correlation between low SES and both obesity measures used.

Conclusively, increasing socioeconomic status is associated with increased risks for cardiometabolic syndrome among female nurses. Such is a mark of danger in the health sector and the society at large when those expected to serve as counselors are themselves careless about the negative consequences attached to obesity. Instituting hospital based fitness programmes might go a long way in reducing this menace.

Key words: Socioeconomic status, health professionals, cardiometabolic syndrome, obesity.

LEPTINEMIA, HYPERINSULINEMIA IN PATIENTS WITH OBESITY ASSOCIATED ARTERIAL HYPERTESSION

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The aim of our investigation was a study of possible connection between the body mass index(BMI), basal plasma levels insulin, leptin plasma levels in the patients with arterial hypertension (AH).

Material and methods: 49 patients with AH were examined. Patients were divided into four groups: 1 group - patients with AH and pre-obesity (AH+PO), 2 group - AH with 1 degree obesity (AH+OB1), 3 group - AH with 2 degree obesity (AH+OB2), 4 group - AH with 3 degrees obesity (AH+OB3). In the group of comparison 14 AH patients entered without overweight (AH), and 21 practically healthy person - control group. Plasma leptin and insulin levels were determined by ELISA.

Results: Statistically higher plasma levels of leptin and insulin were evaluated in the groups of AH+OB1, AH+OB2, AH+OB3 as compared with control and AH group ($p< 0,005$). So the mean values of leptin in control group was 6,21±1,27ng/ml; in AH group - 7,05±1,16ng/ml; in AH+PO group - 8,52±3,34ng/ml; in AH+OB1 group - 9,18±4,57ng/ml; in AH+OB2group - 10,12±4,34ng/ml; in AH+OB3 group - 13,28±3,87ng/ml. Insulin levels in control group was 5,97±2,71µIU/ml; in AH group - 7,85±4,00µIU/ml; in AH+PO group - 8,69±4,49µIU/ml; in AH+OB1 group - 14,88±6,79µIU/ml; in AH+OB2 group - 17,00±15,01µIU/ml; and in AH+OB3 group - 24,22±10,74µIU/ml.

Conclusions: Obtained results suggest that plasma leptin and insulin levels are elevated in the patients with arterial hypertension depend on presence and degree of obesity.

CLINICAL TRIAL TO EVALUATE THE EFFICACY OF MNT WITH EXTRACT OF *PERILLA* LEAVES IN KOREAN OVERWEIGHT AND OBESE SUBJECTS

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This study was conducted to investigate the effects of 12 weeks of medical nutrition therapy (MNT) in accordance of taking *Perilla* leaves extraction in Korean overweight and obese men and women. A total of 70 subjects (14 men, 56 women) who were healthy and overweight or obese (BMI ≥ 25 kg/m^2) took parts in the study during May, 2007-April, 2008. During the study period, all subjects attended MNT program 4 times and they took placebo capsule (PM group) or extract capsule of *Perilla* leaves (TM group). Body weight, fat mass (FM), fat free mass (FFM), blood pressure, fasting blood lipid profiles (triacylglycerol, total-cholesterol, HDL-cholesterol, LDL-cholesterol, free fatty acid), glucose, and insulin were measured at the beginning and end of the study. After 12 weeks of experiment, there were significant reduction of body weight, FM, FFM, waist circumference, hip circumference, and skinfold thickness in both PM and TM groups($p< 0.05$). The mean losses of body weight in men and woman were 1.5 ± 0.3, 1.8 ± 0.1 kg in PM group, and 2.6 ± 0.5 kg, 3.3 ± 0.1 kg in TM group, respectively. The changes of fat mass of PM group and TM group were -4.97 ± 1.25%, -9.25 ± 1.28%, respectively. The levels of plasma TG and total-cholesterol decreased significantly in TM group in both PM and TM group($p< 0.05$). The results confirmed that taking extracts of *Perilla* leaves with MNT had positive effects on body fat mass reduction and on obesity-related blood parameter.

EVALUATION OF EFFECT OF TWO ACCUPUNCTURE ANTIOBESITY TREATMENTS: RANDOMIZED -CONTROLLED CLINICAL TRIAL

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Objective: To evaluate the effects of two acupuncture antiobesity therapies, catgut-embedding and traditional acupuncture.

Design and methods: Randomized-controlled parallel clinical trial. Inclusion criteria include: aged 18-65 years and BMI≥25 kg/m^2. Subjects with anyone of secondary obesity, type 2 diabetes, hypertension, coronary heart disease, stroke, infectious disease, cancer, or under any anti-obesity medication were excluded. In total 60 obese subjects were recruited and randomly divided and allocated to two groups and received different treatments for 4 weeks, catgut-embedding and traditional acupuncture, by using the same acupuncture points. Selected acupuncture points include: Zhongwan, Shuifen, Qihai, Guanyuan, Tianshu, Daheng, zusanli and Yinlingquan. Catgut-embedding treatment was provided once a week. The variation of obesity related measurements, fasting glucose, blood lipids profiles, basic metabolism rate in response to the treatments were evaluated and compared between groups.

Results: During 4-week treatment, the body weight, BMI, waist circumference, and low density lipoprotein levels decreased slightly but significantly in both groups (weight: 2.2±0.3 kg, BMI,by 0.82±0.10 kg/m^2, waist circumference: 5.12±0.55 cm; LDLC, 0.17±0.37 mmol/L) with equal responses between two groups. However, fasting glucose, total cholesterol, triglyceride, high density lipoprotein or low density lipoprotein cholesterol levels did not significantly vary during the treatment.

Conclusions: Both catgut-embedding and traditional acupuncture treatment of 4 weeks can slightly reduce body weight, BMI, waist circumference and LDLC levels, which is not associated with the variation of fasting glucose or lipid profiles in response to treatment.

CAROTID INTIMA MEDIA THICKNESS, LIPID PROFILE AND BODY COMPOSITION IN BRAZILIAN PREPUBERTAL OBESE CHILDREN

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Childhood obesity is increasing worldwide and is strongly associated with greater cardiovascular and all-cause mortality later in life. Increased carotid intima-media thickness (IMT) and metabolic abnormalities observed in obese children may lead to early atherosclerosis. The aim of this study was to measure IMT (high resolution ultrasound techniques) and associate IMT with serum lipid profile (total cholesterol(TC), LDL-c, HDL-c), fasting glucose (FG), waist circumference (WC), body mass (BM), body mass index (BMI), fat-free mass (FFM) and fat mass (FM) by bioelectric impedance and energy and fat intake in overweight and obese children. Statistical analysis was performed using Sigma Stat v.3.0 (VA, EUA) and significance was set to a value of $p \leq 0,05$. Written informed consent was

obtained from parents and this study was approved by Ethical Committee of the Universitary Hospital. Sixteen children (10F/06M , mean age 7.03 ± 1.38 years) were enrolled at the study (4 overweight and 12 obese). The medium values of IMT were right IMT-c: 0.50 ± 0.10mm and left IMT-c: 0.49 ± 0.09mm. Statistical analysis showed positive associations between IMT and BM (r= 0.51, p=0.04), BMI (r=0.64, p= 0.01), TC (r= 0.66, p=0.00), LDL-c (r= 0.73, p= 0.00), FG (r= -0.5, p= 0.03), CC (r= 0.54, p= 0,03), FM (r=0.61, p=0,01) whereas not statistical significant with FFM (r= 0.29, p=0.27). Dietetic data showed no associations with IMT-c. These data of a small group indicates that lipid layers of carotid intima media are influenced by serum lipid profile and total and abdominal adiposity.

OBESITY, SOCIOECONOMIC AND METABOLIC DETERMINANTS IN IRANIAN POPULATION

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Introduction: Obesity is an important risk factor of cardiovascular disease (CVD) morbidity and mortality and is associated with other risk factors of (CVD). This study investigates the association between obesity indices and other behavioural, socioeconomic and some metabolic risk factors in Iranian men and women.

Methods: The data is gathered from 12600 subjects aged ≥ 19 years selected by multistage random sampling who participated in a community based study entitled "Isfahan Healthy Heart programme" conducted in three cities in Iran. Demographic, behavioral and socioechonomic factors were studied.

Results: Mean BMI level, was 26.62±5.51 for women and 24.55±4.62 for men (p< 0.01). Mean WC was 88.39±11.93 in men and 92.62±14.18 in women, while (WHR) was 0.90±0.09 in men and 0.91±0.10 in women. Being married and resident in urban areas were both associated with a higher level of BMI, WC and WHR in both men and women (P< 0.05). Also these factors differed significantly according to the education level(primary, secondary, university) of the participants in both men and women (P< 0.05). The duration of daily sleeping and watching TV was significantly associated with obesity indices .A significant correlation between nutritional index, BMI, and WC was observed both in men and women(P< 0.05).

Conclusion: In general all obesity indices are more prevalent in Iranian woman than men. Special interventional strategies with more emphasis on healthy nutrition are needed to overcome their recent epidemic in Iran particularly in married men and women who have higher educational levels and live in urban areas.

IS THE PHASEOLUS VULGARIS AND CYNARA SCOLYMUS COMPLEX USEFUL TO IMPROVE METABOLIC ASSET IN HEALTHY OVERWEIGHT PEOPLE?

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Aims: Changes in glyco-metabolic set-up were explored in obese people treated with two natural active substances Phaseolus vulgaris and Cynara scolymus together as a dietary supplementation during a trial conducted to evaluate the effect of this complex on satiation feeling (primary end point).

Methods: A 2-months randomized, double-blind, placebo-controlled trial was carried out. 40 overweight and obese (BMI 25-35) people both gender aged 30-65 years were recruited. Twenty subjects were randomized to the complex in association with personalized diet, and 19 to placebo together with diet. The feeling of satiation was measure with Haber's scale, and glyco-metabolic set-up with blood cholesterol, trigliceryds, glucose, ALAT and HOMA levels.Changes from the baseline were tested by paired t test or analogous non-parametric test and between the two groups with unpaired t test.

Results: At the baseline the two groups were homogeneous respect to all the parameters investigated. At the end of supplementation, the treated group showed feeling satiation significantly higher than the controls (0.61±2.27 vs. -2.86±1.51; t=-5.39 p< 0.0001). Blood glucose levels decreased significantly with respect to baseline (104.85±16.5 vs. 90.25±13.34 mg/dl; t=6.51 p< 0.0001), as well as ALAT (22.15±8.51 vs. 19.25±6.29 UI/l; t=2.21 p=0.04) and HOMA ones (2.59±1.3 vs. 2.07±0.93; t=4.51 p=0.0002). Also cholesterol levels decreased (228.5±48.7 vs. 215.7±30.4 mg/dl, p=0.089). At the end of follow-up, treated group evidenced a glycaemia significantly less than the control one (90.25±13.34 vs. 100.21±16.69 mg/dl; t=2.06 p=0.046).

Conclusions: The findings indicate that the assumption of the complex may be an effect on glyco-metabolic asset.

WEIGHT LOSS REDUCES C- REACTIVE PROTEINAND FIBRINOGEN LEVELS IN OBESE WOMEN

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Introduction: Obesity is one of the most important risk factors in chronic diseases , Like coronary heart disease and diabetes mellitus. It is believed that elevated levels of C- reactive protein (CRP) and fibrinogen are associated with increased cardiovascular risk.

We examined the hypothesis that weight loss would reduce plasma CRP and fibrinogen levels in obese women.

Methods: Body weight, fasting glucose, insulin, triglyceride, total cholesterol, high- density lipoprotein cholesterol (HDL-C), low- density lipoprotein cholesterol (LDL-C) and acute phase proteins were measured at baseline and after 12 weeks in 29 obese women.

Results: Weight, BMI,, fasting blood glucose, cholesterol and triglyceride had significant reductions. HDL-C had increased significantly. No significant changes were observed in LDL-C and insulin concentrations. Plasma acute phase proteins levels decreased significantly.

Conclusions: Weight loss may represent an important intervention to reduce acute phase proteins levels, which may mediate part of its cardioprotective effects in obese women.

EFFECT OF CHITOSAN ON INSULIN SENSITIVITY IN OBESE PATIENTS

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Aim: To evaluate the effect of chitosan on insulin sensitivity in obese patients.

Patients and methods: A randomized, double blind, controlled clinical trial was carried out in 12 obese (BMI 30-40 kg/m²) adults (30-50 years) without background of diabetes mellitus. Chitosan 750 mg 3 times at day 30 min before meals was prescribed during 3 mo to six patients; other six volunteers receive placebo. Before and after the intervention the insulin sensitivity, evaluated with the euglycemic-hyperinsulinemic clamp technique and a lipid profile were measured. The statistical analyses were performed with Wilcoxon and Mann-Whitney U tests. The study was approved by an Ethic hospital-based Committee and a written informed consent was obtained in all volunteers.

Results: Both groups were similar in the basal measurements. The insulin sensitivity increased after the administration of chitosan (2.4 ± 1.4 vs. 3.6 ± 1.4 mg/kg/min; p = 0.043). BMI (34.3 ± 2.7 vs. 31.6 ± 2.2 kg/m²; p = 0.028), waist circumference (106 ± 12 vs. 99 ± 9 cm; p = 0.028), triglycerides (218 ± 80 vs. 145 ± 84 mg/dl; p = 0.028) and VLDL (41.9 ± 17.2 vs. 28.9 ± 16.9 mg/dl; p = 0.028) concentrations decreased in the chitosan group, but in the controls.

Conclusion: Chitosan increased the insulin sensitivity and decreased BMI, waist circumference, triglycerides and VLDL.

BASAL SECRETION OF GHRELIN AT PERSONS WITH ABDOMINAL OBESITY AND VARIOUS GLUCOSE METABOLISM ABNORMALITIES

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Aim: To study the difference of the indicators of ghrelin basal levels (BG) at persons with abdominal obesity and various glucose metabolism abnormalities.

Methods: 122 patients aged 35-55 were examined (the 1st group - obesity and normal tolerance to glucose; the 2nd - obesity and IGT; the 3rd - obesity and newly Type 2 diabetes and the control). The insulin, C-peptide, BG levels in serum were measured by the immune-enzyme method with «DRG International» reagents. The index HOMA-IR was calculated according to G0 x INS0 / 22,5.

Results: The lowest BG levels (41,29 ± 5,07 ng/ml) were registered in the 3rd subgroup. At the same time there was marked the progressive decrease of the BG levels with the evidence increase of glucose metabolism disorder from 60,19 ± 5,28 ng/ml in the 1st subgroup, to 51,32 ± 4,56 ng/ml in the 2nd subgroup and 41,29 ± 5,07 ng/ml in the 3rd subgroup (and the BG indicators in the 1st and 3rd subgroups authentically differed between each other, p < 0,05). The connection of ghrelinemia with the glucose metabolism indicators was also confirmed during the correlation analysis. There was registered the significant negative correlation of BG with HOMA-IR (r = - 0,60; p < 0,001), BG (r = - 0,48; p < 0,001), C-peptide (r = - 0,27; p < 0,001), insulin (r = - 0,43; p < 0,001).

Conclusion: The level decrease of BG levels was registered at persons with abdominal obesity in the process of degree increase of glucose metabolism abnormalities.

PSYCHIC EQUILIBRIUM AND OBESITY

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Aims: The aim of the study is to determinate a correlation between psychic equilibrium and obesity.

Methods: We studied a group of 50 patients aged between 28-74 years old, , we used the Life Syle Inventory Scale to determined the life style such a expresion of psychic equilibrium.The scale contained the follow items:obligations/satisfactions spontaneity, toxic in take, insomnia, relaxation, family relantionship, social activity and hobby.The scale was quanticated from 0-6.The obesity rate has been determined with body mass index IBM. We study, the age, sex, enviroment distrubution cases, life style.
Results: We have studied 26(52,0%)women and 24(48%)men, sex distribution of the cases points aut the women´s preponderance, the report women/men being 1:1.More than half (46,0%)of the patients were between 41-50 years old, 28% between 51-60 years old.86% from the patients are activ people.More than half 55%of the patienys presented obesity, and only 10% normal weight.Only 12% of the patients have normal life style, 62,0% have unhealthy life style , and 26,6% are intermediary life style.The obesity prevalence was present at 62,0% to the patients with unhealthy life syle, at 26,0% to the patients with intermediar life style, and only 7,1% to the patients with normal life style.

Conclusions: The obesity prevalence in activ popopulation is high, in our study we observe the high prevalence of obesity in active population and unhealthy life style, we determined a correlation betwen the life style and incidence of obesity.

RIMONABANT CAUSES WEIGHT LOSS WHEN DAILY ENERGY INTAKE IS MAINTAINED AT PRE-TREATMENT LEVELS

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Aim: To investigate in obese subjects the direct effect of rimonabant (i.e. independent from effects on weight loss) on resting energy expenditure (REE) and body fat distribution.

Methodology: 14 obese (33.0±1.9 kg/m²) post-menopausal women were randomised into two groups. Group 1 (n=7) received rimonabant (20mg/d) for 13 weeks with energy intake matched to their energy requirements and group 2 (n=7) followed a dietary intervention to achieve the same weight loss as group 1. Body weight, waist circumference, REE and body fat (by MRI) were measured at baseline (after a 4 week run-in-period) and after treatment. Average daily energy intake was measured by daily diet diary throughout the study.

Results: There was no difference in daily energy intake before and during the treatment in the rimonabant group (1991±99 vs.1963±73 Kcal/day, p= 0.630). Mean weight loss in the rimonabant group was 2.6±1.4kg (p=0.003) and 3.1±2.8kg (p=0.027) in the diet group with a 3.7±3.6cm (p=0.036) and 3.5±6.7cm (p=0.221) waist circumference decrease respectively, with no significant difference between groups. MRI results showed a significant decrease of 2.02±1.82% in total body fat in the diet group (p=0.046) however there was no significant difference between treatments. In the diet group there was a decrease in REE (p= 0.054) but no change in the rimonabant group or difference between groups.

Conclusion: Rimonabant treatment for 13 weeks (without a decrease in energy intake) led to a reduction in body weight. The maintenance of REE in the rimonabant group despite weight loss suggests rimonabant may influence energy expenditure.

PLASMA ADIPONECTIN LEVEL IS DECREASED IN ENOS KNOCKOUT MICE

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Aims: Nitric oxide (NO) synthesized by endothelial NO synthase (eNOS) plays an important role in mitochondrial biogenesis. We recently reported that adiponectin synthesis is regulated by mitochondrial function in adipocytes. This study was undertaken to test the hypothesis that plasma adiponectin level and adiponectin synthesis from adipocytes are decreased in eNOS knock-out mice.

Methods: We measured the plasma adiponectin levels, adiponectin expression and mitochondrial content of adipose tissue in eNOS knockout mice, and examined the effect of exogenous administration of NO donor on adiponectin synthesis.

Results: Plasma total adiponectin levels and high-molecular weight (HMW) oligomers, which are functionally most active in the oligomeric complexes of adiponectin were lower in eNOS knockout mice than in control mice. Chronic treatment of the eNOS knockout mice with exogenous NO donor SIN increased both plasma total adiponectin levels and HMW oligomers. Mitochondrial DNA content, and expression of mitochondrial proteins and adiponectin in adipose tissues were reduced in the eNOS knockout mice, but increased with NO donor treatment.

Conclusions: Reduced mitochondrial function can explain decreased plasma adiponectin concentration in eNOS knockout mice. These results reemphasize the role of mitochondria in adiponectin syntheisis in adipocytes.

THE EFFECTS OF LEPTIN AND ADIPONECTIN ON PANCREATIC BETA-CELL FUNCTION ARE MODULATED BY HIGH GLUCOSE CONCENTRATIONS

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Leptin and adiponectin are adipokines secreted from adipose tissue. Dysregulated secretion of these adipokines had been shown to play a crucial role in the development of diabetes. Leptin and adiponectin have a modulatory effect on insulin secretion. The effects of these adipokines on beta-cell survival is still controversial.

Aims: To evaluate the effect of leptin and adiponectin on beta-cell viability and function, and to determine whether these effects are modified by high glucose concentrations.

Methods: Studies were performed on RINm rat pancreatic beta-cells, grown in different glucose concentrations (5, 11, 33mM). Insulin secretion, cell viability and apoptosis were measured in the absence or presence of leptin (10, 100 ng/ml) or adiponectin (10 nM). Expression levels of several signaling proteins was measured.

Results: Leptin and adiponectin each inhibited mRNA expression of pre-pro-insulin and basal insulin secretion, effects that were blocked by high glucose concentrations. In addition, leptin and adiponectin each increased cell proliferation in 11mM but not in 33mM glucose. The adipokines had protective effects against palmitic acid and H_2O_2 induced beta-cell death, effects that were not blocked by high glucose concentrations. High glucose reduced the expression of the long isoform of leptin receptor, but not the short form or of adiponectin receptor. High glucose modulated RNA expression and protein phosphorylation of AMPK and STAT3, which are involved in adipokine signaling.

Conclusion: We show that leptin and adiponectin affect beta-cell function, but some of these effects appear to be abrogated by high glucose concentrations.

ADIPONECTIN: A MARKER OF THE METABOLIC SYNDROME IN DIABETES

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Aim: The role of adiponectin (ApN) in diabetes and its connection with obesity, dyslipidemia and inflammation as markers of the metabolic syndrome were studied.

Methods: Relevant clinical and laboratory parameters were measured in eighty patients with type 1 diabetes (D1), type 2 diabetes (D2) and a control group (D0).

Results: A significant difference in ApN was found between D1 (ApN=12.22±6.68), D2 (ApN=6.86±5.42) and D0 (ApN=7.85±6.47) (ANOVA) (p=0.018). Kruskal-Wallis ANOVA revealed a significant difference in fasting blood glucose (FBG) (p< 0.0001) and BMI (p=0.007) between D1, D2 and D0. There was an insignificant difference in CRP between D1(2.17±2.88), D2(3.18±3.00) and D0(3.72±3.14). ANOVA revealed a significant difference in ApN and CRP within D2 in relation to BMI [< 25(A), 25-30(B), >30(C)] (p=0.003 and p=0.001, respectively). ApN statistically significantly (p< 0.05) correlated with HDL (r=0.78), AIP (r=-0.63), BMI (r=-0.41), diabetes duration (r=0.35) and leukocyte count (r=-0.33). After stepwise regression in D1 for ApN, the best model (R^2=0.989) included AIP (p< 0.0001), uric acid (UA) (p< 0.0001) and homocysteine (p=0.05). The best model for UA (R^2=0.399) included CRP (p=0.028), pulse pressure (PP) (p=0.013) and gamma-GT (p=0.066). In D2 the best model for ApN (R^2=0.725) included HDL (p< 0.0001), systolic blood pressure (p=0.059) and fibrinogen (p=0.035).

Conclusion: Decreased ApN level in type 2 diabetes could be explained by insulin resistance. In addition, it appears to be significantly associated with markers of the metabolic syndrome, and could therefore be considered to be one of the markers of the metabolic syndrome in diabetes.

METABOLIC SYNDROME AND VASCULAR EVENTS IN GERIATRIC CORONARY PATIENTS

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Aims: The metabolic syndrome (MetS) confers an increased risk of cardiovascular disease and of type 2 diabetes. Older age is associated with an increasing prevalence of the MetS.Our aim was to investigate the prevalence of the MetS and its influence on vascular events in geriatric coronary patients.

Methods: 342 consecutive patients >65 (mean age 71,8±4,8 years) undergoing coronary angiography were recruited 1999-2000. MetS was defined according to the Adult-Treatment-Panel (ATP)-III and to the International Diabetes Federation (IDF), respectively. 112 (32,7%) vascular endpoints were recorded after a follow-up period of 6,2±0,8 years.

Results: 292 (85,4%) patients had a significant stenosis ³50%. 31.9% (n=109) had the MetS according to ATP-III criteria and 43,3% (n=148) according to IDF. The concordance between these two definitions was moderate (Cohen-k-coefficient 0,527, p< 0,001). 77 patients (22,6%) fulfilled either ATP-III or IDF criteria.Event-free survival in patients with MetS according to IDF or ATP-III was not statistically different form those without MetS (p=0.906 and p=0,196, respectively).In a Cox regression model, MetS by ATP-III was independently predictive of vascular events after adjustment for age, sex, smoking, BMI and LDL-cholesterol (HR 1,419 (95%CI 1,101-1,828, p=0,007), and even after additional adjustment for diabetes. MetS according to IDF was not predictive of vascular events (HR 1,087, 95%CI 0,876-1,350, p=0,448).

Conclusions: One out of three elder coronary patients fulfills the MetS criteria. Different patients are identified depending on the definition of the MetS. The ATP-III definition is predictive of vascular events.

CHEMOKINES IN AQUEOUS HUMOR AND SERUM IN PATIENTS WITH CATARACT AND PROLIFERATIVE DIABETIC RETINOPATHY: A PRELIMINARY STUDY

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The chemokines are a large family of chemotactic cytokines, produced by tissue cells and leukocytes, which regulate leukocytes migration in inflammation and immunity. To determine levels of the chemokines CCL2/MCP-1 and CXCL10/IP-10 in the vitreous humor and serum, from patients with proliferative diabetic retinopathy (PDR) and cataract.

Methods: All patients underwent a complete ophthalmic examination, including retinal fluorescein angiography. Indirect immunoenzymatic method was performed on 17 eyes of 17 patients with type 2 diabetes without DR and on 4 eyes of 4 patients with PDR. A control study was performed on 13 normal conjunctiva undertaken during cataract surgery. The analyses of the levels of the chemokines: MCP-1 and IP-10 in the blood serum and aqueous humor of all the patients were performed by ELISA method.

Results: MCP-1 and IP-10 levels were significantly higher in vitreous humor samples from patients with PDR compared to the cataract patients. IP-10 levels in vitreous humor samples were significantly higher than in serum samples. MCP-1 levels in vitreous humor samples patients with PDR were significantly higher than in serum to the cataract patients. There was a significant association between the incidence of IP-10 detection and increased levels of MCP-1 in vitreous humor samples from all patients, and patients with PDR .

Conclusion: MCP-1 and IP-10 may participate in pathogenesis of cataract and PDR.

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SHORT-TERM EFFECTS OF PIOGLITAZONE ON SERUM LEVELS OF ADIPOKINES AND FETUIN-A IN HEALTHY SUBJECTS

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Aims: Pioglitazone is a thiazolidinedione derivative (TZD), which has various pleiotropic effects on cardiovascular diseases and lipid metabolism. Long-term treatment with TZD influences circulating levels of adipokines and fetuin-A, which is associated with insulin resistance, in diabetic patients, although the mechanism is not well understood. In this study, we examined short-term effects of pioglitazone on serum adipokines and fetuin-A in non-diabetic subjects to assess the effects of pioglitazone independently of glycolipid metabolism.

Methods: The study comprised 12 men with normal glucose tolerance (mean ± SE age 34 ± 2 years). Study participants were treated with 30 mg/day pioglitazone for 14 days, and fasting blood samples were obtained at baseline, at days 7 and 14 of pioglitazone treatment.

Results: Pioglitazone treatment did not change fasting plasma glucose, lipid profile, CRP, or fetuin-A levels. Small decreases in fasting plasma insulin, HOMA-IR, and leptin levels were detected, but they were not statistically significant. On the other hand, both total and high-molecular weight (HMW) adiponectin levels rapidly increased (total adiponectin 6.3 ± 0.9 and 12.6 ± 2.0 μg/ml [$P< 0.001$] and HMW adiponectin 3.9 ± 0.8 and 9.6 ± 1.8 μg/ml [$P< 0.001$] at baseline and day 14, respectively). Serum resistin significantly decreased after 14 days of pioglitazone treatment (11.0 ± 1.5 and 9.9 ± 1.4 ng/ml, $P< 0.05$).

Conclusions: Pioglitazone increases serum adiponectin levels and decreases resistin levels, which precedes changes in the status of glycolipid metabolism or inflammation. Our data support the primary effect of pioglitazone on the regulation of these adipokines.

RELATIONSHIP BETWEEN CAROTID INTIMA-MEDIA THICKNESS (IMT) AND ADIPONECTIN, TESTOSTERONE OR SMALL,DENSE LDL-CHOLESTEROL (SLDL-C)

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Aims: To assess the relationship between IMT and High-Molecular-Weight(HMW) adiponectin, testosterone(T) or small, dense LDL-C(sLDL-C).

Methods: Fifty-one out-patients (31 men and 20 women aged 54.0±13.2 years) were enrolled in this study.Carotid atherosclerosis was assessed by carotid IMT on B-Mode ultrasonography. Metabolic Syndrome(MS) was diagnosed according to the definition of MS in Japan. The subjects taking thiazolidine, angiotensin II receptor blocker, pravastatin or fibrates were excluded. Heparin-magnesium precipitation method was employed for the determination of sLDL-C. Statistical analysis was performed using JSTAT for windows version12.5.

Results:

1. Multiple regression analysis showed that the most powerful determinant of carotid IMT was age, followed by HMW adiponectin, presence of Diabetes Mellitus(DM) and gender in non-statin users.

2. In the men including statin users, the most powerful determinant of carotid IMT adjusted for age was T, followed by presence of DM.

3. Excluding statin users, we found significant positive correlation between adiponectin and age, gender, in addition to an absence of MS. Significant inverse correlation was found between adiponectin and smoking, BMI, HOMA-R, sLDL-C,IMT and T. The most powerful determinant of adiponectin adjusted for age was T, followed by sLDL-C and HOMA-R ($P< 0.01$).

Conclusions:

1. HMW adiponectin can be more powerful determinant of IMT than sLDL-C.

2. T can also be a determinant of IMT in men including statin users.

3. SLDL-C was the determinant of HMW adiponectin, indicating that insulin resistance is associated with both HMW adiponectin and sLDL-C.

IMPAIRED INSULIN SENSITIVITY IN OCTOGENARIANS IS ASSOCIATED WITH DECREASED LOW MOLECULAR WEIGHT (LMW) ADIPONECTIN

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Adiponectin circulates in the blood in three different multimer complexes, of which the high molecular form (HMW adiponectin) is presumed to mediate insulin sensitivity.

Adiponectin multimers were determined in 166 individuals older than 80 years (octogenarians) and in 24 normoglycemic younger controls (44±7 years) by an ELISA. Insulin sensitivity has been assessed by a oral glucose tolerance test.

Sex-adjusted values for HMW, MMW, and LMW-adiponectin were significantly higher in normoglycemic octogenarians in comparison to the normoglycemic younger controls, increasing by 95.6%, 88.9%, and 35.2%. The more pronounced increase of HMW adiponectin resulted in higher HMW/total adiponectin and lower LMW/total adiponectin ratios in normoglycemic octogenarians. The impairment of glucose tolerance in octogenarians with type 2 diabetes mellitus (T2D) was associated with a decrease of plasma LMW adiponectin by 25.4%, while the total, MMW, and HMW adiponectin concentrations were not different. The obtained data further revealed a strong inverse correlation of LMW adiponectin with the postchallenge insulin level 150min after glucose load ($r=-0.339$, $p< 0.001$), whereas the correlations of total ($r=-0.285$, $p< 0.001$) and HMW ($r=-0.236$, $p< 0.003$) adiponectin with the insulin at the same time were less pronounced.

In conclusion, our data indicate that the increase of total plasma adiponectin concentrations in octogenarians was characterized by a proportionally increase of HMW and a proportionally decrease of LMW multimer complexes. The impairment of insulin sensitivity in 80-year-old patients with T2D primarily could be associated with a significant decrease of LMW adiponectin.

ADIPOKINES AND CARDIOVASCULAR RISK IN HIV INFECTED PATIENTS

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Aims: Cytokines and adipokines may contribute to cardiovascular risk (CVR) both in general population and in HIV infected. To value the role of leptin, adiponectin and ghrelin in HIV infected HAART treated patients subdivided for CVR.

Methods: 54 HIV+ HAART treated patients were screened by Framingham score and subdivided in 2 groups: A) "high" CVR (>10%) and B) "low" CVR (< 10%). CD4 and CD8 cell counts, HIV-RNA, TCh, HDL-C, LDL-C, TGs, blood pressure, microalbuminuria, fasting glucose, insulinemia, HOMA-IR, CRP, cistatin-C, beta-2-microglobulin, IL-18, IL-6, leptin, adiponectin, ghrelin and antropometric parameters were measured.

Results: Group A showed statistically higher levels of TCh, LDL-C, TGs, blood pressure, glicemia, insulinemia, HOMA-IR, cistatin-C, microalbuminuria and BMI. Moreover levels of IL-6, IL-18 and leptin were statistically higher in group A, whereas adiponectin was statistically increased in group B (Table 1). Data showed a positive correlation between VAT, leptin levels ($r=0.20$, $p=0.007$) and IL-18 ($r=0.34$, $p=0.01$), and a negative correlation between VAT and adiponectin ($r=-0.03$, $p=0.01$).

Conclusions: Literature shows that low adiponectin levels are associated with obesity and insulin resistance and are inversely correlated to CVR factors. Serum levels of adiponectin are directly associated with HDL-C and inversely to TGs levels in general population. Our data show that HIV+ patients with high CVR have increased lipidic and VAT levels. In this patients increased CVR is associated to high levels of IL-18, ghrelin, leptin and decreased levels of adiponectin. Thus adipokines and visceral adiposity are important markers of CVR so in HIV+ subjects as in HIV negative population.

INFLUENCE OF ADIPONECTIN +45A/G AND +276G/T POLIMORFISMS ON HDL SIZE DISTRIBUTION IN MEXICAN CHILDREN WITH METABOLIC SYNDROME

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Aims: To establish adiponectin +45A/G and +276G/T polymorphisms frequencies in Mexican children with metabolic syndrome (MS) and to determine their influence on HDL size distribution and plasma paraoxonase-1 (PON1) activity.

Methods: Sixty children with MS and 60 controls matched by age and sex were recruited. MS was diagnosed by the ATPIII criteria using age and gender specific 90 percentiles for lipid levels, blood pressure and waist circumference. Assent was obtained from participants and their parents gave their signed informed consent. HDL size distribution was determined by electrophoresis in polyacrilamide 5-30% gradient gels in native conditions. PON1 activity was determined by using phenylacetate as substrate.

Results: MS patients had a lower relative proportion of large HDL2b (7.7±0.7) than controls (12.9±1.7, $p< 0.05$), whereas small HDL3b and HDL3c relative proportions were higher in the MS patient ($p< 0.05$ for both). AD+45 TT, TG and GG frequencies were 75%, 25% and 0% in controls, whereas in the MS group they were 54.1%, 41.6% and 4.3% respectively. AD+276 TT, TG and GG frequencies were 12.8%, 37.5% and 50% in controls, whereas in the MS group they were 0%, 37.5% and 62.5% respectively. PON1 activity was lower in SM group than in controls (57±2 vs. 116±3U/mL, $p< 0.05$). Finally, we found a significant correlation of AD+276 polymorphism with HDL2b and HDL3b ($p< 0.05$).

Conclusions: Our results suggest that adiponectin AD+276 polymorphisms contribute to determine the abnormal HDL size distribution which could be related to the low plasma levels of PON1acitivities in children with MS.

ARE CIRCULATING INFLAMMATORY MARKERS RELATED TO INSULIN RESISTANCE AND GLUCOSE INTOLERANCE IN THE METABOLIC SYNDROME?

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Cytokines may influence insulin signaling and worse insulin sensitivity, leading to glucose intolerance in MS. We compared the inflammatory status of 187 individuals with MS (33.2% men, 55.3±12.6yrs), with (pre-diabetes) or without abnormal glucose metabolism. Mean BMI and waist were 31.4±5.6kg/m^2 and 103.1±12.5cm. Groups had similar male-to-female ratio, age, BMI, waist and blood pressure.

	Normal glucose tolerance	Pre-diabetes	Overall	p
Fasting plasma glucose (mg/dL)	87.8 ± 7.5	105.9 ± 7.9	97.4 ± 11.9	0.000
HDL-cholesterol (mg/dL)	40.2 ± 8.6	42.7 ± 11.9	41.5 ± 10.6	NS
Triglycerides (mg/dL)	171.0 ± 71.7	144.5 ± 76.9	157.0 ± 75.5	0.016
HOMA-IR	2.12 ± 1.37	2.62 ± 1.69	2.37 ± 1.56	0.043
*C-reactive protein (mg/dL)	0.55 ± 0.55	0.57 ± 0.58	0.56 ± 0.56	NS
*Interleukin-6 (pg/mL)	3.06 ± 3.28	3.07 ± 3.57	3.07 ± 3.42	NS
Leukocyte count (cels/mm3)	7109 ± 1662	6751 ± 1849	6922 ± 1767	NS
Adiponectin (ng/mL)	10.36 ± 5.87	9.97 ± 6.69	10.19 ± 6.16	NS
TNF-alfa (ng/mL)	13.24 ± 5.73	12.45 ± 6.44	12.84 ± 6.09	NS

*log-transformed for analysis

Pre-diabetic group showed higher HOMA-IR but inflammatory markers were similar between the groups. Significant correlations were detected between inflammatory markers (leukocyte count, IL-6, CRP, adiponectin) and waist; HOMA-IR was correlated to CRP, leukocyte count and adiponectin. Pre-diabetic status was associated with a more insulin resistant condition in individuals with MS. Inflammatory markers in circulation were not sensible to detect differences of glucose tolerance status; this may be attributed to their similar body adiposity. Determinations of those biomarkers did not support that inflammatory markers are able to differentiate glucose tolerance categories in MS.

EVALUATION OF ADIPONECTIN AS A POTENTIAL COMPONENT OF THE CRITERIA FOR THE METABOLIC SYNDROME

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First-degree relatives (FDR) of patients with type 2 diabetes (T2DM) have increased risk of developing diabetes because of aggregation of cardiometabolic risk factors. This study explores the potential use of adiponectin as a marker of the metabolic syndrome (MS) in normoglycemic FDR of T2DM patients. Fasting adiponectin, insulin, glucose, and full lipid profile were determined in 423 and 53 healthy control subjects without family history of diabetes. Clinical and anthropometric data were recorded and subjects were classified on the basis of the degree of adiposity, insulin resistance (IR) (HOMA-IR) and the number of criteria of the MS (International Diabetes Federation). Adiponectin concentration was higher in females than males (mean 9.7 vs. 6.9 ug/ml) despite similar waist circumference (WC). In both FDR and controls, adiponectin was inversely correlated with WC and HOMA-IR and positively correlated with HDL-cholesterol (HDLC). Adiponectin showed stepwise decrease with increasing number of MS criteria. Binary logistic regression showed that the odds ratio of MS as predicted by adiponectin was 0.55 [95% confidence interval 0.41-0.73; $p < 0.0001$]. At cut-off points of 7.5 ug/ml, the diagnostic sensitivity and specificity of adiponectin for the MS were 90% and 70% respectively compared to 42% and 95% for triglycerides and 80% and 54% for HDLC at standard cut-off points. Receiver Operating Characteristic analysis showed that adiponectin (0.859) had significantly higher area under the curve compared with HDLC (0.745) and triglycerides (0.823) for detection of MS. We conclude that adiponectin should be an additional and useful criterion for identification of the MS.

SERUM ADIPONECTIN, ADIPOSITY AND PRE-DIABETES IN A SUB-SAHARA AFRICAN POPULATION

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The rising prevalence of obesity, diabetes and cardio-vascular diseases in Sub Sahara Africa requires a clear understanding of the role of obesity as a risk factor for chronic diseases in this population. We examined the association between pre-diabetes, serum adiponectin levels and obesity indices in adult Cameroonians aged between 25 to 55 years (n = 223 M, 382 F).

Fasting blood glucose (FBG) and 2 hours post-load blood glucose (2h BG) were measured during a standard 75g OGTT. Global and abdominal obesity were assessed by BMI, body fat (measured by bio-impedance) and waist circumference respectively. Sex-specific quartiles of serum adiponectin and body fat were used in the logistic regression models.

There was not significant difference in prevalence of pre-diabetes between men and women (16% vs. 19%, p=0.4). Women had a significantly higher serum adiponectin level (6.8±3.8 vs. 4.9±2.5 mg/L, p< 0.001), BMI (27.1±5.6 vs. 24.9±3.9 kg/m^2, p< 0.001), body fat (33.8±8.9 vs. 18.0±6.9 %, p< 0.001) and waist circumference (90.0±12.9 vs. 86.0±10.3 cm, p< 0.001). In multivariate logistic regression models adjusting for age, serum adiponectin, smoking, alcohol consumption, family history of diabetes and self-reported physical activity, abdominal obesity showed the highest risk for pre-diabetes in both men (OR=3.31; 95% CI: 1.18, 9.27) and women (OR=3.31; 95% CI: 1.18, 9.27). In a similar model, serum adiponectin (quartile-4 vs. quartile-1) showed discordant effects in men (OR=3.65; 95% CI: 0.90, 14.82) and women (OR=0.58; 95% CI: 0.24, 1.43), though these were not significant.

Abdominal obesity measured by the waist circumference in this population is more strongly predictive of pre-diabetes compared to other indices of adiposity. These results imply that emphasis should be placed on measurement of waist circumference in primary care in this population as a clinical surrogate of excess adiposity.

THE RELATIONSHIP BETWEEN BODY SURFACE AREA AND INSULIN RESISTANCE, SERUM IL-6 LEVELS IN PATIENTS WITH TYPE 2 DIABETES

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Background and aims: In this study, we aimed to evaluate the relationship between body surface area and insulin resistance, serum IL-6 levels in type 2 diabetic patients.

Material and methods: Twenty-five type 2 diabetic patients and 14 non-diabetic controls who don't have any chronic inflammatory disease were enrolled in the study. All subjects underwent a diagnostic protocol including

serum fasting insulin, hsCRP, fibrinogen, HbA1c, fasting serum IL-6 levels analysis and the routine laboratory tests.

Results: The study results showed that the mean insulin sensitivity index of study patients was lower than normal ranges (HOMA-IR: 4.5 ± 3.0), serum fasting insulin levels (12.2 ± 7.4 μU/ml) were higher than normal ranges. The study population had a mean serum fasting glucose level: 143.2 ± 42.2 mg/dl, mean HbA1c: % 7.3 ± 1.8, mean hs-CRP level: 42.5 ± 45.3 mg/L.

The correlation analysis (Pearson) have shown that in type 2 diabetic patients, there was a statistically significant correlation between body surface area and fasting serum IL-6 levels (r=0.49, p< 0.05), BMI (r=0.78, p< 0.001). There was no statistically significant correlation between body surface area and HOMA-IR (r=0.36, p>0.05). There was statistically significant correlation between BMI and HOMA-IR (r=0.41, p< 0.05).

Conclusion: Previous clinical studies have shown that the low grade inflammation in type 2 diabetic patients has an important role for developing diabetic cardiovascular complications. Because of that, the increased body surface area values must be accepted as an important additive prognostic indicator for diabetic vascular complications.

CORRELATIONS OF GLUCOSE METABOLISM WITH ADIPOKINES AND MARKERS OF INFLAMMATION

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There are speculations that inflammation process has negative influence on glucose metabolism and cardiovascular diseases (CVD) development.

Aim: To evaluate correlations of glucose, insulin and homeostatic model assessment (HOMA) index with adipokines and markers of inflammations.

Methods: In forty-eight outpatients without CVD and fifty-two inpatients with arterial hypertension, correlations between levels of glucose, insulin and HOMA index with adiponectin , leptin, C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and plasminogen activator inhibitor-1 (PAI-1) were detected by using Pearson correlation coeficient (PCC).

Results: Correlations of glucose metabolism parameters with adipokines and markers of inflammation are shown in table.

Parameters		Adiponectin	Leptin	CRP	IL-6	TNF-α	PAI-1
Glucose	PCC	-0.293	0.083	0.439	0.092	0.192	0.144
	p	0.003	0.410	0.000	0.362	0.058	0.154
Insulin	PCC	-0.345	0.199	0.349	0.103	0.168	0.435
	p	0.001	0.050	0.000	0.313	0.100	0.000
HOMA index	PCC	-0.359	0.162	0.553	0.147	0.185	0.336
	p	0.000	0.112	0.000	0.150	0.069	0.001

Parameters of glucose metabolism have positive correlation with CRP and negative with adiponectin. Insulin and HOMA index correlated positively with PAI-1, while only insulin has correlation with leptin.

Conclusions: Levels of CRP and PAI-1 are increased in patients with disturbance of glucose metabolism. Given markers could be advisable factors for risk calculation in these patients.

THE ROLE OF RESISTIN, ADIPONECTIN, AND TUMOR NECROSIS FACTOR-A WITH INSULIN RESISTANCE IN OBESE NON DIABETIC MEN

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Objective: Adipokines, proteins produced by the adipose tissue, can be expressed primarily in adipocytes (adiponectin), macrophages (resistin), or both (TNF-α), identified as potential contributors to insulin resistance in humans. The aim of this study is to assess whether these adipokines are contributed to the development of IR in obese non diabetic men.

Method: This is a cross-sectional study using 74 obese men (WC > 90 cm). Fasting glucose, fasting insulin, ALT serum, AST serum, creatinine, bilirubin, c-reactive protein, triglyceride, HDL-C, blood pressure, resistin, adiponectin, and TNF-α were measured. The associations of these adipokines with insulin resistance were assessed using Somers'd Test.

Result: A weak linier correlation was found between resistin and HOMA-IR (r=0.151, p=0.284), TNF-α and HOMA-IR (r=0.096, p=0.501), adiponectin and HOMA-IR (r=0.030, p=0.715). High HOMA-IR was found mostly in obese men with high resistin serum concentration (58.3% of population). A significant correlation was found between the 3 risk factors (high resistin, low adiponectin and high TNF-α) with HOMA-IR (r=0.214, p=0.047). Subjects having 3 risk factors have 6.7 fold higher risk of insulin resistance, meanwhile subjects with 1 or 2 risk factors have 2.3 fold higher risk of insulin resistance, compared to subjects with no risk factors.

Conclusion: According to our study, resistin has the strongest correlation with IR, compared to adiponectin and TNF-α. Subjects with more risk factors having higher risk of IR. Finally, we concluded that high resistin, high TNF-α, and low adiponectin were correlated with higher risk of IR.

THE INFLUENCE OF PLASMA ADIPONECTIN CONCENTRATION ON STRUCTURE AND FUNCTION OF THE LEFT VENTRICULE IN PATIENTS WITH METABOLIC SYNDROME

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Objective: Several studies have revealed an association between low serum adiponectin level and cardio-vascular diseases. However, consensus is still lacking in regard to the influence of adiponectin on the heart of patients with metabolic syndrome. The purpose of our work was to elucidate the influence of adiponectin levels on the structure and function of the left ventricle in patients with metabolic syndrome.

Methods: One-hundred seventy-five patients with metabolic syndrome and 53 age-, gender- and blood pressure-matched control subjects without metabolic syndrome were studied. Serum adiponectin concentrations were measured by an ELISA kit from BioCat (Germany).

Two-dimensional M-mode echocardiography and Doppler echocardiography were performed using the "Acuson Aspen Echo" (USA). Statistical analyses were carried out with StatSoft "Statistica 6.0".

Results: Left ventricular mass index in both groups positively and significantly correlated with blood pressure, fasting blood glucose, body mass index and age (p< 0,05). Serum adiponectin concentrations were significantly lower in the metabolic syndrome group than in the control group (4,5 ± 3,1 μg/ml versus 15,2 ± 3,5 μg/ml, p < 0,05) and showed an

inverse correlation with left ventricular mass index (r = -0,352; p< 0,05) and isovolumetric relaxation time (r = -0,456; p< 0,05) only in the group of patients with metabolic syndrome.

Conclusions: Low plasma adiponectin concentrations are associated with more severe left ventricular hypertrophy and diastolic dysfunction in patients with metabolic syndrome. The identification of efficient ways to increasing the serum adiponectin might help to reduce cardiovascular complications.

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THE RELATIONSHIPS BETWEEN SERUM ADIPONECTIN MULTIMERS AND THE COMPONENTS OF METABOLIC SYNDROME IN KOREANS

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Aims: Metabolic syndrome is characterized by the clustering of multiple cardiovascular risk factors. Adiponectin is a well known anti-atherogenic adipocytokine secreted from the adipocyte, and circulating as diverse forms i.e. low (LMW), middle (MMW), and high molecular weight (HMW) multimers. HMW multimer form is supposed to be mainly involved in the metabolic benefits. We evaluated the relationships between adiponectin multimers and the components of metabolic syndrome in Koreans.

Methods: The subjects of this study, visited for health screening, were 15 people with metabolic syndrome (male 9, female 6) and 15 without metabolic syndrome (male 10, female 5). The definition of metabolic syndrome was based on the definition of IDF in 2005. Insulin resistance was measured by HOMA-IR. Serum total adiponectin level was measured by ELISA. Adiponectin multimers were fractionated by SDS-PAGE, followed by immunoblotting and densitometry.

Results: Total adiponectin level was marginally reduced in metabolic syndrome group than normal group (13.45±5.191 vs 16.82±4.969 μU/mL, P = 0.044). HMW adiponectin multimer(%) was significantly reduced in metabolic syndrome (39.7±14.46 vs 55.6±11.98%, P = 0.005). Waist circumference (r=-0.51, P = 0.004), triglyceride (r=-0.52, P = 0.003), systolic pressure(r=-0.53, P = 0.003), and diastolic pressure (r=-0.51, P = 0.004) showed significant negative correlation with HMW adiponectin multimer(%). HDL cholesterol (r=0.4, P = 0.003) had significant positive correlation with HMW(%). Fasting plasma glucose and HOMA-IR did not show significant correlation.

Conclusion: The percentage of HMW adiponectin multimer showed better correlation with the components of metabolic syndrome in Koreans than total serum adiponectin level.

CORRELATION BETWEEN PLATELET AGGREGATION ACTIVITY AND PROINFLAMMATORY CYTOKINES IN PATIENTS WITH COMBINATION OF METABOLIC SYNDROME AND ISCHEMIC HEART DISEASE

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Aim: Investigation of correlation between platelet aggregation activity and content of proinflammatory cytokines in patients with combination of metabolic syndrome and ischemic heart disease.

Methods: There were examined 23 patients with combination of ischemic heart disease and metabolic syndrome, diagnosed according to IDF criterions (2005), and 18 healthy volunteers. Interleukin 1β (IL-1β), interleukin 8 (IL-8), tumor necrosis factor α (TNF α) were measured by ELISA. ADP- and adrenalin-induced platelet aggregation activity in platelet reach plasma was estimated using dual-channel aggregometer.

Results: It was revealed significant increase of IL-1β, IL-8 and TNFa in plasma of patients as compared to healthy volunteers. Increased degree of aggregation, induced by 5 μg/ml ADP according to the light transmission curve was detected as well as increased rate of aggregation, induced by 1.25 μg/ml ADP according to the mean radius curve. In group of patients growth of adrenalin-induced (5 μg/ml) aggregation degree according to the light transmission and mean radius curves was revealed. There were also detected positive correlation dependences between level of IL-1β and adrenalin-induced platelet aggregation parameters, between content of TNF-α in serum and degree of adrenalin-induced platelet aggregation, between level of IL-8 and degree of ADP-induced platelet aggregation in the group of patients (all according to the mean radius curve).

Conclusions: Obtained results showed interdependence between activation of platelet aggregation capacity and elevated content of proinflammatory cytokines in patients with combination of ischemic heart disease and metabolic syndrome.

TOTAL, HMW AND TOTAL/HMW RATIO OF ADIPONEKTIN CONCENTRATION IN CHILDREN: COMPARISON BETWEEN NORMAL, OVERWEIGHT AND OBESE CHILDREN

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Background: Childhood obesity is associated with metabolic disease. Adiponectin is the most abundant adipose-specific protein and is exclusively expressed and secreted from adipose tissue. Adiponectin exists in serum as a trimer, a hexamer, and a high-molecular weight (HMW) form. HMW adiponectin may be biologically active.

Objective: To determine the difference of Total, HMW and ratio of Total/HMW Adiponectin concentration between normal, overweight and obese Indonesian children.

Design: Cross Sectional Study.

Material and methods: There were 40 of 6 - 11 year olds childrens, devided in three major of groups, consist of overweight children (IMT≥85-94 percentile) (n=10), obese children (IMT≥95 percentile) (n=10) and normal weight children (IMT≥5-84 percentile) (n=20) base on criteria percentile by sex and age.

Result: Concentration adiponectin had significant difference (p>0.05) in overweight compare with normal weight children, either in concentration of total (p=0.389), HMW (p=0208) or HMW/Total adinopenctin ratio (p=0.075) and in major group of obese compare with overweight children in concentration of total (p=0,009), HMW (p=0.255) or HMW/Total adinopenctin ratio (p= 0.700). Significant differences concentration of adiponectin either in concentration total adiponectin in obese compare with normal weight children (p=0.008) and HMW adiponectin (p=0.020) or in major group of obese children compare with non obese children either in total (p=0.012) and HMW adiponectine (p=0.041). Furthermore, concentration adiponectin had significant difference in obese & overweight children compare with normal weight (p=0.0310).

Conclusion: The result showed adipoenctin concentration in obese children or overweight children were different than normal weight children.

CORRELATION MODELS OF INFLAMMATION AND ANGIOGENESIS IN ADULT MEN WITH CENTRAL OBESITY: THE ROLE OF TNF-A, IL-1B, VEGF AND LEPTIN BIOCHEMICAL MARKERS

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Background: Adipose tissue is highly vascularized, and each adipocyte is nourished by an extensive capillary network. Adipose cell enlargement leads to a pro-inflammatory state in the cell with increased secretion of several cytokines, including IL-1β and TNF-α, as well as multiple angiogenic factors, namely leptin, and VEGF, which either alone or collectively stimulate neovascularization during fat mass expansion. The pro-inflammatory state in the adipose tissue also leads to a local insulin resistance. Anti-angiogenic agents provide a novel therapeutic option for prevention and treatment of human obesity and its related disorders. Therefore, relations between biochemical markers of inflammation like TNF-α and IL-1β, with biochemical markers of angiogenesis like VEGF and leptin need to be explored in a comprehensively to understand more about their links to obesity development.

Objective: To investigate the correlation between inflammation and angiogenesis in adult men with central obesity.

Methods: We performed a cross-sectional study on 81 healthy adult men, aged 25-50, with waist circumference ranged from 64-116 cm.

Results: This study showed that IL-1β and leptin concentrations in central obesity subjects were correlated with increased waist circumference. Increasing TNF-α was correlated only with IL-1β and VEGF, but not with waist circumference. This study also demonstrated that each increase in TNF-α concentration was followed by 2,4 times increase in leptin concentrations.

Conclusion: These findings suggest that TNF-α is a potent inflammatory cytokine that links between inflammation and angiogenesis. Inflammatory state in central obesity is an important signal in the cross-talk between angiogenesis and development of adipose tissue.

MARKERS OF INFLAMMATION AND ADIPOKINES IN THE CASE OF METABOLIC SYNDROME

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There is evidence that metabolic syndrome (MS) is characterised by reaction of inflammation.

Aim: To evaluate markers of inflammation and some adipokines in patients with MS.

Methods: The trial compared the following biochemical parameters: total cholesterol, low and high density lipoprotein cholesterol (LDL-C and HDL-C), triglycerides (TG), glucose, insulin, the homeostatic model assessment (HOMA) index, levels of adiponectin, leptin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and plasminogen activator inhibitor-1 (PAI-1) in fifty-five patients without MS and forty-five patients with MS separately. Significance of difference between the two groups was determined by significance indicator-p.

Results: The inflammation markers and adipokines in both groups of patients are shown in table.

MS	CRO	Adiponectin	Leptin	IL-6	TNF-α	PAI-1
No	1.50±1.49	5.64±2.91	13.53±14.29	0.59±1.20	3.01±2.19	4.65±2.37
Yes	6.72±10.29	2.97±1.70	19.96±15.13	0.56±0.91	4.54±3.61	6.58±3.22
p	0.000	0.000	0.032	0.874	0.010	0.001

In the case of MS the level of adiponectin was significantly lower, but CRP, leptin, TNF-α and PAI-1 were higher.

Higher level of TG (2.39±1.24 v. 1.25±0.58mmol/L; p=0.000) and lower HDL-C (1.15±0.28 v. 1.76±0.40mmol/L; p=0.000) for patients with MS than without MS was detected. Patients with MS had significantly higher level of insulin (15.36±8.64 v. 6.85±4.7μIU/mL; p=0.000) and HOMA index (4.59±3.55 v. 1.55±1.10; p=0.000).

Conclusion: In patients with MS substantial activation of inflammation (CRP and TNF-α) and thrombosis formation (PAI-1) was detected. The given markers could be advised as additional factors for total CVD risk calculation.

ADIPONECTIN LEVEL AND ITS RELATIONSHIP TO CAROTID INTIMA MEDIA THICKNESS IN CHILDREN WIYH TYPE 1 DIABETES

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Background: Adiponectin is an anti-inflammatory and antiatherogenic hormone. It inhibits neointimal thickening and vascular smooth muscle cell proliferation.

Aim: The aim of this study to evaluate adiponectin level and its relation to carotid intima media thickness (cIMT) in children with T1DM.

Subjects and methods: Forty-six diabetic children mean age (13.59±3.64 years). The mean duration of diabetes (4.35±2.19 years), the mean BMI (20.56±3.54)the mean HbA1C (8.35 ±2.92).Thirty six healthy control subjects matched in age, sex and BMI took part in this cross-sectional study. All children had normal blood pressure for age and sex and no microalbuminuria. Adiponectin, albumin/ creatinine ratio in early morning urine sample, lipid profile, and HbA1c, were measured.

Results: Adiponectin level was significantly lower in children with T1 DM than control (9.49±1.74) and (10.31±1.45) respectively (P 0.02). Children with T1DM had significantly higher cIMT than control (0.57±0.08) and (0.43±0.07) respectively (P 0.00). Adiponectin level correlated negatively with cIMT (P0.01). Diabetic children with good metabolic control (A1C < 7) had no significant difference in Adiponectin level compared to control (10.22±0.81) and (10.31±1.45) (P0.82), although children with diabetes had higher cIMT (0.49±0.064) than control (0.43±0.049) (P0.00) .The most fitting factor that can predict cIMT was BMI (t3.61, P0.00). Adiponectin was significantly higher (10.22±0.81) and cIMT was significantly lower (0.49±0.064) in children with good metabolic control than those with poor metabolic control (9.27±1.74) (0.62±0.081).

Conclusion: Diabetic children had lower level of Adiponectin than control. Diabetic children with good metabolic control had no significant difference in adiponectin level than healthy children.

ADIPONECTIN AND NEW-ONSET HYPERTENSION: THE COPENHAGEN CITY HEART STUDY

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Aims: The aim of this study was to investigate the relationship between adiponectin, a hormone secreted by adipose tissue, and new-onset hypertension in the Copenhagen City Heart Study, since adiponectin has been proposed to play a major role in the pathogenesis of overweight-related diseases.

Methods: The present study was a prospective population-based study. We studied 613 normotensive women and 324 normotensive men from the third Copenhagen City Heart Study examination, which was performed in 1992 to 1994. New-onset hypertension was defined as systolic blood pressure ≥140 mm Hg, or diastolic blood ≥90 mm Hg, or use of antihypertensive medication.

Results: Between the third and the fourth Copenhagen City Heart Study examination, which was performed in 2001 to 2003, 173 of the 613 women and 77 of the 324 men had developed hypertension. In multiple logistic regression models, adjusting for age, creatinine clearance, high-density lipoprotein cholesterol, triglycerides, and fibrinogen, adiponectin was not significantly associated with new-onset hypertension having an odds ratio (95% confidence interval) of 0.96 (0.78-1.18; P=0.68) per standard deviation increase in women and 0.94 (0.70-1.25; P=0.66) in men. However, if body mass index was included in the models, body mass index was a significant predictor of new-onset hypertension with an odds ratio of 1.28 (1.03-1.58; P=0.026) per standard deviation increase in women and 1.59 (1.15-2.19; P=0.005) in men.

Conclusions: Our results indicate that adiponectin is not an important intermediary between adipose tissue and hypertension in women and men from the Copenhagen City Heart Study.

THE INFLUENCE OF METABOLIC SYNDROME COMPONENTS AND ADIPONECTIN CONCENTRATION ON THE ENDOTHELIUM-DEPENDENT DILATION OF THE BRACHIAL ARTERY

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Objective: Endothelial dysfunction is considered as an early event in the development of atherosclerosis. A noninvasive ultrasound technique to evaluate brachial artery flow-mediated dilation has recently been established for studying the vaso-dilating function of the endothelium. Adiponectin is one of the vascular regulators that has important consequences for cardiovascular risk. The aim of this study was to examine the influence of the metabolic syndrome components and serum adiponectin concentration on the vaso-dilating function of the endothelium.

Methods: Analysis was performed on 175 patients with metabolic syndrome and 53 patients of the control group aged between 42 and 65 years. Metabolic syndrome was defined using the NCEP ATP III criteria. Doppler ultrasound was used to analyse endothelium-dependent vascular dilation in the brachial artery. Serum adiponectin concentrations were measured by an ELISA kit (BioCat, Germany). Statistical analyses were carried out with 'Statistica 6.0' (StatSoft, Germany).

Results: Patients with metabolic syndrome showed impaired flow-mediated dilation and significantly lower adiponectin level than patients from the control group (4,5 ± 3,1 ng/µl and 15,2 ± 3,5 ng/µl, respectively). Endothelial dysfunction increased and adiponectin level decreased with increasing numbers of metabolic syndrome components. The greatest correlation with the changes of the brachial vascular diameter at 60 s after decompression had systolic blood pressure (r = -0,18) and abdominal-type obesity (r = -0,17).

Conclusions: Blood pressure control, body weight reduction and increasing the serum adiponectin level might help to reduce disturbances of endothelial functions and the risk of cardiovascular complications in patients with metabolic syndrome.

ADIPOCYTOKINES AND MARKERS OF INFLAMMATION IN ADOLESCENTS WITH METABOLIC SYNDROME

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Introduction: Obese children constitute a valuable population to study the mechanisms leading to numerous obesity-related patology like metabolic syndrome (MS). Factors released from adipose tissue, like inflammatory cytokines, fatty acids, adipocytokines exert biologic actions beyond the adipose tissue and influence peripheral metabolic and cardiovascular processes.

The aim of the study was to evaluate the concentration of selected adipocytokines and markers of inflammation in adolescents with MS.

Material and methods: We selected 23 patients with recognized MS (based on the IDF criteria), aged 15,5±2,1. The control group consisted of 20 healthy adolescents aged 16,0+1,5 years. Levels of adiponectin, leptin, resistin and TNFα were evaluated with use of immunoenzimatic ELISA kits, hsCRP - with use of immunoturbidimetric method.

Results: In children with MS we found, in comparison with control, lower level of adiponectin (p=0,001), higher of leptin (p= 0,001), resistin levels did not differ between groups. Adolescents with MS had also higher hsCRP levels (p< 0,001) as well as TNFα (p=0,002). We showed significant negative correlation between adiponectin with hsCRP and TNFα as well as positive correlation between leptin and hsCRP.

Conclusions:

1. In adolescents with MS we found significant differences in adipocytokines and inflammatory markers concentration compared to healthy control group. This may confirm considerable biological activity of adipose tissue in obesity already in young patients.

2. Numerous significant correlations between studied particles with components of MS as well as with other atherosclerosis risk factors show the important influence of adipose tissue released substances on obesity-related pathology already in adolescents.

VITAMIN E INDUCTION OF ADIPONECTIN EXPRESSION INVOLVES PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR GAMMA

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Several studies performed in human or in animal models, have reported a positive effect of vitamin E on insulin resistance. Because adiponectin is one the major actor involved in this physiopathological process, we evaluate the ability of vitamin E to regulate adiponectin expression, which could provide a molecular basis for the reported observations. Vitamin E force feeding resulted in an induction of adiponectin in mice at both mRNA and protein levels. Adiponectin mRNA and protein levels were also induced by vitamin E (both a- and g-tocopherol) in 3T3-L1 cells, independently of an antioxidant effect. In transient transfections, both a and g vitamers were able to induce the luciferase gene reporter under control of human adiponectin promoter. This effect seems to be PPARg-dependant since the

transactivation of luciferase reporter required PPARg expression vector co-transfection. The involvement of PPARg was confirmed by using a specific antagonist GW9662, which blocked adiponectin induction. Finally, we showed that PPARg mRNA levels were induced under tocopherol effect, independently of PPARg ligand properties. Vitamin E up-regulates adiponectin expression. This regulation implies PPARg, and could be a molecular basis for positive effect of vitamin E on insulin resistance.

SHOULD HYPOADIPONECTINEMIA BE INCLUDED AS A COMPONENT OF THE METABOLIC SYNDROME?

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Aim: To evaluate the relationship between adiponectin levels and the metabolic syndrome (MetS) in obese women.

Methods: We studied 80 premenopausal obese women anthropometrically characterized. Blood pressure (BP) was evaluated and a fasting blood sample was collected for adiponectin, glucose, triglycerides and HDL-c levels. We looked for correlations between adiponectin levels and waist circumference (Wc), glucose, triglycerides, HDL-c and BP levels. We compared adiponectin levels whether MetS was present or not (by the IDF definition) and according to the presence or absence of each of its components.

Results: Women were characterized by mean age=34.3±8.2 years, BMI=43.1±8.5 Kg/m^2, Wc=117.8±15.7 cm, waist:hip ratio (WHR)=0.88±0.07, systolic BP=123.7±18.3 mmHg, diastolic BP=79.5±11.5 mmHg, glucose=98.8±33.5 mg/dl, triglycerides=121.2±67.3 mg/dl, HDL-c=51.2±12 mg/dl and adiponectin=6.44±2.82 µg/ml. MetS was present in 34 women (42.5%) with hypertriglyceridemia present in 23.8%, low HDL-c in 52.5%, hyperglycemia in 27.5% and high BP in 38.8% of the sample. No significant difference in adiponectin was evident comparing groups with and without MetS, low HDL-c, hyperglycemia or high BP; those with hypertriglyceridemia presented significantly lower levels of adiponectin (p=0.039). Adiponectin was inversely correlated with Wc (p=0.008; r=-0.293), WHR (p< 0.001; r=-0.483) and triglycerides (p=0.004; r=-0.321).

Conclusions: Adiponectin do not associate with most part of the components of the MetS. Diagnosis of the MetS as well of the majority of the pathologies that enter in its definition do not serve as differentiation factors for adiponectin levels. We conclude that hypoadiponectinemia should not be included as a component of the MetS, in premenopausal obese women.

EFFECT OF SINGLE NUCLEOTIDE POLYMORPHISMS IN THE ADIPONECTIN GENE ON CIRCULATING ADIPONECTIN AND CARDIO-METABOLIC RISK FACTORS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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The genetic mechanisms underlying the hyperandrogenism and metabolic disorders in polycystic ovary syndrome (PCOS) are complex. We postulate that polymorphisms in the gene for adiponectin play a role. We studied 92 PCOS patients and 108 controls, we used PCR to determine the 45T>G (rs2241766) and 276G>T (rs1501299) polymorphisms in the adiponectin gene; measured LH, FSH, estradiol, testosterone, androstenedione, DHEA-S, SHBG, lipid profile, adiponectin, glucose and estimated insulin resistance (HOMA-IR). Regression analyses were used to find the associations of these variables with each other, adiponectin gene polymorphism and PCOS. Adiponectin showed significant inverse correlations with waist circumference, fat percentage, HOMA-IR, free androgen index (FAI) and triglycerides but showed positive correlation with HDL-cholesterol and SHBG. Multivariate regression analysis showed that adiponectin is a significant determinant of insulin, HOMA-IR, SHBG and FAI. The distributions of the genotypes of both polymorphisms were not significantly different in PCOS patients and controls but TT and GT genotypes of rs 2241766 and TT and TG genotypes of rs 1501299 were associated with significantly lower adiponectin and HDL and significantly higher insulin, HOMA-IR, triglycerides and FAI despite similar obesity indices. Binary logistic regression analysis showed that the TT (OR = 0.89) and GT (OR = 0.83) genotypes of rs 2241766 and TT (OR = 0.90) and TG (OR = 0.87) genotypes of rs 1501299 were significant determinants of PCOS risk. We conclude that polymorphisms in the adiponectin gene are associated with lower adiponectin that contribute to the pathogenesis of insulin resistance and hyperandrogenism in the patients.

PLASMA LEVELS OF LEPTIN AND ADIPONECTIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) WITH AND WITHOUT METABOLIC SYNDROME (MS)

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Aim: The aim of this work was a comparative study of the leptin and adiponectin plasma levels in patients with T2DM with and without MS.

Materials and methods: The 58 patients of both genders [26 men (M), 32 women (W)] aged 30 to 70 years, under study represented three equivalent groups: MS, T2DM, and T2DM + MS, and control subjects: with BMI < 25 kg/m^2 and BMI >25 kg/m^2. The diagnosis of MS was made based on ATPIII (2001), fasting leptin and adiponectin were measured by ELISA.

Results: The highest level of leptin was reported in W with MS (43.7±15.5 ng/ml), and T2DM + MS (29.8±6.8 ng/ml). In M and W patients with T2DM, leptin content (6.1±1.8; 9.5±4.5 ng/ml, respectively) did not differ from both control subgroups. Level of leptin in W of control group with BMI >25 kg/m^2, (28.7±5.2 ng/ml) were significantly higher than in the control group with BMI < 25 kg/m^2 (14.5±2.3 ng/ml, p< 0.05). Adiponectin content, contrary to leptin, was decreased in the presence of MS (13.9±2.9 ng/ml) and T2DM + MS (14.2±1.2 ng/ml) vs. both control subgroups (20.6±2.9; 26.9±3.4 ng/ml, p< 0.05).

Conclusion: Leptin content both in M and W with T2DM without MS was close to normal values. An increase in leptin levels in T2DM was mainly reported in W only in the presence of MS, and it correlates with obesity degree. Adiponectin content, contrary to leptin, was decreased in the presence of MS and T2DM + MS.

SERUM CONCENTRATIONS OF ADIPOCYTE BIOMARKERS IN INSULIN RESISTANT HIGH WAIST PERSONS

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Aims: Biomarkers of adipose tissue, additional criteria for investigations on the Metabolic Syndrome (MetS), may affect glucose and lipid metabolism and present pro-inflammatory properties.The aim of the study was to asses

serum adiponectin, leptin and resistin concentrations in central obese persons according to their insulin resistance.

Methods: White central obese Europids were screened for MetS (IDF 2005 criteria). Persons with no acute disease or severe chronic disorder underwent physical examination (ie. systolic, SBP and diastolic blood pressure, DBP; body fat, FAT). During OGTT fasting (G 0') and 2h-glycemia (G 120') were determined (enzymatic-bioMérieux, France) and t.2 diabetics were excluded. Fasting blood sample were determined: lipids: T-C, HDL-C, LDL-C, TAG (enzymatic-bioMérieux, France); insulin, Ins (ELISA-BioSource, Belgium); adiponectin, Adp, leptin, Lep, resistin, Res (ELISA-R&DSystems, US). Ins/G 0' ratio, IR and HOMA-IR were calculated. IR was used to study non-insulin resistant, non-IR, IR< 0,3 (n=25; 13 males, 12 females; age 49±10) and insulin resistant, IR group, IR≥0,3 (n=25; 12 males, 13 females; age 46±11).

Results:

1. Decreased Adp (p=0,001), increased Res (p=0,04) and Lep (p=0,04) were found in IR comparing with non-IR group.
2. In IR group negative correlations Adp&Ins0' (R=-0,50), Adp&IR (R=-0,51), Adp&HOMA-IR (R=-0,50), and Adp&Res (R=-0,61) were found, and positive correlations: Res&Waist (R=0,54), Res&DBP (R=0,53), Res&Ins0' (R=0,49), Res&IR (R=0,49), Res&HOMA-IR (R=0,49) were calculated.
3. Both groups presented positive correlations Lep&BMI (R=0,55) and Lep&Fat (R=0,65).

Conclusion: In the studied central obese persons insulin resistance influenced adiponectin and resistin concentrations in blood, while leptin was affected by BMI and FAT independently of insulin sensitivity.

INSULIN SENSITIVITY AND ADIPOCYTOKINES IN PATIENTS WITH DIABETES AND PREDIABETES

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Aims: The aim of study was to evaluate insulin sensitivity and level of adipocytokines in patients with newly diagnosed Type 2 diabetes (T2D) and prediabetes.

Methods: 82 patients and 28 healthy subjects were recruited in the study including 48 with T2D, 21 with impaired glucose tolerance (IGT) and 13 with impaired fasting glucose (IFG); mean age was 58,5±9,7 years, BMI 30,2±5,1 kg/m^2. Insulin sensitivity was measured by euglycaemic clamp (insulin infusion rate 1 mU/kg/min).

Results: The glucose disposal rate (M-index) was lower in patients with T2D (3,94±2,48 mg/kg/min) compared with IGT (5,71±0,45, p< 0,01), IFG (5,95±0,79, p< 0,01) and control group (7,72±1,89, p< 0,001). There was no difference of M-index between male (3,96±2,20 mg/kg/min) and female (4,13±2,29). There was significant correlation of M-index with BMI (r=-0,34, p< 0,001), HbA1c (r=-0,37, p< 0,001), triglycerides (r=-0,26, p< 0,001), adiponectin (r=0,23, p< 0,01) and visfatin (r=-0,30, p< 0,01) levels. Data for adiponectin, resistin, leptin and visfatin in patients with T2D, IFG, IGT and control group are presented in Table 1.

Conclusions: Insulin sensitivity was associated with obesity, metabolic control, triglycerides, adiponectin and visfatin levels in patients with T2D and prediabetes.

Level of adipocytokines in patients with T2D and prediabetes						
	T2D (1)	IGT (2)	IFG (3)	healthy subjects (4)	p	
Adiponectin µg/ml	6,08±2,54	8,03±2,48	7,17±0,92	14,33±5,78	p1-2<0,05, p1-4<0,01, p2-4<0,01, p3-4<0,01	
Resistin ng/ml	3,36±1,12	3,21±0,64	3,49±0,34	4,54±1,94	p1-4<0,05, p2-4<0,05, p3-4<0,05	
Leptin ng/ml	23,9±17,4	12,5±6,9	9,9±1,3	8,3±7,0	p1-2<0,01, p1-3<0,001, p1-4<0,001, p2-4<0,05	
Visfatin µg/ml	3,57±2,63	1,24±0,70	3,17±0,56	2,25±1,86	p1-2<0,01, p1-4<0,01, p2-3<0,05	

ASSESSMENT OF RELATIONSHIP BETWEEN SERUM LEPTIN AND ADIPONECTIN WITH METABOLIC SYNDROME IN 40-60 YEARS OLD POST MENOPAUSAL WOMEN

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Objective: Leptin and adiponectin are secretary hormones from adipose tissue, and closely correlate with cluster of metabolic syndrome (MetS) risk factor. The aim of this study is assessment of relationship between serum leptin and adiponectin with metabolic syndrome in 40-60 years old post menopausal women.

Materials and methods: The present cross-sectional study was done on 85 women 40-60 years old. MetS was identified with national cholesterol education program adult treatment panel III (NCEP ATP III) criteria. Serum leptin and adiponectin, blood pressure and other related factors were measured and data was analyzed by spss software.

Results: Women with MetS had higher leptin levels and lower adiponectin levels (p< 0.0001 for both variables) compared with women without MetS. Adiponectin was significantly correlated with waist size, triglycerides, high density lipoprotein (HDL) cholesterol (r= -0.33, -0.26, and 0.451 respectively, p< 0.0001 for all variables). The relation between adiponectin and HDL cholesterol and triglycerides remained significant after adjustment for age and body mass index (BMI). Also lepton was strongly correlated with waist size (r= 0.63, p< 0.0001); however, its relationship to the lipid profile was weak (for cholesterol r= 0.16, p< 0.05 and for triglycerides r= 0.17, p< 0.05) and disappeared after adjustment for BMI.

Conclusion: Our results show that leptin directly and adiponectin indirectly correlated with MetS in post menopausal women 40-60 years old.

Keywords: Leptin, adiponectin, metabolic syndrome.

ADIPOCYTOKINES IN OBESITY-ASSOCIATED HYPERTENSION

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Objective: Accumulating evidence indicate that abdominal obesity is more closely related with hypertension. In was proposed that adipocytokines such

as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), in addition to their role in immune response in hypertension, are involved in the development of obesity. The aim of our clinical study was to assess plasma TNF-α and IL-6 levels depend on presence of overweight, obesity and abdominal obesity.

Methods: Anthropometric parameters (height, body mass, body mass index (BMI), waist circumference), plasma TNF-α and IL-6 levels by ELISA were measured in 90 hypertensive patients. Abdominal obesity was defined according IDF (2005).

Results: Patients were divided into two groups depend on BMI means: 1 group (n=20) with BMI < 25 kg/m^2; 2 group (n=70) overweight and obese subjects with BMI > 25 kg/m^2. Plasma TNF-α (7.11±1.38 pg/ml) and IL-6 (11.93±0.21 pg/ml) levels 2 group patients were statistically higher as compared with 1 group - TNF-α (3.09±0.18 pg/ml; p=0.005), IL-6 (10.27±0.39 pg/ml; p=0.001). Comparison of adipocytokines levels in hypertensives depend on presence of abdominal obesity showed that TNF-α (7.78±1.69 pg/ml) and IL-6 (11.96±0.24 pg/ml) levels in hypertensives with abdominal type of body fat distribution (n=56) exceed TNF-α (3.63±0.52 pg/ml; p=0.021) and IL-6 (10.91±0.33 pg/ml; p=0.012) levels in hypertensive patients without abdominal obesity. It was found that TNF-α positively correlated with waist circumference (r=0.277; p=0.039) in patients with abdominal obesity.

Conclusion: Results of our clinical study indicate increased adipocytokines production in overweight and obese hypertensive patients more closely related to abdominal obesity presence.

EFFECT OF VERY-LOW-CALORIE-DIET(VLCD) ON CYTOKINE AND ADHESION MOLECULES IN PATIENTS OF METABOLIC SYNDROME(MS) WITH OBESITY

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Background: With diabetes and obese patients, we found increase of cytokines and adhesion molecules. It is thought that they play an important role for the onset and development of a complication such as arteriosclerosis. However, a change of them in patients of Metabolic Syndrome (MS) with obesity by dieting and a weight change are not clarified enough.

Purpose: To clarify an influence to cytokines and adhesion molecules by VLCD in patients of MS with obesity.

Objects and methods: We enforced VLCD treatments (600-800 kcal/ day) more than minimum 1week for persons with obesity (MS(+); N=8, MS(-); N=4), then We measured and examined comparison blood IL-18, Adiponectin, hs-TNF-α, VCAM-1, ICAM-1 and L-selectin before start and after one-two weeks and more than three weeks.

Result: In both MS(+) and MS(-) groups, BMI, total cholesterol and Triglyceride decreased significantly in both one-two weeks later and more than three weeks, compared with before the VLCD. In MS(+) group, VCAM-1 increased significantly after VLCD for one-two weeks, but appearing did not show a change at more than three weeks. Adiponectin in MS(-) group rise significantly after VLCD more than three weeks, but appearing did not show a change for one-two weeks. IL18, hs-TNF-α, ICAM-1, L-selectin did not show a meaningful change after a VLCD treatment in both MS(+) and MS(-) groups.

Conclusion: In the start early stage of a VLCD for a person having MS with obesity, it was suggested that sudden weight decrease might give vessels damage from an aspect of adhesion molecule.

THE ASSOCIATION BETWEEN SERUM ADIPONECTIN AND ANTHROPOMETRIC MEASUREMENTS IN MALAY ADULTS

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Objective: Low level of serum adiponectin is associated with low physical activity and high caloric intake. It is also proposed to vary between ethnicity. Hence, we aimed to investigate the association between serum adiponectin and anthropometric measures in adults from the Malay ethnicity.

Method: This is a cross-sectional study involving 43 adults aged between 30 to 70 years old living in a rural village in Malaysia. Anthropometric measurements include height, weight, waist circumference and hip circumference. Body composition was measured using InnerScan™ Body Composition Monitor (Tanita, Japan). Body mass index (BMI) and waist-hip-ratio (WHR) was calculated using standard formula. Serum adiponectim was measured using a commercial adiponectin Enzyme Linked Immunosorbent Assay (Millipore, USA).

Results: Serum adiponectin ranged from 3.7 µg/ml to 42.6 µg/ml with mean of 16.2 µg/ml. Adiponectin level was significantly (P< 0.001) higher in female (18.8 µg/ml) compared to male (9.4 µg/ml) subjects. Adiponectin was significantly correlated with waist circumference (r=-0.4, P< 0.05), waist-hip-ratio (r=-0.4, P< 0.01) and visceral fat (r=-0.3, P< 0.05). No significant association was found between adiponectin with BMI and percentage body fat.

Conclusion: Adiponectin is associated with measures of central obesity such as waist circumference, WHR and visceral fat. Hence, it has potential to appear as a biomarker for central obesity and could be possibly used as one of the component for metabolic syndrome criteria.

DIETARY PATTERNS AND MARKERS FOR THE METABOLIC SYNDROME IN ADOLESCENTS

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Aims: Overweight and other risk factors for cardiovascular disease (CVD) as well as their clustering, or the metabolic syndrome, are increasingly prevalent among children and adolescents. We examined relationships between dietary patterns and CVD risk factors and the clustering of these risk factors in a cohort of 14 year old adolescents living in Perth, Western Australia.

Methods: Two dietary patterns, 'Western' and 'Healthy', were identified in food frequency questionnaire data using factor analysis. Associations between these dietary patterns and BMI, waist circumference, systolic blood pressure, plus fasting levels of serum glucose, insulin, total cholesterol, HDL-C, LDL-C, triglycerides and insulin resistance (HOMA) were assessed using ANOVA. The clustering of these risk factors was examined in relation to both dietary patterns using logistic regression. Aerobic fitness and socio-demographic factors were considered as potential confounders.

Results: 1,139 adolescents provided complete data. The 'Western' dietary pattern was associated with a higher odds of clustering several risk factors (p for trend =0.02) as well as higher mean scores for total cholesterol (p for trend=0.03), waist circumference (p for trend=0.03) and BMI (p for trend =0.02) in girls, but not boys. The 'Healthy' dietary pattern was not related to the clustering of risk factors but was inversely associated with serum

glucose in boys and girls (p for trend=0.01 and 0.04 respectively) and was positively associated with HDL-C concentration in boys (p for trend=0.02).

Conclusions: Dietary patterns are associated with having CVD risk factors and the clustering of these risk factors in adolescence.

FAVORABLE EFFECTS OF MEDITERRANEAN DIET ON CHILDREN AND ADOLESCENTS WITH PRE-METABOLIC AND METABOLIC SYNDROMES

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Aims: To examine short- and long-term effects of individually adjusted Mediterranean diet on abdominal obesity, lipid status, hypertension and insulin resistance in children and adolescents with pre-metabolic and metabolic syndromes.

Material and methods: 60 children and adolescents aged 7 to 20 were studied, sub-divided by follow-up duration into three groups of 20 patients each and analysed through 6, 12 and 24 months diet, respectively. They all received individually adjusted Mediterranean diets rich in complex carbohydrates, dietary fibres and monounsaturated fats.

Results: Waist circumference (WC) was reduced after 6 months from l0l±17.8 to 92.5±12.1cm (p< 0,05) in the first group and after 12 months from 9l.8±14.5 to 86.6±10.9cm in the second group, while WC slightly increased in the third group. The increased blood pressure found in the first group normalised after 6 months: systolic from 123.1±17.5 to 119.3±19.7mmHg, diastolic from 8l.2±13.0 to 78.1±14.3mmHg. HDL-cholesterol improved in all groups. Triglycerides normalised after 6 months, from 1.86±0.8 to 1.39±0.52mmol/l (p< 0,05). Hyperinsulinism improved: (i) insulin mean value during OGTT test improved from 142.2±99.0 to 62.4±31.5U/l (first group), from 69.7±66.9 to 59.1±44.5U/l (second group) and from 79.8±38.6 to 58.4±57.6.8U/l (third group); (ii) HOMA IR improved from 14.0±15.2 to 6.1±3.5µmol/mU/ml (first group), from 7.9±4.8 to 6.0±2.2µmol/mU/ml (second group) and from 8.2±4.1 to 6.2±1.2µmol/mU/ml (third group). Increased CRP in the first group normalised after 6 months, from 7.1±4.6 to 3.7±2.2mg/l.

Conclusion: The cardioprotective Mediterranean diet applied resulted in favourable effects on insulin resistance, abdominal obesity, lipid status, hypertension and prevention of pre-diabetes, diabetes and vascular complications.

INCREASED INSULIN RESISTANCE, PLASMINOGEN ACTIVATOR INHIBITOR AND MICROALBUMINURIA, AND REDUCED ANTIOXIDANT STATUS, IN ADOLESCENTS WITH PRE-METABOLIC AND METABOLIC SYNDROMES

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Aims: To analyze thrombotic and atherosclerotic factors and antioxidant status in adolescents with pre-metabolic (pre-MS) and metabolic (MS) syndromes.

Material and methods: The study included 43 obese individuals (age 16 to 20). Three of the following five criteria were used for MS diagnosis: waist circumference (WC) > 90 Pct.; triglycerides (TG) >1.7 mmol/L; high density lipoprotein cholesterol (HDL-C) < 1.0 mmol/L; hypertension > 90 Pct.; glycemia >6.0 mmol/L. Patients with less than three afore mentioned criteria were indicated as patients with pre-MS. Insulin sensitivity was determined by HOMA IR, lipid status and total antioxidant status (TAS) by spectrophotometry. Activities of markers of antioxidant defense, superoxide dismutase (SOD) and glutathion peroxidase (GSH-Px) were determined in erythrocytes. Plasminogen activator inhibitor (PAI-1) was determined by plasminogen substrate essay. Microalbuminuria was determined immuno-nephelometrically.

Results: Adolescents with MS had increased WC (113.4±11.9cm), HOMA IR (8.7±4.4µmol/mU/ml), mean insulinemia (99.8±84.5U/l), PAI-1 (6.3±1.1U/ml) and microalbuminuria (41.2±28.0mg/24h), and decreased SOD and GSH-Px (1039.3±144.9 U/grHg and 27.3±6.5 U/grHg) and TAS (1.36±0.28U/g/Hb). Adolescents with pre-MS had increased WC (99.0±16.1cm), HOMA IR (6.2±3.4µmol/mU/ml), mean insulinemia (57.1±35.7U/l), PAI-1 (6.1±1.3U/ml) and microalbuminuria (52.7±29.5mg/24h), and decreased SOD and GSH-Px (1079.1±169.0 U/grHg and 31.6±7.6 U/grHg) and TAS (1.29±0.22U/g/Hb).

Conclusion: Pre-metabolic and metabolic syndromes in adolescents are characterized by abdominal obesity, hyperinsulinism, insulin resistance, increased thrombotic factors and miicroalbuminuria, and decreased antioxidant status. Glycoregulation, hypertension and lipid status disorders exist in metabolic syndrome and are absent in pre-metabolic syndrome. A risk for early atherosclerotic complications exists. If not intervened, pre-MS will become MS.

THE EFFECT OF 12 MONTHS METFORMIN TREATMENT ON OBESE CHILDREN AND ITS FACTORS ANALYSIS

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Objective: To compare the 6 and 12 months effect of metformin treatment on obese children and learn characteristics of the affecting parameters.

Subjects and method: 132 obese children were grouped based on OGTT, Grp1 consisted of 31 simple obese cases. Grp2 were 50 with hyperinsulinemia cases, among of them, 20 cases managed by lifestyle interferering and 30 cases treated with metformin. Grp3 were 51 IGR/T2DM cases treated with metformin and lifestyle interfering. Metformin Dose: 8-12yr-old, 0.25 tid, >12yrs. 0.5 tid.

Results:

1. Baseline HOMA-IR were high in Grp2 patients and HOMA-β were low in Grp3 patients.

2. After metformin treatment, all speculated parameters were improved remarkablely, while comparing data between 6 and 12 months there were no significant differences. Data in treated cases were better than that with simple lifestyle interfering.

3. Metformin treated patients in grp2, HOMA-IR and lgHOMA-β decreased. Grp3, FBG and HOMA-IR decreased, but the lgHOMA-β increased.

4. Treated patients in Grp2 and3, the change value of parameters were related to ΔBMI.

Conclusion: Metformin are safe and effective when treated on obese patients who had Hyperinsulinemia and IGR/DM. Comparing the results of Metformin treatment between 6 and 12 months, almost all parameters were no significant differences, this gives us a hint: Metformin might

discontinued after 6-12 months treatment in case the adverse effect.longer duration observation and further investigation to conform. Decreasing BMI had good relationship with decreasing Glucose, Insulin, Lipid and LFT. So BMI is the most effective, cheapest and non-invaded index of treatment.

METABOLIC SYNDROME IN CHILDREN OF A CITY IN COLOMBIA, SOUTH AMERICA (SIMBA STUDY)

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Aims: Determine the differences of prevalence between the consensus of metabolic syndrome-MS in a pediatric population, in a developing country.

Methods: Observational study, cross sectional analytical type, was realized. Children between 6 to10 years old, from Bucaramanga, Colombia were recruited. The sample was determined by random-cluster sampling. A detailed medical and family history was obtained and physical examination performed on all participants who were required to be in good health. The MS prevalence was estimated using different consensus considered for a pediatric population: Adult Treatment Panel III modified-ATP III, Research Group on diabetes and Chronic Illnesses-REGODCI, European Group for the Study of Insulin Resistance-EGIR and Lambert study.

Results: The data of 1282 children (51.1% male), who had medium of 8.5 [RIC7.2-9.6], were analyzed. The prevalence of the MS is described on the table.

ATPIII: BMI as central obesity indicator	2.6(34)
ATPIII: Waist circumference as central obesity indicator	2.2(28)
ATPIII: Scapular fold as central obesity indicator	2.2(28)
EGIR: BMI as central obesity indicator	7.4(95)
EGIR: Waist circumference as central obesity indicator	7.4(94)
EGIR: Scapular fold as central obesity indicator	7.1(91)
REGODCI	5.8(74)
LAMBERT1	9.6(123)
LAMBERT2	8.6(110)

Conclusions: The differences between MS prevalence in Colombian children, according to the consensus used is in the reported range for children of other countries, despite the differences among the consensus.

COMPARISON OF METABOLIC AND NUTRITIONAL PROFILES AMONG MEXICAN CHILDREN LIVING IN MÉXICO, MEXICAN CHILDREN LIVING IN THE US, AND NON-HISPANIC WHITE CHILDREN IN THE US

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Purpose: To compare the metabolic profile of Mexican children living in Mexico and children living in the United States, environmental factors, diet and physical activity.

Material and methods: A total of 595 children 6 to 13 years old were randomly selected from schools in México (MEXMCS), and 1283 Data from Mexican-American (MA) and Non-Hispanic Whites (NHW) children aged 6 to 15.9 from the National Health and Nutrition Examination Survey (NHANES 2003-2004). Variable set included: weight, height, waist circumference, BMI, systolic and diastolic blood pressure, fasting glucose, triglycerides, total cholesterol, LDL, HDL. Twenty-four-hour dietary recalls data was used to assess diet and exercise.

Results: We found significant difference between the groups for weight, height, waist circumference ($p< 0.0001$), higher overweight and obesity for the MA (BMI 17.9±4.5 kg/m^2) as compared with Mexican (BMI 17.4±4.5 kg/m^2) and NHW (BMI 17.3±5.1 kg/m^2) ($p< 0.01$). We also found differences for total cholesterol, HDL-cholesterol and diastolic blood pressure ($p< 0.0001$). We found higher energy intake for the Mexican group (2292±925 Kcal), as compared with MA (1998±771 kcal) and NHW (1953±834 kcal) ($p< 0.0001$). Higher intake of protein ($p< 0.0001$), carbohydrate ($p< 0.0001$), and saturated fat was higher for the NHW (25.3±14.7g) as compared with Mexican (20.5±12.7g), and MA (24.9±14.8g) ($p< 0.0001$).

Conclusions: We concluded that there are higher overweight and obesity in the MA group, the Mexican group had higher intake of energy, protein and carbohydrate and the Non-Hispanic white had intake higher amount of saturated fat.

PREVALENCE OF METABOLIC SYNDROME AMONG YOUNG ADOLESCENTS IN TAIWAN

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Objects: The purpose of this study is to evaluate the prevalence of the metabolic syndrome (MetS) among young adolescents in Taiwan. We also address the importance of anthropometric index such as body mass index (BMI) and/or waist circumference (WC) on the risk of MetS among study subjects.

Methods: After multistage random sampling, we totally enrolled 1562 adolescents (764 boys and 798 girls) with age 11-15 years in 2003. We used modified NCEP-ATP III criteria the diagnosis for metabolic syndrome in the young adolescents including: blood pressure$\geq 90^{th}$, fasting glucose$\geq 90^{th}$, TG$\geq 90^{th}$, HDL-C$\leq 10^{th}$, and BMI or WC$\geq 90^{th}$ with age and sex specification respectively.

Results: The overall prevalence of MetS was 4.1% for boys and was 3.8% for girls. After adjusting for age, cigarette smoking, alcohol drinking and pubertal status, BMI and WC were significantly associated with MetS for boys and girls. After further adjusting for BMI or WC, WC for boys (OR=1.14, 95%CI=1.05-1.24) and BMI for girls (OR=1.36, 95%CI=1.13-1.64) were the more significantly anthropometric index associated with MetS.

Conclusion: Further intervention study may be indicated for the overweight and obese young adolescents to evaluate the effectiveness of weight control in prevention of MetS in the future.

BODY FAT AND ITS RELATIONSHIP WITH METABOLIC SYNDROME INDICATORS IN OVERWEIGHT AND OBESE ADOLESCENTS IN LEBANON

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Aim: To examine whether obesity is accompanied by the development of metabolic syndrome indicators in Lebanese adolescents of both sexes.
Methods: One hundred and twenty adolescents, 58 males and 62 females, attending private or public schools across Lebanon were recruited as follows: 99 were overweight (BMI ≥85th percentile) and 21 were of normal weight (BMI< 85th percentile). Anthropometric measurements, glucose, insulin, serum lipids, blood pressure and dual energy X-ray absorptiometry were performed. Dietary food intake was also collected.

Results: Twenty three percent of obese subjects were diagnosed with the metabolic syndrome according to IDF criteria. The most frequently observed abnormalities among the obese subjects were elevated waist circumference in 97.1%, followed by hyperinsulinemia (≥19.9μU/ml) in 74.3%, low HDL in 38.2%, hypertension in 17.6%, elevated triglycerides in 16.1%, and high glucose in 5.4%. Pearson coefficient showed that BMI and waist circumference were significantly positively correlated with TG, SBP, DBP and insulin concentration and significantly negatively correlated with HDL ($p \leq 0.05$). HDL and TG were significantly negatively correlated. The intake of carbonated beverages was significantly higher among the obese adolescents versus the control ($p \leq 0.05$).

Conclusion: Obesity in adolescents may be associated with metabolic syndrome abnormalities that may arise in childhood and adolescence and track to adulthood. Whether this state increases the risk of developing cardiovascular diseases and type 2 diabetes mellitus remains to be investigated.

PREVALENCE OF THE METABOLIC SYNDROME RISK FACTORS IN OBESE SAUDI CHILDREN AND ADOLESCENTS

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Objective: This study aims at evaluating the prevalence of risk factors associated with the metabolic syndrome in obese Saudi children and adolescents.

Methods: Fifty-seven obese Saudi children and adolescents with a mean age of 9.8±3.5 years were evaluated at King Faisal Specialist Hospital and Research Centre-Jeddah between 2004 and 2008 . We reviewed their medical records and collected data on their age, weight, height, body mass index (BMI), blood pressure (BP), fasting lipid profile, fasting glucose and insulin concentrations. The degree of insulin resistance was estimated using the homeostasis assessment model- insulin resistance (HOMA-IR) score.

Results: Mean weight and body mass index (BMI) were 63.7±28.3 kg and 31.6±8.0 kg/m^2 respectively. Systolic and diastolic BP were elevated in 44% and 4% of the subjects respectively. 25.6% of the children had hypertriglyceridemia, 20% had hypercholesterolemia, 16.2% had elevated LDL cholesterol levels, and 15.8% had low HDL cholesterol levels. Impaired fasting glucose was found in 10 out of 38 (26.3%) of the patients. 9 out of 25 patients (36%) had fasting hyperinsulinemia. 11 out 37 patients (29.7%) met the diagnosis of the metabolic syndrome. Diastolic BP correlated positively with BMI (r=0.440, p=0.001), and HDL cholesterol correlated negatively with weight and BMI (r=-0.487, p=0.002 and r=-0.317, p=0.05). HOMA-IR correlated positively with BMI and triglyceride levels and negatively with HDL cholesterol levels.

Conclusions: Obese Saudi children and adolescents have multiple risk factors associated with the metabolic syndrome. At least 30% of obese Saudi children and adolescents meet the diagnosis of the metabolic syndrome.

RELATIONSHIP BETWEEN HYPERURICEMIA AND LIFESTYLE-RELATED DISEASES AMONG JAPANESE JUNIOR HIGH SCHOOL STUDENTS

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Aims: The present study was designed to examine whether serum levels of uric acid (UA) were associated with the metabolic disorders among Japanese junior high school students.

Methods: A total of 600 students (333 boys and 267 girl, aged 12.1 to 15.0 years) who were enrolled between April 2005 and June 2007 were included in this study. They underwent measurement of body height and weight, blood pressures, and blood chemistry, including serum levels of UA, lipids, and fasting plasma glucose (FPG) at the time of the annual school health check-up.

Results: The serum UA levels in boys were significantly increased compared with those of girls, and asymptomatic hyperuricemia (defined as serum UA levels > 7.0 mg/dL) was present in 32 (9.6 %) of the boys and 2 (0.7 %) of the girls. Of the 34 students who showed hyperuricemia, 20 (59 %) had one or more of the lifestyle-related diseases, such as obesity, hypertension, dyslipidemia, and increased FPG levels. There was a strong association between hyperuricemia and the presence of two or more of the lifestyle-related diseases in boys (odds ratio 5.74, 95% CI: 2.16-15.26, $p < 0.01$).

Conclusions: There was a close relationship between the serum levels of UA and the presence of lifestyle-related diseases among male Japanese junior high school students. The results of the present study may provide new insights into the development of educational programs for the prevention of lifestyle-related diseases in the Japanese population of the school children.

THE IMPACT OF ABDOMINAL OBESITY ON BLOOD PRESSURE IN CHILDREN AND ADOLESCENTS

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Aim: The Aim of the study was to investigate the influence of abdominal obesity (AO) on blood pressure (BP) in children and adolescents.

Methods: In the study group of 2391boys (B) and 2393 girls (G), age range 3 to 20 years from Slovakia anthropometric parameters and BP were measured. AO was classified as 90 th percentile according the abdominal circumference Slovak standards. Mean and median BP in children with AO were compared with non obese peers by ANOVA, $p< 0.01$.

Results: Incidence of AO (regardless of BMI) in ***B*** increased with age from 6 to 16%, in ***G*** it was highest at the age of 12 years (13%). Significantly higher mean SBP values in AO were found in school age, moreover 50% of them achieved the optimal SBP (120 mmHg) at the age of 10 y. This median of SPB was observed in non obese ***B*** older than 15 years, whereas in the non obese ***G*** the median of SBP 115 mmHg reached at the age of 12 y remained unchanged up to 20 y. The "high normal" or even hypertensive SBP values were observed in 30% of school age children with AO Average values of DBP were also higher in children with AO, but their median exceed the limit of optimal DBP (80 mmHg) only in 16-20 years old ***B***.

Conclusions: Attention should be paid to abdominal obesity also in children with normal BMI, as excessive abdominal circumference

regardless of BMI substantially increases the risk of incidence of hypertension.

ANALYSIS OF LEVELS OF ANGIOGENIN IN CHILDREN AND ADOLESCENTS WITH DIABETES MELLITUS TYPE 1 IN RELATION TO THE DURATION OF THE DISEASE

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The objective of the study was to analyse levels of angiogenin in children and adolescents with long-standing diabetes mellitus type 1 (DM1) in relation to the duration of the disease. We examined a group of 83 children with type 1 DM. Control group consisted of 51 healthy children. All of the diabetic patients had daily urinary albumin excretion, HbA1c level, C-peptide measured. Also 24hrs blood pressure monitoring and ophthalmologic examination was performed. Serum level of angiogenin was measured by immunoenzymatic ELISA technique. The patients with less than 5 years after diagnosis and no complications of the disease demonstrated a significantly shorter duration of the disease, significantly lower HbA1c level, CRP, albumin excretion rate, systolic and diastolic blood pressure as well as angiogenin levels in relation to patients over 5 years from diagnosis and showing complications of the disease. Additionally, the patients with DM1 showed significant correlation between serum angiogenin and duration of the disease (R=0.41, p=0.03). Our results indicate that angiogenin is involved in the process of angiogenesis and they provide information about the possibility of detecting late diabetic complications.

THE TENDENCY FOR LOWER T REGULATORY CELLS PERCENTAGES IN THE PERIPHERAL BLOOD OF CHILDREN WITH METABOLIC SYNDROME

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Background: The role of the immune system in the development of metabolic syndrome has received considerable interest in recent years. Regulatory T cells, a subset of CD4+ cells, can suppress inflammation and induce tolerance and are considered to play a role in the pathogenesis of this disease.

The aim of our study was to test the hypothesis that the number of T regulatory cells is reduced in children with metabolic syndrome.

Material: The metabolic syndrome was diagnosed according to the International Diabetes Federation definition (2007). A total of 25 children with metabolic syndrome were studied (median age - 17, boys - 12, girls - 18), and compared to the control group consisted of 30 healthy children with no signs of autoimmune, chronic, inflammatory and neoplastic disease.

Methods: Flow cytometric analysis of T-cell subpopulations was performed using the following markers: anti-CD3, anti-CD4, anti-CD25 and anti-CD127 (IL-7R).

Results: We found no differences in the percentages of T helper cells (CD4+) between examined and control groups. The percentages of T regulatory cells i.e. CD4+/CD25high and CD4+/CD25high/CD127low cells in children with metabolic syndrome were lower comparing to the healthy children (3.1% vs. 4.2%, $p< 0.05$ and 6.1 vs. 6.7%, $p>0.05$ respectively).

Conclusion: We noted the tendency for lower T regulatory cells in the peripheral blood of children with metabolic syndrome. This finding suggests their role in the pathogenesis of the disease and could be used as a potential therapeutic avenue in the future.

LOOKING FOR METABOLIC SYNDROME IN OBESE CHILDREN AND ADOLESCENTS

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Aim: To evaluate the prevalence of Metabolic Syndrome (MS) in a population of obese children.

Methods: From January 2005 to December 2007 all grossly obese children (428 patients, 210F/218M, mean age 10.5±2,9yrs, BMI above the 95th percentile for age and sex, according to Cacciari normograms), referred to our Department, were studied for waist circumference (WC), blood pressure (BPS and BPD), fasting cholesterol and fractions, triglycerides, glucose and insulin, calculated HOMA. The above mentioned parameters were used for MS classification according to 2007 IDF definition.

Results: The patients were subdivided in 2 age-groups: group A (247 adolescents, 114F/133M, mean age 12,55±1yrs, BMI 29,9±4,34 Kg/m^2, WC 92,24±10,5cm) and group B (181 children, 96F/85M, mean age 7,6±1,6yrs, BMI 25,92±3,22 Kg/m^2, WC 79,1±8,5cm). SM was found in 18 adolescents of group A (14M/4F, mean age 13,83±2yrs, BMI 33,94±5,48 Kg/m^2, WC 98,66±7,47cm, BPS 123,75±13,35mmHg, BPD 82,81±7,29mmHg, total cholesterol 185,17±43,11mg/dl, LDL cholesterol 188,12±39,44mg/dl, HDL cholesterol 36,94±5,3 mg/dl, triglycerides 170±91,45mg/dl, glycemia 93,26±9,93mg/dl insulinemia 25,13±12,03µU/ml, HOMA 5,89±2,81), with a prevalence of 7,29%. The SM patients had statistically higher BMI, total cholesterol, HDL, triglycerides, fasting glycemia, BPS and BPD than group A subjects without SM ($p< 0.05$).In group B subjects 135 children (66F/69M with family history of SM) were identified as at risk of developing metabolic syndrome (prevalence of 74,59%).

Conclusion: High prevalence of SM is found in grossly obese adolescents above 10 yrs of age when IDF criteria are used. Prospective careful follow-up has to be performed in younger (< 10 yrs) obese children with family history of SM.

IDENTIFICATION OF CD40 (CD154) LIGAND EXPRESSION ON THE SURFACE OF CONGLOMERATE PLATELET - MONOCYTE IN CHILDREN WITH METABOLIC SYNDROME

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Background: The increased expression of the transmembrane protein CD40 on macrophages, endothelium, smooth muscle cells, platelet - monocyte conglomerate is connected with enlarged risk of the occurrence of diseases of the cardiovascular system in metabolic syndrome.

The aim of the work was to establish whether metabolic syndrome in children can already be a precursor of cardiovascular diseases.

Material: The study was carried out on 35 children aged 10-18 years with the metabolic syndrome recognized according to IDF 2007 criteria. The control group determined 26 healthy children, without risk factors.

Methods: In examined children we evaluated BMI, the blood pressure, lipids, hsCRP, and the HOMA index. The analysis of the expression CD 40L (CD154) was performed using three-color flow cytometer. The

identification surrendered 10^4 cells. Statistical analysis was performed with use of U - Mann Whitney test, for correlation analysis we used Spearman and Pearson tests.

Results: We observed elevated expression of CD40 ligand on the surface on platelet-monocyte conglomerate in patients with the metabolic syndrome compared to healthy children (12.7% vs 4.95%, p=0.0036). In addition, we found statistically significant correlation between expression of the CD40L and HOMA index ($r = - 0.33$, $p < 0.028$).

Conclusions: Enlarged expression of the transmembrane protein CD40L not only initiate and influence the progression of the atherosclerosis, but modulate the architecture of atherosclerotic plaque as well.

THE FEATURES OF METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS AGED 7-16 YEARS IN THE CITY OF ZGIERZ (POLAND)

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The aim of this study was to evaluate the frequency of features of metabolic syndrome in children and adolescents living in the city of Zgierz (Poland).

A total of 504 of children and adolescents aged 7-16 years were studied. Weight, height, waist cirumference, fasting blood glucose concentration and blood pressure were measured. The WHO defined criteria for the diagnosis of overweight, obesity and hypertension were used. Self-report questionnaire prepared for the study purpose was used to assess lifestyle.

In the studied group, the frequency of overweight and obesity was 22,4% and 11,5% respectively. Obesity was more common in boys (14,5%), than in girls (9,8%). Abdominal obesity was observed in 14,5% of participants and was more common in boys (20,4%), compared to girls (11%). Elevated blood pressure was seen in 19,2 % of participants - 13,5% and 29% in girls and boys respectively. Non of the participants presented with an elevated fasting plasma glucose level.

The significant, positive correlation between overweight, obesity, abdominal obesity and hypertension was seen. Inappropite eating habits also correlated with overweight, obesity and hypertension. Additionally, physical activity was nagatively correlated with overweight and obesity in the examined population, although it did not reach statistical significance.

The early detection of the features of metabolic syndrome will help to define and develop preventive strategies in order to stop the progression of cardiometabolic diseases.

METABOLIC SYNDROME IN ADOLESCENT BOYS: DIAGNOSTICS AND TREATMENT

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Puberty is a crucial time for metabolic syndrome (MS) development. In spit of some MS components are present in children and adolescents as well as in adults, diagnostic criteria of the MS in pediatric population are still under discussion.

Aims: To investigate association between insulin resistance and some components of metabolic syndrome in adolescent boys. To estimate the efficacy of Metformin for MS treatment in young.

Methods: 292 boys (12-17 years) with clinical manifestation of the metabolic syndrome, according to IDF consensus (2007), were under investigation in the Department of Pediatric Endocrinology. Blood samples for insulin (IRI), glucose and lipids measurements were taken in fasting state. Insulin sensitivity and B-cell function were estimated by HOMA Calculator v.2.2. Metformin in dose - 1000 mg/day has been administrated to individuals with obesity and high blood pressure with therapeutic purpose.

Results: It was found that in insulin resistant individuals (HOMA-%S < 100%) prevalence of triglyceride (≥1.7 mmol/l) - OR = 16.6 [16.4 - 16.8]; HDL(< 1.03 mmol/l) - OR=3.36 [1.9 - 5.2]; BP(SBP > 130 mmHg, DBP > 85 mmHg) - OR= 2.13 [1.2 - 6.09]. Fasting glucose intolerance (≥5.6 mmol/l) was associated with B-cell dysfunction (50% < HOMA-%B < 100%) - OR = 14.7 [10.3 - 19.1].

Conclusions: According to our results triglyceride and HDL levels are the major MS components, which are strongly associated with resistance to insulin in young patients. Metformin (1000 mg/day) efficacy in body mass and blood pressure lowering is 88%.

Sponsored by "Berlin-Chemie Menarini Group".

BODY MASS INDEX AND INSULIN RESISTANCE AMONG MEXICAN CHILDREN , ADOLESCENTS AND YOUNG ADULTS

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Objective: To report the insulin resistance (IR) prevalence in a Mexican population of children, adolescents and young adults and its association with the body mass index. (BMI).

Methodology: The study enrolled 1366 participants between 7-24y. Previous signed inform consent , glucose and insulin levels were determine. Hyperinsulinemia was defined as >20mU/I .The IR was estimated by HOMA. The cut point of HOMA value is 3.16 to determine IR in adolescents. The BMI was determine through the Center of Disease Control 's charts, according to age and height percentiles. Normal weight was defined as < p85, overweight ≥p85 and < p95 , and obesity >p95. According to WHO's BMI cut points for >18y and older, overweight was defined as >27 and obesity >30.

Results: Fifty four percent were female, with an age average of 14.9±4.3y . Overweight was determined in 18.4%, obesity 13.3% hyperinsulinemia 12% and IR 23.3% from the entire population. Comparing by age group, we observed a higher prevalence in obesity (18.4%, p< 0.00), hyperinsulinemia(14.9% p=0.03) and IR (28.2% p< 0.004) in children 10-14 years old. The IR increased in direct relation with a BMI. Overweight increased 2.7 times the risk to develop IR (p=0.00; IC95% 1.99-3.78), obesity increase 6.8 times the risk of IR (p< 0.001; IC95% 4.87-9.68).

Conclusions: Overweight and obesity are associated with the developing of IR. The IR prevalence was higher than in other populations. It is required immediate actions in households and schools to avoid a mayor damage in health issues for this population.

ASSOCIATION OF ALANINE AMINOTRANSFERASE WITH AEROBIC FITNESS IN HEALTHY CHILDREN AND ADOLESCENTS IN WALES, UK

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Introduction: Alanine aminotransferase (ALT) is the liver enzyme with the closest association with liver fat accumulation and consequently has been used as a circulating marker of non-alcoholic fatty liver disease (NAFLD). This study examined the prevalence of elevated ALT in apparently healthy children and adolescents from Wales, UK and subsequently assessed the association of ALT with physical fitness.

Methods: 107 children (70 male) aged 11-14 years were assessed for ALT and VO_2max. Aerobic fitness was assessed using a progressive 20m shuttle run test. Test scores were converted using the equation of Mahar *et al.* (2006). VO_2max values were arranged into quintiles (Q1, lowest fitness - Q5, highest fitness).

Results: Elevated ALT levels were found in 13.1%, with a higher prevalence in boys than in girls (14.7% and 10.3% respectively). ALT in the children that displayed the lowest fitness (Q1) was significantly greater than those with higher fitness (Q3-5; $p = 0.002$, $p = 0.001$, $p = 0.012$). Multivariate regression analysis showed that aerobic fitness explained ~16% of the variation in ALT ($R^2 = 0.160$; $P< 0.0001$).

Conclusions: In conclusion, we have shown for the first time in apparently healthy Welsh school children that elevated ALT levels were highly prevalent and were associated with low aerobic fitness. These data suggest that children and adolescents with the lowest aerobic fitness may be at risk of developing NAFLD.

INSULIN RESISTANCE AND THE ASSOCIATION WITH HYPERTENSION AMONG CHILDREN, ADOLESCENTS AND YOUNG ADULTS ACCORDING TO THE BODY MASS INDEX

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Objective: To research the association between Insulin Resistance (IR) and hypertension among children, adolescents and young adults according to the Body Mass Index (BMI).

Material and methods: Data on 1366 participants between 7-2y were enrolled. Glucose and insulin levels were determined. Hyperinsulinemia was defined as >20mU/I. Participants were hypertense when the systolic or diastolic blood pressure (BP) was above the $P95^{th}$ percentile by gender and age for < 18y and for >18y, values of >140/90mmHg. Overweight/Obesity were establish by the BMI, based on CDC charts. Overweight was $\geq P85^{th}$ and obesity $\geq P95^{th}$. The IR was estimated by HOMA, considering it IR>3.16.

Results: There were 741 women (54.3%), average age was 14.9±4.3y, and the 13.3% showed obesity. According to the increase of BMI the insulin levels do so. The 12% has hyperinsulinism, hypertension (7.1%) and RI (23.2%), being the most affected those < 14y. Differences between the mean value of HOMA and insulin were found independently of age in all categories of BMI. Obesity increases 6.8 times the risk of IR (IC95% 4.8-9.6, p< 0.00), 3.8 times the risk of hypertension (IC95% 2.5-5.7, p< 0.00) and 9.6 times the risk to develop hyperinsulinism (IC95% 6.4-14.3, p< 0.00). IR increased 1.3 times the risk of hypertension (IC95% 0.82-2.16, p=0.20).

Conclusion: Overweight/Obesity increase the risk of develop IR and hypertension. Epidemiologic data showed that young people with high levels of arterial tension are more likely to develop hypertension in adulthood, causing a high morbility and mortality in future generations, therefore immediate actions are needed to prevent future damage in health issues.

LONGITUDINAL VECTOR PLOTTING OF INSULIN SECRETION AND INSULIN SENSITIVITY REVEALS GENDER DIFFERENCES IN GROWING CHILDREN: THE EARLYBIRD STUDY

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Aim: Insulin secretion and action interact in the feedback loop that controls blood glucose concentration. Longitudinal plotting of this interaction produces 'vectors', the direction of which may illuminate the earliest steps in the pathogenesis of diabetes. We have previously shown a significant gender difference in insulin sensitivity. We wished to establish the impact of this on vector plotting.

Methods: Subjects: 80 girls and 115 boys from the EarlyBird cohort. These were studied annually from 5y to 12y. Measures: BMI (kg/m^2), fasting concentrations of glucose and insulin, derived insulin sensitivity (HOMA-%S) and secretion (HOMA-%B).

Results: BMI SDS was higher in girls at all ages. Girls had lower HOMA-%S at all ages ($p< 0.001$ at 5y, 6y, 9y, 11y, 12y), and higher HOMA-%B ($p< 0.001$). As a result, the vector plot of HOMA-%B v HOMA-%S for girls was shifted upwards and leftwards compared with boys. Vector plots from 5y to 12y in both sexes revealed inflexions, indicating profound changes in the disposition of loop control. For example, in boys the inflexion was seen at 7y, with HOMA-%S falling from 327% at 7y to 298% at 8y; HOMA-%B at 7y was 58% (60% at 8y). The inflexions occurred at different ages in boys and girls, suggesting that glucose homeostasis may differ.

Conclusions: Girls are more insulin resistant (less insulin sensitive) than boys, and this is associated with differences in behaviour of loop control. In both sexes, falling insulin sensitivity post-inflexion is associated with rising beta-cell response, perhaps indicating strain on beta-cell reserve.

THE PRESENCE OF CARDIOVASCULAR RISK FACTORS AMONG CHILDREN WITH PARENTAL HISTORY OF PREMATURE ISCHEMIC HEART DISEASE

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Objective: The aim of this study is to evaluate the presence of cardiovascular risk factors in children of parents with premature ischemic heart disease (IHD).

Methods: Children between the age 5-18 y/o with parental history of premature IHD are included. BMI, BP, waist and hip circumference, cholesterol, LDL and HDL levels, fasting glucose, liver enzymes, CRP were measured. Carotid intima media thickness (CIMT) were evaluated.

Initial results: Thirty nine children, aged 4 - 18 y/o, with parental premature IHD were checked.

BMI percentiles were 15 to 90, BP percentiles were normal, and fasting glucose was normal. Thirty four children had familial hypercholesterolemia (FH), with LDL values above 160 mg/dl, 27 of them were evaluated for

CIMT and 11/27 were found to have increased CIMT. Four of them had already carotid plaques.

Conclusion: To date, there is not enough information regarding children of parents with premature ischemic heart disease. Intensive follow up and treatment are thus required in order to establish more data and allow primary prevention of future morbidity.

In our study, the main cardiovascular risk factor was hypercholesterolemia, Characterization of the cardiovascular risk factors in this population will provide usefull information required to establish recommendations for screening and early treatment of these children, in order ot prevent future morbidity and mortality.

ABDOMINAL OBESITY AND SERIC LEVELS OF C REACTIVE PROTEIN AMONG MEXICAN CHILDREN, ADOLESCENTS AND YOUNG ADULTS

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Aim: To identify the association between abdominal obesity (AO) and the plasmatic concentrations of C reactive protein (CRP).

Methods: 1077 participants between 7-24y were enrolled, who has a fasting stage, with no antinflammatories intake background and/or infections 15 previous days. The measurement of CRP in serum was determined by RANDOX inmuneturbidimetric essay. High CRP was established as >3mg/L. Waist circumference (WC) was measured at the high point of the iliac crest at the end of normal expiration, to the nearest 0.1cm, with a steel measuring tape. Central obesity was defined as a WC ≥75th percentile by age and gender, according to Fernandez's charts.

Results: About the participants, 52% were women, the mean of age was 14.8±4.34y. The mean value of CRP was 3.58±1.48mg/L. A high prevalence of CRP levels was found in the 13.4% of the population. The mean of WC was 77.13±12.7 cm. The 28.9% of all participants had AO. In those who had AO a higher CRP mean (3.83±1.76 vs 3.48±3.48mg/L) was identified. Differences were shown in the mean of CRP according to the presence of AO (p=0.0005). An OR crude of 2.33 (IC 95% 1.63-3.43) and an adjusted OR by sex, age, physical activity and tobacco consumption of 2.88 (IC 95% 1.92-4.32).

Conclusions: Even in young ages there is risk of having elevated CRP levels according to the presence of AO. The amount of intrabdominal fat is the most important determinant for a high inflammatory cytokines production, causing the increase of CRP levels, which contributes to the endothelial dysfunction.

ASSOCIATION BETWEEN PHYSICAL INACTIVITY AND INSULIN RESISTANCE AMONG CHILDREN AND ADOLESCENTS

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Objective: To evaluate the association between physical inactivity and insulin Resistance (RI) among children and adolescents.

Methods: The study enrolled 1117 participants between 7 to 19 years old. Glucose and insulin levels were determined by conventional methods. Hyperinsulinemia was defined as >20mU/I. Overweight was >P85 and obesity >P95 accord CDC percentile´s charts. The RI was estimated by HOMA, considering it RI when >3.16. Physical activity (PA) of the children and adolescents was classified as active and inactive ≥60 minutes/day 5 days per week, accord with CDC guidelines.

Results: More than half of the population were females (52%), with a mean age of 13.5±3 years, 14.5% were obese, and 12.9% had hyperinsulinemia, with the highest prevalence observed among females (p>0.05). Almost 25% of the population suffered from RI, the youngest (< 14 years) were the most affected. Seven of each ten participants were inactive. Males were more active (59 vs 38 min/day; p< 0.001). Participants < 10 years do less PA per day (35 vs 53 min/day, p=0.001). Participants who doing less 60 minutes of PA were 1.5 more likely to suffer from RI independently of sex, age and BMI (IC 95% 1.07- 2.19; p< 0.05).

Conclusions: Our study indicates that realize less than 60 minutes of PA among children and adolescents increase the likelyhood to present IR. Immediate action should be taken to reduce obesity during childhood to prevent the increase of several diseases in adulthood.

HYPERLEPTINAEMIA WITH POSSIBLE LEPTIN-RESISTANCE IN OBESE BOYS WITH DELAYED PUBERTY

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Background: The adipocyte-derived hormone, leptin, is supposed to play a permissive role in initiating the onset of puberty.

Objective: The study aim at measurement of serum leptin level in obese boys with delayed puberty (DP) and its relation to some other puberty-relevant hormones and some somatic and sexual anthropometric indices.

Subjects and methods: Delayed puberty was defined as absence of signs of puberty at upper limit of the chronological age for onset of puberty (Mean ±SD) equal 13.8 years. Twenty-five obese boys with DP (group1) their BMI ≥95th for age and twenty normal age-matched control subjects with normal onset of puberty (group 2) were included. The mean age in obese and control was (14.3±0.4) and (13.8±15.8) respectively. For all subjects, heights and body weights were measured; body mass index, fat percentage and fat mass were calculated. Sex Maturity Rating stages were identified. The levels of leptin, FSH, LH, GH, T_4 and free testosterone were determined. Bone age was determined for group1 only.

Results: All variables showed significant differences between the two groups except serum levels of GH and T4. Serum leptin was significantly higher in obese (25.2±17.1) than control (6.16±2.9) P< 0.001 . In group1 there were significantly positive correlations between serum leptin and body weight, BMI, fat mass and fat percentage. Obese with DP exhibited a subtle retardation of bone age.

Conclusion: Obese boys with DP are hyperleptinaemic. Presence of defective expression of leptin receptors might be responsible for this distinctive association of obesity and delayed puberty.

REFERENCE INSULIN RESISTANCE MARKERS AT BIRTH. THE MÉRIDA COHORT

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Background: Several endocrine regulators are implicated in the metabolic syndrome development.

Aims: To assess normal ranges for glucose, insulin, cortisol, GH, IGF1, and the Quantitative Insulin Sensitivity Check Index (QUICKI) for newborns and some Homeostatic Model Assessment (HOMA)-related equations, proposed as indicators of insulin sensitivity (HOMA-S) and insulin resistance (HOMA-R).

Methods: The indexes used to test insulin resistance or sensitivity were QUICKI, calculated as: 1/[(log Insulin)(μUI/mL) + (log Glucose)(mg/dL)]; HOMA-R, calculated as: Glucose (mmol/L) x Insulin (μUI/mL)/22.5 and HOMA-S, calculated as 1/HOMA-R. The study included 115 singleton, normoweight, Spanish Caucasian neonates delivered without foetal distress from mothers of the Mérida (Spain) Birth Cohort who tested negative in the O'Sullivan screen.

Results: Neonatal normal values (mean and 95% CI) were: Cortisol (7.4, 6.85-7.97(μg/dL), GH (16.7, 14.87-18.60 ng/mL), insulin (5.5, 4.12-6.88 μUI/mL), IGF-I (55.2, 50.82-59.53 ng/mL), Glucose (75.3, 68.29-82.29 mg/dL), QUICKI (0.45, 0.43-0.48), HOMA-R (1.36, 0.84-1.88), HOMA-S (4.07, 2.66-5.49). Hormone ranges (except for cortisol, whose values were lower) were equivalent to those of other studies. Cortisolaemia values cannot be associated with the type of delivery, as only 2.6% of births were by caesarean section, while 17.4% were instrumental deliveries. No significant differences were found between males and females. Differences were not significant after adjusting data for weight and gestational age.

	Mean	95% CI
Glucose (mg/dL)	75.3	68.29-82.29
UI/mL)□Insulin (	5.5	4.12-6.88
g/dL)□Cortisol (	7.4	6.85-7.97
IGF-I (ng/mL)	16.7	14.87-18.60
GH (ng/mL)	55.2	50.82-59.53
QUICKI	0.45	0.43-0.48
HOMA-S	4.07	2.66-5.49
HOMA-R	1.36	0.84-1.88

Conclusions: Due to the strict criteria used in the neonate selection, present mean and CI data will be used as reference of insulin resistance markers in future studies.

POOR CARDIORESPIRATORY FITNESS IN ADOLESCENTS WITH METABOLIC SYNDROME

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Objectives: Obesity and sedentary life style are the most important pathophysiology factors of the metabolic syndrome and type 2 diabetes in association with poor cardiorespiratory fitness. The aim of present study was to assess the relationship between cardiorespiratory fitness and parameters for metabolic syndrome in obese adolescents with and without metabolic syndrome.

Patients and methods: Thirty centrally obese (15 boys and 15 girls, age: 13.6±2.2 years, waist circumference>90 centile) and 30 metabolic syndrome (15 boys and 15 girls, 13.7±2.0 years, IDF criteria) adolescents (Tanner stage 2-4) were involved in the study. Components of metabolic syndrome were recorded and cardiorespiratory fitness at pulse rate of 170/min (physical work capacity: PWC170) was assessed using bicycle ergometer and HOMA-IR was calculated in every case.

Results: PWC170 was significantly lower in adolescents with metabolic syndrome as compared with those having simple central obesity (mean±SE: 1.20±0.13 vs. 1.52±0.14 W/kg, p=0.03). After controlling for age, sex and pubertal stage, PWC170 showed independent negative association with waist circumference and HOMA-IR while no relation was observed with fasting plasma glucose, lipid and blood pressure parameters in the group of simple obese adolescents. However, in the group of adolescents with metabolic syndrome, PWC170 related independently with waist circumference, HOMA-IR, fasting plasma glucose, trigliceride and systolic blood pressure

Conclusions: Adolescents with metabolic syndrome have significantly lower level of cardiorespiratory fitness than cases with simple central obesity. Poor cardiorespiratory fitness independently contributes to the development of insulin resistance and blood glucose, lipid and blood pressure abnormalities in adolescents.

THE CONTRIBUTION OF THE SELECTED PARAMETERS OF LIPID METABOLISM TO THE DEVELOPMENT OF DIABETIC NEPHROPATHY IN CHILDREN AND ADOLESCENTS WITH DIABETES MELLITUS TYPE 1

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Objectives: The aim of the work was to evaluate lipid metabolism and its influence on the development of diabetic nephropathy in children and adolescents with diabetes mellitus type 1 (DM1).

Material and methods: 185 children with DM1 were enrolled in the study. The control group consisted of 86 healthy children. All the children had HbA1c, triglycerides, total cholesterol and its HDL and LDL fractions as well as daily urinary albumin secretion assessed.

Results: No statistically significant differences were observed between DM1 children and the healthy controls. When comparing DM1 children presenting with microalbuminuria (group A) to DM1 patients without overt microalbuminuria (group B) and healthy children it come out that the levels of total cholesterol and its LDL fraction were statistically significantly higher in group A with regard to the healthy children but were not significantly different between group B patients and the control group. Statistical analysis of the selected lipid parameters and HbA1c levels has shown a statistically significant increase in the level of total cholesterol ($p< 0.001$) its LDL fraction ($p< 0.001$) and triglycerides ($p< 0.001$) correspondingly to the duration of the disease.

Conclusions: Presence of the proper lipid profile during the first years of diabetes mellitus type 1 in children cannot guarantee that afterward the patient will not demonstrate clinical symptoms of the diabetic nephropathy.

PHYSICAL ACTIVITY AND C-REACTIVE PROTEIN IN MEXICAN ADOLESCENTS: THE OPERATIONALIZATION OF THE ACTIVITY IT MATTER?

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Objective: To evaluate the association between physical activity (PA) and the C-Reactive Protein (CRP), comparing 3 methods to operationalizate the physical activity.

Methods: The population base of this report are children of participants of the project "Cohort of Workers IMSS-INSP-UAEM". The methods have been described previously. Briefly, the PA level was evaluated with a questionnaire used previously that allows measuring the PA during the daily life and in the free time. The CRP levels were determined using the highly sensitive technique. By means of models of multiple logistic regression the association between the PA (measured in minutes per day in the free time, in MET´s of total PA and like reason of the time of PA in the free time and the time in activities of low energetic expenditure - RAI-) and the levels of CRP was evaluated (< 5 mg/l Versus. 5-10 mg/l), adjusting by diverse covariables.

Results: The information of 1.007 clinically healthy adolescents was analyzed. 139 (13,8%) adolescent with levels elevated of CRP were detected. The PA min/day, METS/day and RAI were inversely associated with the CRP; (OR=0.32 CI95% 0.18-0.58; OR=0.44 CI95% 0.23-0.85; OR=0.42 CI95% 0.23-0.75, respectively).

Conclusions: The PA is associates with the CRP levels. We could observe that the operationalization of the PA does not modify the observed association, this finding is relevant since in our knowledge there is no previous report of the same. However, Is necessary to confirm these findings in other populations.

METABOLIC RISK FACTORS IN GUADELOUPEAN ADOLESCENTS

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Aims: To quantify the presence of selected cardiovascular and metabolic risk factors among adolescents of Guadeloupe.

Methods: 808 voluntary students aged 11-17 yo from 6 schools participated. They fulfilled the modifiable activity questionnaire over a 7-day period. Their height, weight, body composition and blood pressure were measured. Elevated blood pressure was defined as systolic or diastolic blood pressure above the 95th percentile adjusted for age, gender and height percentile given by the fourth report of the American national high blood pressure education program working group on high blood pressure in children and adolescents.

Results: Based on IOTF threshold of body mass index, 18.9% of the participants were overweight and 7.3% were obese. The distribution of the weight status was affected by the gender (χ^2 = 13.2, p< 0,001), with moderate or severe hypertension identified among 9.7% of boys, and 12.9% of girls. As other authors, we observed a strong association between the weight status and the blood pressure status, but no specific profile of physical activity was identified according to the blood pressure profile.

Conclusions: This study confirms in a Caribbean population that the screening of blood pressure is necessary in adolescents presenting overweight or obesity. Our results suggest that it is not pertinent in this population to target one or the other of the metabolic or cardiovascular risk factor with exercise programs likely to prevent the development of metabolic abnormalities in general population.

ASSOCIATION BETWEEN C-REACTIVE PROTEIN AND ALANINE AMINOTRANSFERASE AS CARDIOVASCULAR RISK FACTORS IN ADOLESCENTS

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Aim: To identify the association between C-reactive protein (CRP) and alanine aminotransferase (ALT) and cardiovascular risk factors (CV) in adolescents 10 to 18 years.

Materials and methods: 795 subjects participated, the CV was determined by the criteria of the Adult Treatment Panel III for pediatric ages. The BMI was established by the boards of the CDC, according to percentiles for age and sex. Elevated values of CRP and ALT were defined as those above the median (> 3.3mg / L and> 15mg/dL, respectively) classified into four groups.

Results: The average age was 14 ± 2.5a. 52% were women. Prevalence of elevation CRP and ALT was 48% and 43% respectively. Overweight / obesity was found in 31%, hyperinsulinemia in 14.5%, and insulin resistance in 26.54% of yhe population.

The prevalence of ALT elevated was higher in males (p< 0.001). ANOVA analysis showed that the mean value of CV as: BMI, waist circumference (WC), systolic blood pressure (s-BP), triglycerides (TG), HDL-c, insulin and HOMA-IR, was higher in the elevated groups of CRP and ALT (p < 0.001 in all), but not for blood pressure and glucose.

After adjusting for age and sex observed that: BMI, WC, TG, HDL-c, insulin and HOMA-IR were positively associated with elevation of CRP and ALT. The OR´s ranged from 2.1 (TG) and 8.6 (BMI), all statistically significant.

Conclusions: Our data suggest that elevated concentrations of CRP and ALT are associated with CV in children and adolescents however is necessary to confirm this in other populations.

INSULIN RESISTANCE AND ADIPOCYTOKINES IN YOUNG OBESE CHILDREN

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Aims: To evaluate the prevalence of insulin resistance (IR) and dyslipidemia in obese children and their possible relation to the plasma levels of adipocytokines.

Methods: 56 children (29 boys; 27 girls; BMI>95th percentile) between 7-9 year-old participated in a lifestyle intervention program. Assessment at baseline included weight, height, BMI, BMI-Zscore (BMI-Zs), waist circumference (WC), Tanner stage, blood pressure, and fasting serum level of glucose, insulin, C-peptide, total cholesterol, HDL, LDL, triglycerides (TG), leptin, adiponectin, TNF-a, interleukin 6 (IL-6), C-reactive protein (CRP) and homocysteine. Insulin resistance (IR) was calculated by HOMA-IR method. Results with statistical significance (p< 0.05) are presented.

Results: At baseline, all children presented with abdominal obesity (WC≥90th percentile). IR was observed in 11% of children. Total cholesterol ≥180 mg/dl, HDL≤40 mg/dl, LDL≥110 mg/dl and TG≥100 mg/dl were found, respectively, in 36%, 9%, 45% and 16% of the sample. Correlation analysis showed a linear relationship between BMI and the

following variables: C-peptide, IR, leptin, TG and CRP. WC correlated positively with BMI, BMI-Zs, C-peptide, insulin, leptin, PCR and homocysteine, and negatively with adiponectin. IR correlated linearly with leptin and TG. Leptin showed a positive correlation wit C-peptide, TG and CRP. However, adiponectin levels were inversely correlated with BMI, insulin, TG, CRP, homocysteine, leptin and TNF-a.

Conclusions: These obese children showed a significant prevalence of IR and dyslipidemia. Leptin levels correlated with a low-grade inflammatory state and IR, contributing to the future development of metabolic syndrome. In contrast, adiponectin seems to have an important protective role.

EPIDEMIOLOGICAL FEATURES OF TYPE 1 DIABETES MELLITUS IN PEDIATRICS

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The type 1 diabetes mellitus is the most frequent in pediatrics, the epidemiological studies shows a regular increase of frequency.

The objective of the study was to describe the epidemiological features of type 1 diabetes mellitus among children attending the pediatrics department at Tlemcen Hospital, Algeria.

Prospective study was conducted on 202 patients at the pediatrics department; from 01-01-1999 to 09-15-2008. For each patient a questionnaire was field. A clinical examination was performed. We used the World Health Organization (WHO) type 1 diabetes mellitus definition for patients ≤ 15 years old.

This study showed for 202 patients; 98 males (48%) and 104 females (52%) was diagnosed with type 1 diabetes mellitus. The mean age at diagnosis was 7.5 years old. For 14 families, at least 2 members have had type 1 diabetes mellitus. Three types of regiments used for the treatment. The diabetes wasn't controlled well; the mean of HbA1C was 11.23% /patient/year. Association with others autoimmune diseases noticed: celiac disease for 3 patients, thyroiditis for 8 patients. This association complicates the management of the diabetes.

Statural growth was satisfactory with sometimes non significant puberty retardation. Degenerative complications were reported: retinopathy for 20 patients, cataract for 5 patients, and renal impairment for 8 patients.

The finding indicates that pediatricians as well physicians in charge of child with diabetes, should seriously and continuously consider the diabetes degenerative complications. For the patient futures all the consequences are related to the well control of diabetes from the childhood period.

MENTAL HEALTH PARAMETERS IN GREEK OVERWEIGHT AND OBESE ADOLESCENTS

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Objective: To assess the prevalence of behavioral, emotional symptoms and mental disorders in Greek overweight and obese adolescents.

Methods: 538 adolescents, 226 boys (Mean ± SD) 14.4 ± 2 years and 312 girls (Mean ± SD) 14.9 ± 2.03 years followed at the Center for Health and Prevention in Adolescence, were included. 69 boys and 82 girls were overweight/obese. Mental health parameters were assessed by the use of the Youth Self Report (Achenbach System of Empirically Based Assessment). For the statistical analysis of the collected data SPSS 16.0 was used and t-test was performed.

Results: Descriptive statistics in the group of obese adolescent boys showed: depression - anxiety 7.2%, withdrawal-depression 2.9%, social problems 2.9%, attention problems 4.3%, delinquent behavior 2.9%, aggressive behavior 11.8%, thought problems 0%. Additionally, in the group of obese girls showed: depression - anxiety 12.2%, withdrawal-depression 11%, somatic complains 2.4%, social problems 11%, thought problems 1.2%, attention problems 11%, delinquent behavior 3.7%, and aggressive behavior 7.3%. In the group of obese boys there is a higher prevalence of thought problems and delinquent behavior ($p < 0.05$). In the group of obese girls there is a higher prevalence of somatic complains and attention problems ($p < 0.05$).

Conclusion: The epidemic of obesity not only affects the physical health but also the mental health of the adolescents. Therefore, personalized psychological support is needed along with the dietary intervention.

ESTIMATION OF QUALITY OF LIFE IN ADOLESCENCE WITH DIABETES MELLITUS

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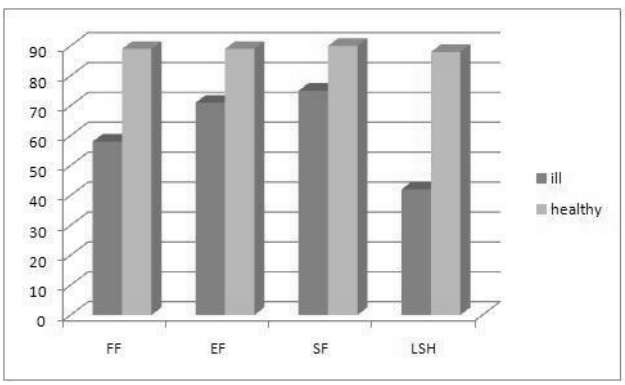
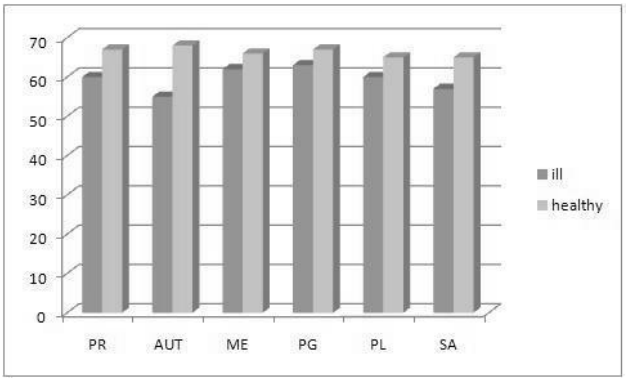
Aims: To implement an estimation of quality of life (QOL) in adolescence with diabetes type one, comparing it with quality of life of healthy adolescence.

Methods: We used the international pediatric questionnaire of quality of life - PedsQL ™ 4.0 General Score, Diabetes Module (Varni J., 2001), «The Scale of psychological well-being» (K. Ryff, 1989). Adolescence with diabetes in number of 58 persons aged on the average 15,8 ± 2,4 have been inquire.

Results: Indicators of general QOL of patients with diabetes in comparison with control group: considerable decrease in indicators are established: physical functioning (58,4±16,2; $p < 0,01$), emotional functioning (70,8±18,8; $p < 0,01$), social functioning (75,1±17,4; $p < 0,01$), school functioning (42,3±22,1; $p < 0,01$); Patients with diabetes have law level of psychological well-being: positive relations» (60,0±9,6; $p < 0,01$), «an autonomy» (55,5±9,7; $p < 0,01$), «management of environment» (58,6±9,7; $p < 0,01$), «personal growth» (61,3±10,7; $p < 0,01$), «purposes in life» (62,4±11,0; $p < 0,01$), «self-acceptance» (56,1±10,6; $p < 0,01$). The correlation analysis: positive correlation between complications of a diabetes and positive relations with associates ($r = 0,56$; $p < 0,05$); an autonomy ($r = 0,40$; $p < 0,05$); personal growth ($r = 0,37$; $p < 0,05$); purposes in life ($r = 0,41$; $p < 0,05$); self-acceptance ($r = 0,60$; $p < 0,05$).



[QOL of ill and healthy adolescence (PedsQL)]



[QOL of ill ana healthy adolescence (PWB)]

Conclusions: QOL in adolescence with diabetes more lower than at healthy teenagers and depend on the psychological well-being of tee-nagers with diabetes.

CHILDREN AND THE METABOLIC SYNDROME

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There are well documented proofs dislipoproteinemia, as a major coronary artery disease (CAD) risk factor (RF) is mostly of nutritional origin and can be prevented. It´s also well known adults, even those after cardiovascular events are very "rigid" in changing nutrition and behavior habits.

Objective:

1. to analyze the food pattern and lipoprotein profile in children and to screen the dislipoproteinemia and
2. to focus the importance of preventive strategy in children.

The analysis was conducted in a children population group sample of 290 children, aged 7-15 years, selected at random in schools.

In this study total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and tryglicerdie (TG) were measured in a fasting plasma of mentioned participants. An standard questionnaire was filled for all participants concerning their eating and lifestyle habits.

Results: Mean TC, HDL, LDL and TG were: 4.6mmol/L, 1.67mmol/L, 2.55mmol/L, and 1.0mmol/L respectively. In 23 children (7.9%) the high cholesterol (above 5.20mmol/L) was found; in 19 (6.6%) the cholesterol values were under 6.5mmol/L, while in 4(1.3%) cholesterol was above 6.5mmol/L. The triglycerides were within normal ranges in all children.

Discusion and conclusion: Our data indicate there are many anhealthy habits in children. Dislipoproteinema, especially a high number of children with a low level of HDL cholesterol, as a important component of metabolic syndrome is present in children too.

Nutrition education as component of community based Interventional program must begin in our country too, especially in children, who are adaptive to lifestyle changes.

THE HEREDITARY PREDISPOSITION TO BLOOD PRESSURE INCREASE IN CHILDREN WITH SIGNS OF METABOLIC SYNDROME

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Objective: To determine a sense of genotype and influence of hereditary predisposition in formation of raised blood pressure in children with signs of metabolic syndrome. Subjects: We studied 110 obese boys (80 - 72.7%) and girls (30 - 22.3%) aged 6-17 years old with varying degrees of obesity (I-IV).

Methods: Height, weight, body mass index and blood pressure level were measured. Lipid profile and level of glucose were analyzed. The estimate of findings was carried out by percentile tables. In 80 patients, randomly sampled from our group, ACE I/D gene polymorphism were genotyped by PCR method. Their near relations were cross-examined by questionnaire.

Results: The prevalence of the components of metabolic syndrome was: 20.9% for persistent and 45% for episodic hypertension, 54.5% for pro-atherogenic lipid disorders, 23.6% for impaired glucose homeostasis. 10 out of 17 carriers (58.8%) of the ACE gene D/D genotype, which is estimated as an independent risk factor for development of sustained hypertension, had episodic (20%) and persistent (80%) high blood pressure. And 4 out of 8 children (50%) with resistant hypertension already had the hypertonic retinal angiopathy. There were found that in 10 out of 17 families at least 1-2 of near relations of children - D/D genotype carriers, complained of high blood pressure.

Conclusion: The significant part in formation and intensity hypertension in children with signs of metabolic syndrome plays the variant of genetic polymorphism. The presence hypertension in near relations more than in 50% cases permits to talk about existent hereditary predisposition.

CONNECTIONS BETWEEN OBESITY AND SOME ASPECTS OF OBESITY: LOCUS OF HEALTH CONTROL IN ADOLESCENTS

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Introduction: The substantial health enhancing potential of physical and psychological activity can be realized by incorporation of physical activity in everyday style of life. Health can be understood as an aim of activities but also adolescents may not take into consideration activities toward health improvement.

Aim of the study: The aim of the study was to estimate differences in psychological functioning locus of health control in adolescents with obesity.

Methods: The method was The Scale MHLC - Multidimensional Scale of Health Control Localization.

Material: 60 persons growing with obesity (over 90 percentile) participated in investigations in age of 12-18 years. 60 healthy persons well-chosen made up the group of the reference under in relation to age, sex, educations. The results were important on the level 0,05.

Results: The locus of health control was internal in both groups, but internal locus in healthy group has appeared more often.

Conclusion: Obesity may be a risk factor of disturbing of locus of control and may make some difficulties in creating motives for health behaviors.

THE MAIN PROBLEMS OF MOTOR ORGAN APPEAR IN OBESE CHILDREN

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Childhood obesity is an important health problem because an excessive body mass affects the body posture. It leads to deteriorate the biological condition of child, its motor skills and physical efficiency. But the most important thing - obesity is the essential factor loading the motor organ.

Scientists' findings show that intensity and frequency of irregular body posture is related to the degree of obesity. They evaluate the body posture in two planes : sagittal and frontal. In the sagittal plane the degrees of thoracic kyphosis and lordosis was measured. In the frontal plane the symmetry of chosen osseous points in relation to the spine was analysed. (I.a. distances from the shoulder - blades to the spinous line and height of triangles of waist). And these are the most often disorders in frontal plane.

The most often problems in sagittal plane were concerned with reduction kyphosis's angle and increase lordosis. It is closely connected with deformations of pelvis. It tilts forward and the lordosis's angle enlarges.

Excessive body mass results in developing four main disorders: enlarged lordosis (the abdomen is convex), flat feet, knocked knees (genu valgum) and asymmetry of the spine. There are a lot of methods of treatment. Kinesiotherapy, hydrotherapy, physical therapy are the most popular and effective ways of relieving pain, reducing inflammation and improving range of motion in occupied and loaded joints.

METABOLIC COMPLICATIONS OF OBESITY IN CHILDREN

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Increase of metabolic complications in obese children results in high morbidity in young adults.

Aim: To reveal frequency of metabolic complications in children with obesity.

Methods: We examined 119 obese children aged 4-17 (BMI > 95 percentile). All patients were examined by clinical, biochemical, ultrasound methods. Liver elastography was performed if necessary. In children with fatty liver chronic hepatitis were excluded.

Results: We selected 50 children (42%) with metabolic complications of obesity (NAFLD - 40, metabolic syndrome (IDF, 2005) - 27, both - 17 children). Mean age of children was 13,26 years (boys - 19, girls - 31), weight - 96,4 kg, height - 163,5 cm, BMI - 34,4 (98,3 percentile). Waist circumference - 105,42,8 cm (90 percentile), hip - 110,6±4,1 cm. Obesity in children manifestated at 6,2±0,5 years. Arterial hypertension was documented in 19 children. Family anamnesis characterized by obesity in 74%, diabetes type 2 - in 26%, hypertension - in 50% of children. Increase of serum cholesterol was revealed in 24%, triglycerides - in 18%, low-density lipoproteins - in 14%, decrease of high-density lipoproteins - in 52% children. In most of children hyperuricemia was noted (429,9±22,8 mcmol/l). Ultrasound signs of fatty liver were shown in 40 patients with NAFLD. Left lobe size was 81,3±1,8 mm, right - 141,5±2,2 mm. Portal hypertension wasn`t noted in any patients. Liver elastography (n=22) showed 1-3 stage of fibrosis in 13 children.

Conclusions: Children with overweight and obesity has high risk of metabolic complications. Risk factors are the early start of obesity and specific family anamnesis.

NUTRITIONAL STATE ANALYSIS, METABOLIC SYNDROME AND FOOD INGESTING IN A VALLADOLID ADOLESCENT POPULATION (SPAIN)

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Objectives:

Valladolid adolescent nutritional state.

Metabolic syndrome (MS) risk factor analysis.

Food ingesting study.

Materials & methods:

Transversal descriptive observational study on a 557 adolescents sample between 14-18 years old (2005-2007).

Variables: age, gender, weight, height, waist perimeter (WP), systolic and diastolic blood pressure (SBP/DBP), body mass index (BMI) and food list weekly rations.

BMI was classified using z-score and International Obesity Task Force (IOTF) criterions, while WP and SBP/DBP were classified with International Diabetes Federation (IDF) ones.

Results:

Results show 11,9% overweight and 5,2% obesity using z-score; and a 13,9% and 2,4% respectively employing IOTF cut-off points.

A 15,2% women in undernutrition range.

A 1,3% have a main criterion of SM diagnosis.

A 42,4% have SBP/DBP greater or equal that 130 and 85 respectively.

Normal group have greater food ingesting than the ones with overweight or obesity.

Daily energy distribution: 32% lipids, 45% carbohydrates and 17% proteins.

Exists an iodine, zinc, A and E vitamin ingesting deficit in males and a calcium, iodine, zinc and E vitamin in females.

Conclusions:

There is lower weight excess than in AVENA and enkid.

SM development risk is lower than in British and Americans.

Exists a carbohydrate, iodine, zinc, calcium and A and E vitamin ingesting deficit.

OBESITY IN ADOLESCENT-PREVALENCE AND RELATIONSHIP WITH CARDIOVASCULAR RISK FACTORS

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If obesity in adults is largely evaluated, the same issue in child and adolescents is only at the beginning

The aim of this study was to evaluate the prevalence of the overweight and obesity in adolescents from a highschool in Oradea and to establish, if there is, the relationship between this metabolic disease and cardiovascular risk factors (family history, smoking, physical inactivity and arterial hypertension).

Method: We included in our screening 712 adolescents, 390 (54,1%) girls and 331 (45,9%) boys aged 15-19 years. For all of them we determinated: high, weight, blood pressure and they were invited to answer the questions from a questionnaire about lifestyle (smoking, physical activity, nutrition) and about family history.

Results: The relationship with cardiovascular risk factors obesity and overweight was hyghly prevalent in sedentary adolescents and in those whose parents werw obese.

Conclusion: Owerweight and obesity are highly prevalent in adolescents; our result are comparative with those from the literature. Because the relationship between obesity and cardiovascular risk factors is significant and strong, overweight and obese adolescent needs a special attention from the physician.

HYPERTENSION IN ADOLESCENTS

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Essential hypertension, independent cardiovascular risk factor, becomes a diseases of adolescent. Because of tracking phenomen hypertension in adolescent is a risk factor for adult´s hypertension.

The aim of this screening was to evaluate hypertension´s prevalence in a group of 712 adolescents aged 15-19 years and to estabilish the relation with other cardiovascular risk factors. Hypertension´s prevalence was 10,1% slightly high in boys. Risk factors that had a strong influence in hypertension´s prevalence are smoking, cholesterol level, obesity and presence of the disease in parents.

Method: In our screening we included students from 9-12 grades in a highschool of Oradea - 721 students - 390 (54,1%) girls and 331 (45,1%) boys aged 15-19 years. For all of them we evaluated: high, weight, body mass index, blood pressure and cholesterol levels. The adolescents werw invited to answer the questions included in a questionnaire composed of two parts - one about lifestyle (nutrition, smoking, physical activity) and one about family history.

Results: Obesity and hypertension are strongly linked: hypertension is a mark of metabolic syndrom frequently in adolescents.

Conclusions: Primary hypertension becomes the dominant aetiology in adolescents.

Prevalence of hypertension in childhood and adolescence depends strongly to the values considered normal.

Primary hypertension in adolescents is related to cardiovascular risk factors.

METABOLIC SYNDROME IN OBESE CHILDREN

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Introduction: Insulin resistance (IR) is a common feature of childhood obesity and a key component of the metabolic syndrome (MS).

The aim of this study was to evaluate the prevalence of MS among obese children.

Methods: We examined 1760 schoolchildren at age 7-17 years. Obesity was revealed in 91 children (5.2%). Risk factors in the family such as DM2, hypertension, hyperlipidemia, obesity were recorded for the first degree relatives. All children underwent anthropometric measurements, an oral glucose tolerance test, assessment of blood pressure, plasma lipids. OGTT accompanied by four point of insulinemia was performed. HOMA index was calculated according to the standard formula. MS was diagnosed according to a classical definition (Weiss's criteria).

Results: In the group of obese children metabolic syndrome was found in 18 (19.8%). BMI was 30.9 ± 3.4 kg/m^2 . The prevalence of the single components of the MS was follows: hypertension 52.6%, hypertriglyceridemia 38.2%, glucose intolerance 17.6%, IR revealed in 25% children. HOMA index was 4.6 ± 3.3, peak insulinemia was 112 ± 24.1 mIU/l.

Conclusion: This study showed a high prevalence of the MS among obese schoolchildren.

ALANINE AMINOTRANSFERASE AND METABOLIC SYNDROME IN MEXICAN CHILDREN AND ADOLESCENTS

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Objective: To evaluate the association between alanine aminotransferase levels (ALT) and the Metabolic Syndrome (MS).

Methods: The population base of this report are children of participants of the project "Cohort of Workers IMSS-INSP-UAEM". The methods have been described previously. Briefly, the MS was defined with the criteria of ATP III. The ALT levels were categorized in quartiles. We evaluated if the ALT levels were associated with the presence of MS by means of models of multiple logistic regression, stratifying for sex and adjusting by some covariables.

Results: The information of clinically healthy 534 females (53.1%) and 472 males was analyzed (age 14.8±4.4). MS was found in 21.1% of participants with no differences by sex. The prevalence of MS was greater in the fourth vs. first quartile, both men and women (46.2% vs. 8.3% in men and 31.4% vs. 16.1% in women). Men in fourth quartile were more likely than men in first quartile to have MS (OR:14.3 95% CI:6.5-31.7) The same pattern, although with different risk was found in females (OR:2.8 95% CI:1.5-5.3).

Conclusions: The ALT levels were associated with the presence of MS, especially in men. This finding is consistent with previous reports in the literature. However, is necessary to confirm these findings in other populations.

INSULIN RESISTANCE AND ALANINE AMINOTRANSFERASE IN MEXICAN CHILDREN AND ADOLESCENTS

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Objective: To evaluate the association between insulin resistance (IR) and alanine aminotransferase (ALT) levels.

Methods: The population base of this report are children of participants of the project "Cohort of Workers IMSS-INSP-UAEM". The methods have been described previously. Briefly, the IR was assessed with HOMA-IR(>3.16). The elevated ALT was defined as >p75 by sex (24U/L for men and 19U/L in women). We evaluated if the IR was associated with the ALT levels by means of models of multiple logistic regression, stratifying for sex and adjusting by some covariables.

Results: The information of clinically healthy 534 females (53.1%) and 472 males was analyzed (age 14.8±4.4). IR was found in 25.6% of participants with no significant differences by sex. The prevalence of IR was greater in the group of elevated ALT, both men and women (42.6% vs. 16.8% in men and 49.5% vs. 22.3% in women). Men with ALT elevated were more likely to have IR (OR:3.8 95%CI:2.3-6.3) The same pattern, although with different risk was found in females (OR:4.2 95%CI:2.6-6.9).

Conclusions: The elevated ALT levels were associated with the presence of IR, especially in women. This finding is consistent with previous reports in the literature. However, is necessary to confirm these findings in other populations.

CONSEQUENCES OF PARTIAL GENETIC INHIBITION OF HORMONE-SENSITIVE LIPASE ON INSULIN SENSITIVITY AND ADIPOSE TISSUE INFLAMMATION

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Aims: Hormone-sensitive lipase (HSL) participates together with adipose triglyceride lipase (ATGL) in the hydrolysis of triglycerides in adipocytes. In human adipose tissue, HSL protein content correlates with maximal stimulated lipolysis. Expression and activity of HSL is decreased in overweight, obese and insulin resistant patients.

Methods: We used HSL heterozygous mice ($HSL^{+/-}$) as a model of partial lipolytic inhibition to examine insulin sensitivity and adipose tissue inflammation upon different diets.

Results: Lipase activity and lipolytic capacity of $HSL^{+/-}$ mice was 50% lower than in WT mice. When fed a chow diet, insulin sensitivity of WT and $HSL^{+/-}$ mice was comparable whereas the latter presented a higher respiratory quotient indicating that these mice preferentially metabolized carbohydrates. Upon 20 weeks of high fat diet, $HSL^{+/-}$ and WT mice became obese while HSL knock out mice did not. However, $HSL^{+/-}$ mice were more insulin sensitive than WT mice. Surprisingly, $HSL^{+/-}$ mice had larger adipocytes than control animals. No compensation by ATGL was observed in terms of adipose tissue expression and activity level. Plasma lipid profiles indicated no change in non-esterified fatty acid concentration whereas triglyceride content was diminished in $HSL^{+/-}$ mice. On a fructose-enriched diet, no difference in insulin sensitivity was seen between $HSL^{+/-}$ and WT mice after 15 weeks. However, HSL knock out mice were more insulin-resistant than other genotypes.

Conclusions: We are currently analyzing gene expression of inflammatory markers and adipose tissue secretions to determine the mechanisms linking a reduced lipolytic capacity with modulation of insulin sensitivity.

DNA MICROARRAY ANALYSES OF GENES EXPRESSED DIFFERENTIALLY IN 3T3-L1 ADIPOCYTES CO-CULTURED WITH MURINE MACROPHAGE CELL LINE RAW 264.7 IN THE PRESENCE OF BACTERIAL ENDOTOXIN

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Objective: Recent studies have suggested macrophages were integrated to adipose tissues to interact with adipocytes, thereby exacerbating inflammatory responses. Furthermore, both adipocytes and macrophages appear to express toll-like receptor-4 (TLR-4), and free fatty acids may stimulate cells via TLR-4. Herein, we analyzed genes differentially expressed in adipocytes when co-cultured with macrophages in the presence of a ligand for TLR-4, bacterial endotoxin.

Methods: RAW264.7, a murine macrophage cell line and differentiated 3T3-L1 adipocytes were co-cultured using a transwell system. Genes differentially expressed in adipocytes were analyzed by the DNA microarray method following 4, 8, 12 and 24h stimulation with 1 ng/ml of *E. coli* lipopolysaccharide (LPS). Randomly selected genes with high expressions were confirmed by quantitative methods at both the gene and the protein level.

Results: Co-culture of macrophages and adipocytes with a low LPS concentration (1 ng/ml) markedly up-regulated gene expressions associated with inflammation and/or angiogenesis, such as those of *interleukin-6 (IL-6)*, *monocyte chemoattractant protein-1 (MCP-1)*, *regulated upon activation, normal T expressed and secreted (RANTES)* and *CXCL1/KC*, in adipocytes. Furthermore, several genes associated with insulin resistance were differentially expressed, such as up-regulation of *suppressor of cytokine signaling (SOCS)* and down-regulation of *GLUT-4*. Up-regulations of genes encoding *IL-6*, *MCP-1*, *RANTES* and *CXC/KC* were confirmed by quantitative methods. Cluster analyses indicated marked up-regulation of NF-kB-associated gene expression.

Conclusions: The results suggest that ligands for TLR-4 stimulate both adipocytes and macrophages to markedly influence the expressions of many genes associated with inflammation, angiogenesis, and to further accelerate inflammatory changes in adipose tissue.

PPARA CONTROLS PGC-1A GENE EXPRESSION IN BROWN ADIPOCYTES AND CONTRIBUTES TO CAMP-MEDIATED REGULATION THROUGH INTERACTION WITH PRDM16

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Aims: PPARα is a distinctive marker of the brown fat phenotype which has been proposed to coordinate lipid oxidation and thermogenic pathways in brown fat. Our objective was analyzed whether PPARα is involved in the transcriptional control of the PGC-1α gene.

Methods: Analysis of gene expression by RT-PCR in primary cultures of brown adipocytes and in brown fat from PPARα-null mice. The PGC-1α promoter was studied using chromatin immunoprecipitation and promoter reporter gene assays.

Results: PPARα activation induced PGC-1α mRNA expression and the transcriptional activity of the 2kb-mPGC1α-luciferase construct in brown adipocytes. Binding of PPARα to the PGC-1α gene promoter was evidenced by ChIP assays. In PPARα-null brown fat, we observed a decrease in PGC-1α gene expression in basal conditions and also in response to thermogenic activation. A synergistic interaction between the PPARα and cAMP-mediated pathways in the control of PGC-1α transcription was observed, which required the PPRE element. Co-transfection with a PRDM16 expression vector resulted in a dramatic enhancement in the capacity of PPARα to induce PGC-1α gene transcription, especially when the protein kinase-A pathways were activated. This was associated with the interaction of PRDM16 with the PGC-1α promoter, which occurred at the PPRE site. On the other hand, PRDM16 gene expression is controlled by PPARα in brown adipocytes, as evidenced by the study of PPARα-null mice and of cultured brown adipocytes.

Conclusions: We propose that the interaction of PPARα with PRDM16 is required for the full thermogenic activation of PGC-1α gene transcription in brown fat.

REPRODUCIBILITY OF DETERMINATIONS OF MICROVASCULAR BLOOD VOLUME IN SUBCUTANEOUS, ABDOMINAL ADIPOSE TISSUE IN MAN WITH REAL-TIME CONTRAST ENHANCED ULTRASOUND IMAGING (CEU)

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Aim: To investigate the reproducibility of real-time CEU for determination of microvascular blood volume in human abdominal wall adipose and skeletal muscle tissue.

Methods: 5 healthy subjects (two females) were studied. Each subject was given three intravenous bolus injections of 1.5 ml of the ultrasound contrast media SonoVue®. About 10 minutes elapsed between the injections. Harmonic imaging ultrasound was used to monitor the non-linear response of the micro-bubbles in regions of interest in abdominal subcutaneous adipose tissue and abdominal skeletal muscle at rest using a 9 MHz linear ultrasound probe. Care was taken to avoid compression of the examined tissues during the measurements. The relative microvascular blood volume in the tissues was determined as the signal intensity in dB during the first plateau phase. For a region of interest the maximum plateau of signal intensity is given as dB mm^{-2}.

Results: The signal intensity was significantly higher in abdominal subcutaneous adipose tissue than in the underlying skeletal muscle. The maximum plateaus of signal intensity were 0.43 ± 0.23 dB mm^{-2}, and 0.19 ± 0.09 dB mm^{-2} ($p < 0.004$) respectively. The coefficient of variation of consecutive determinations was on average 11% and 8% in adipose tissue and skeletal muscle. The ratio of the signal intensity between abdominal subcutaneous adipose tissue and abdominal skeletal muscle was on average 0.5 ± 0.2.

Conclusion: After a bolus injection CEU has a good reproducibility in adipose tissue and is therefore well suited for examinations of changes in microvascular volume in this tissue in man.

THE PRODUCTION OF ANGIOGENIC FACTORS FROM ADULT THYMUS FAT THE MOLECULAR MECHANISMS ASSOCIATED

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Aims: Many works are proving specific angiogenic properties of adipose tissue. In the adult thymus degenerates and becomes a mass of fat tissue. In this work we study the thymus fat from Ischemic cardiomyopathy patients as a hypothetical source of angiogenic factors and cell repair. For this end we analyzed the expression of angiogenic factors, and also the physiological role of this tissue on endothelial cells. On the other hand we analyzed whether this angiogenic factor production was accompanied by inflammatory or anti-inflammatory mechanisms.

Methods: The detection of gene expression and protein of different proteins in this study was performed by immunohistochemistry and real-time PCR. The physiological function of the thymus adipose tissue was analyzed by testing the migration and proliferation of endothelial cells from the umbilical cord.

Results: Evidence of the presence of angiogenic factors such as VFGF, Ang and I Tie2.

1. The activation of cyclooxygenase-2 and heme oxygenasa-1 showed the existence of both inflammatory and cyto-protective mechanisms in this adipose tissue;
2. The expression of both PPARgamma 1 and gamma2 indicated the adipogenic activity of this tissue; and finally
3. Adipose tissue thymus extract induces in a dose-dependent manner, proliferation and migration of endothelial cells of the cordon.

Conclusions: The evidence of presence of angiogenic factors in thymus adipose tissue, and that this tissue has a big capacity of angiogenesis. Both inflammatory and cytoprotective characteristics of this tissue lead to think that it will be interested to determine the mechanisms underlying angiogenic factor production and angiogenesis regulation.

DIFFERENT THIAZOLIDINEDIONES ELICIT DISTINCT RESPONSES IN HUMAN PREADIPOCYTES

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The distinct side effect profiles of different thiazolidinediones have recently become the focus of considerable attention, particularly differences between pioglitazone and rosiglitazone. To dissect responsible mechanisms, we treated differentiating human abdominal subcutaneous, mesenteric, and omental preadipocytes with pioglitazone (10μM), rosiglitazone (0.5μM), ciglitazone (1μM), AICAR (2nM), or control medium for 15 days and assayed adipogenesis and gene expression profiles. Pioglitazone-induced adipogenesis (lipid accumulation, differentiation-dependent gene expression) was intermediate between that of rosiglitazone and ciglitazone. Pioglitazone had effects on gene expression profiles highly distinct from the other thiazolidinediones. 2977 out of 22,000 expressed genes differed by at least 2 fold with pioglitazone versus the other thiazolidinediones (FDR< 0.001). This was confirmed by RT-PCR analyses of select genes in cells from additional subjects using different thiazolidinedione preparations. Genes that pioglitazone affected distinctly included secreted proteins (including angiopoietin-like 4), transcription factors, and signaling and effector pathway components (including caveolin) on some of which pioglitazone, but not the other thiazolidinediones, had depot-specific effects. CMAP analysis indicates a PPAR gamma-independent glucose transport mechanism is differentially activated by pioglitazone. Thus, thiazolidinediones have different effects on target cells, potentially contributing to their distinct clinical effects.

ANALYSIS OF CLONAL EXPANSION IN ADIPOCYTE DIFFERENTIATION: LESSONS FROM 3T3-L1 PREADIPOCYTE IN CONDITIONED MEDIA

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Aims: The differentiation of 3T3-L1 preadipocytes involves characteristic cellular events before the acquisition of mature phenotype. Treatment with hormonal agents causes the cells to synchronously reenter the cell cycle and to undergo clonal expansion. We found that conditioned media caused the escape from clonal expansion, but not from terminal differentiation. In this study, we investigated the role of clonal expansion using this system.

Methods: 3T3-L1 cells were differentiated on a standard protocol. After 2 days, we harvested medium which is designated as D2M (Day 2 medium). Postconfluent 3T3-L1 preadipocytes were treated with D2M or media containing standard MDI cocktail, and the change in the differentiation profiles was investigated.

Results: Under standard protocol, 3T3-L1 cells undergo one or two rounds of mitosis, however, most cells under D2M remained in G0/G1 phase in FACS analysis. Surprisingly, the differentiation under D2M was even enhanced shown by Oil-red O staining, without any significant increase in cell number. D2M accelerated terminal differentiation into adipocytes as evidenced by up-regulation of PPARgamma, C/EBPalpha, and FAS. We analyzed several genes which are thought to be critical in the difference between standard medium and D2M. Small interfering RNA against some candidate genes blocked the differentiation of cells under standard protocol, but not under D2M, suggesting that cells in D2M can be differentiated without clonal expansion.

Conclusions: Our data showed that preadipocytes treated with D2M do not require cell division to enter the terminal differentiation. This system is useful to investigate why clonal expansion is required in 3T3-L1 cell differentiation.

HUMAN ADIPOCYTES EXPOSE PHOSPHATIDYLSERINE DURING HYPOXIA; A POTENTIAL MECHANISM INVOLVED IN MACROPHAGE-ADIPOCYTE INTERACTION AND ACTIVATION IN WHITE ADIPOSE TISSUE

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Macrophage infiltration and activation in white adipose tissue (WAT) is considered an initiating inflammatory event that underlies the development of metabolic complications during obesity. The mechanism(s) for macrophage-adipocyte interaction and macrophage activation in WAT are currently unclear. Changes in adipocytokine release during adipogenesis and under hypoxic conditions are options we investigate. Alternatively, surface exposed phosphatidylserine, resulting from collapse of lipid asymmetry, provides a recognition signal for phagocyting macrophages, with subsequent release of inflammatory cytokines. We thus hypothesized that human adipocytes expose PS during cytotoxic conditions as part of an apoptotic response. We investigated this by using human Simpson Golabi Behmel Syndrome (pre-)adipocytes subjected to hypoxia. PS exposition was explored microscopically by measuring cellular binding of fluorescently-labeled annexin A5, a PS recognizing protein. (Pre-) adipocytes stimulated with the Ca2+ ionophore ionomycin bound annexin, indicating the presence of a mechanism for Ca2+-induced PS exposure in both cells. Adipocytes differentiated for > 10 days were PS negative, however, when subjected to chemically induced hypoxia, mature adipocytes showed PS exposure. Remarkably, only part of the adipocytes appeared PS-positive, while others in the same culture dish were PS-negative. Possible explanations are differences in calcium homeostasis, differences in redox status or loss of membrane integrity, which are currently investigated. Together, our data show that human adipocytes expose PS during hypoxia. Hypoxia is involved in deregulation of adipose tissue and our data provide a potential mechanism involved in macrophage-adipocyte interaction and macrophage activation in WAT during hypoxia.

INFRAPATELLAR FAT PAD : AN ECTOPIC ADIPOSE TISSUE IMPLICATED IN OSTEOARTHRITIS?

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Purpose: Relations between obesity and osteoarthritis (OA) are complex and not only due to a mechanical stress. In the knee joint, they may also be the consequence of the release of systemic mediators by the infrapatellar fat pad (IFP).

The goal of this study was to provide evidence for the contribution of IFP to local inflammation in knee OA of obese patients by characterizing the pattern of cytokine production in this tissue and comparing it to that of subcutaneous (SC) adipose tissue (AT) from the same individuals.

Method: IFP and SCAT were obtained from 11 women (74.6±1.93 years; BMI: 31.6±1.44 kg/m²) during total knee replacement. Gene expression was measured by RT-PCR. Cytokine secretion in serum and conditioned media of cultured AT explants was determined by ELISA or Luminex technology.

Results: IFP expressed several AT markers, when compared with SCAT . Major proinflammatory cytokines were expressed but only IL-6 expression showed a 2-fold increase in IFP while macrophage infiltration remained unchanged. Cytokine secretion measurements showed that IL-6 and its soluble partner, IL-6sR, were increased by 2 and 3.6 respectively in IFP. Adiponectin secretion was also increased by 40% suggesting a possible role in inflammation.

Conclusion: Our results strongly suggest that IFP from obese OA patients could contribute to paracrine inflammation via the local production of IL-6 and its soluble receptor and thus potentiate the damage of joint and cartilage.

THE EFFECT OF GROWTH HORMONE SECRETION BY EXERCISE AT ANAEROBIC THRESHOLD ON VISCERAL FAT ACCUMULATION

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Aims: We have reported that growth hormone (GH) stimulates lipolysis in visceral fat and the serum GH level increased by exercise. The aim of this study is to investigate the effect of GH secretion by exercise on visceral fat in obese subjects with type 2 diabetes.

Methods: Nineteen subjects (mean; age: 50.3 years, BMI: 27.9 kg/m^2, HbA1c: 9.9 %) were enrolled and were divided into two groups randomly; exercise group (n=11) and non-exercise group (n=8). Exercise was performed at anaerobic threshold for 30 min twice a day and all subjects were treated with a low calorie diet (25 kcal/kg) for 4 weeks. Blood samples were obtained in the morning at week 0 and 4. To evaluate GH response to the exercise, serum GH was also measured before and after exercise at week 0. Visceral and subcutaneous fat area (VFA, SFA) were evaluated by CT.

Results: VFA in exercise group decreased by 22% ($p< 0.001$) while that in non-exercise group was unchanged during this study. SFA showed no significant change in both groups. The decrease of HOMA-R in exercise group was greater than non-exercise group, but was not significant. The change in serum IGF-1 levels in exercise group was higher than in non-exercise group, although there was no significant. In exercise group, the change in VFA correlated negatively with GH response to the exercise ($r=-0.565$, $p=0.090$).

Conclusions: These results suggest that exercise at anaerobic threshold may decrease VFA and the decrease may be associated with GH response to the exercise.

EXPRESSION OF FUNCTIONAL TISSUE FACTOR BY HUMAN (PRE-)ADIPOCYTES IMPLIES FIBROSIS AND THROMBOSIS IN WHITE ADIPOSE TISSUE

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Tissue factor (TF) expression by adipocytes is considered to be involved in obesity-related cardiovascular complications and non-insulin-dependent diabetes mellitus. However, expression of functional TF on human (pre-)adipocytes has not been demonstrated yet. The objective of this study was to examine the ability of human Simpson Golabi Behmel Syndrome (pre-)adipocytes to initiate TF-dependent blood coagulation, i.e. factor Xa (FXa) and thrombin generation and fibrin deposition. Cultured pre-adipocytes and adipocytes, as well as conditioned medium from these cells, initiate FXa and thrombin generation to different extents. Both processes were inhibited by a polyclonal anti-human TF IgG and (partly) by annexin A5, an anionic phospholipid-binding protein. This suggests that FX activation and thrombin generation induced by human (pre-)adipocytes is TF driven and involves anionic phospholipids. Adipocytes appeared to have a ~10-fold higher TF activity per cell compared to pre-adipocytes. Treatment of cultured pre-adipocytes and adipocytes with simvastatin, an inhibitor of HMG-CoA reductase, resulted in a significant reduction of TF activity that was reversed with mevalonic acid. Perfusion experiments with recalcified whole blood and platelet free plasma showed platelet interactions with pre-adipocytes but not with adipocytes. Fibrin deposition was observed on both cell types. In conclusion, our study demonstrates that cultured human (pre)adipocytes are highly procoagulant with imminent implications of disorders of extravascular fibrin formation (fibrosis) and haemostasis (thrombosis) in white adipose tissue.

INHIBITORY EFFECT OF KIOM-201 ON ADIPOGENESIS IN 3T3-L1 PREADIPOCYTE THROUGH DOWNREGULATION OF PPAR-GAMMA AND C/EBP-ALPHA

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Adipocyte dysfunction is associated with the development of obesity, which is a major risk factor for metabolic disorders, such as diabetes, atherosclerosis, and hypertension. It is generally accepted that the regulation of adipogenesis prevents obesity. Our study shows that KIOM-201, extract of natural product, prevents the development of obesity in diet-induced obese (DIO) rats and reduces the body weights in obesity rats. The principal aim of this study was to investigate whether KIOM-201 can have biological activity on adipogenesis in 3T3-L1 preadipocytes as an antiobesity drug. Here, we showed that KIOM-201 inhibits adipocyte differentiation, as evidenced by reduced formation of lipid droplets and glycerol-3-phosphate dehydrogenase (GPDH) activity. Protein expression levels of peroxidase proliferator-activated receptor-gamma (PPAR-gamma) and CCAAT/enhancer-binding protein-alpha (C/EBP-alpha), which are the major adipogenic transcription factors, were markedly reduced by KIOM-201. Moreover, protein expression of adipocyte differentiation-related protein (ADRP) and perilipin (a protein that coats lipid droplets in adipocytes) were reduced by KIOM-201. ADRP, C/EBP-alpha, and perilipin mRNA expressions were also reduced by KIOM-201. We also showed that phosphorylated AMP-activated protein kinase (pAMPK), a key role as a master regulator of cellular energy homeostasis, were elevated by KIOM-201 (5, 10, 25 μg/ml) in a dose dependent manner. Taken together, these results suggest that antiobesity effect of KIOM-201 involves the AMPK signaling pathway and inhibition of adipogenesis through downregulation of PPAR-gamma and C/EBP-alpha.

STEAROIL CO-A DESATURASE (SCD) AND ADIPOSE TISSUE DEVELOPMENT

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Aim: Test the hypothesis that SCD can modulate the adipose tissue variability during the childhood.

Material and methods: 183 chidren between 0-14 years old operated of inguinal hernia have been study.

Antropometric variables of children were measured, and they answered a nutritional and physical activity inquiry, also a sample of subcutaneus adipose tissue was taken during the operation.

BMI and hip-waist ratio were calculated, and in tissue sample we study preadipocyte and adipocytes number, the adipocyte volumen, fatty acid composition of adipose tissue, and relative gene expression of SCD in adipose tissue.

SCD-activity index was stimated as palmitoleic acid/palmitic acid ratio, and as oleic acid/steric acid ratio.

Resultados: Age correlates with weight ($r=0.935$; $p< 0.001$), height ($r=0.949$; $p< 0.001$), waist/hip ratio ($r=-0.556$; $p< 0.001$), and sum of skin folds ($r=0.331$; $p< 0.001$).

The SCD-activity index has shown correlations with anthropometric variables (BMI:r=0.173; p=0.04, the sum of skin folds:r=0.333; p< 0.001)), and with the cellularity of adipose tissue (adipocyte volume: r=0.350; p< 0.001 and number: r=-0.291; p< 0.001)), whilst SCD relative gene expression just show a significant correlation with SCD-activity index (r=0.3; p=0.001) and with adipocyte volume (r=0.18; p=0.03). Correlations were adjusted by age.

Conclusions: Fatty acid composition of adipose tissue reflects the dietary intake and correlate with the habits and with the anthropometric measurements of the subjects.

The SCD activity is related with the cellularity of adipose tissue and with the sum of skin folds of the subject, however SCD relative gene expression is only related with adipocyte volumen.

INCREASED MACRO- AND MICROVASCULAR COMPLICATIONS IN TYPE 1 DIABETES PATIENTS WITH METABOLIC SYNDROME

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The significance of metabolic syndrome (MetS) in Type 1 diabetes (T1D) remains unclear. We sought to estimate the prevalence of MetS and investigate the association between the presence of MetS features and vascular complications in T1D population.

Methods: Retrospective study included all T1D (n=1044) currently attending diabetes outpatient clinics. They were grouped according to the presence or absence of MetS (BMI>30 in addition to two or more features of MetS based on IDF criteria). Clinical characteristics and vascular complications obtained from the most recent clinic review were compared between the two groups. Data expressed in mean (SD).

Results: A total of 162 out of 1044 (15%) patients fulfilled the criteria for MetS (57% (n=92) were men). Those with MetS were older (mean age 52.0 (14.3) vs 44.8 (15.9) years, P≤ 0.0005) with longer duration of diabetes (21.1 (13.2) vs 16.5 (12.6) years, P≤ 0.0005) and higher daily insulin requirement (0.9 (0.4) vs 0.7 (0.3) unit/kg, P ≤ 0.0005). They had higher microvascular complications (21.6% vs 10.4%, P≤ 0.0005 [retinopathy (53.1% vs 23.3%; P≤0.0005), nephropathy (21.0 vs 14.4; P=0.03), neuropathy (37.9% vs 20.7%; P≤0.0005)]. Similarly, macrovascular complications were also higher in those with MetS (70.8% vs 40.5%, P≤0.0005) [Ischaemic heart disease (12.3% vs 5.7%; P=0.002), stroke (4.3% vs 1.3%; P=0.007), peripheral vascular disease (11.7% vs 5.3%; P=0.004). There was a linear relationship between the prevalence of vascular complications and the number of MetS component.

Conclusion: The presence of MetS in T1D was associated with higher macrovascular and microvascular complications.

METABOLIC SYNDROME IN A GROUP OF TYPE 1 DIABETIC PATIENTS. A NEW VARIANT OF DIABETES?

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Metabolic Syndrome (MS) has been connected to insulin resistance and to type 2 diabetes mellitus. However, it has been observed that patients with type 1 diabetes mellitus (T1DM) may develop this condition as well.

Aims: To determine the prevalence of MS in patients with T1DM and its correlation with some factors that could predict it.

Methods: MS presence was defined according to the criteria of the Adult Treatment Panel III. Fifty two patients were included, all older than 18 years, with 5 years or more since their diagnosis of T1DM, and who had been evaluated during the last year. Acanthosis nigricans (AN), daily dose of insulin, glycosylated hemoglobin (HbA1c) and microalbuminuria were evaluated.

Results: The prevalence of MS was 25 % (13/52). Patients with MS were using on average a major daily dose of insulin (p=0.018); they had more presence of AN (p=0.022) and more presence of obesity (IMC > 30 Kg/mt2) (p=0.002) than T1DM without MS. Direct association between waist circumference and dose of insulin, with Pearson`s index of 0.519 (p< 0.0001) was found. Association between MS presence, time of evolution of T1DM, HbA1c or microalbuminuria was not observed.

Conclusions: The present study found there was a high prevalence of MS in patients with T1DM, similar to the general population according to the Chilean National Survey of Health (2003). The use of major doses of insulin in these patients might indicate the reason and/or the consequence of the SM, which needs further evaluation.

CONTRIBUTORS OF ABNORMAL 24-HOUR SYSTOLIC BLOOD PRESSURE IN TYPE 1 DIABETES FAMILIES

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Aims: Oxidative damage is increased in families of type 1 diabetics (T1D) and normotensive non-diabetic relatives of T1D have an abnormal blood pressure response to exercise testing that is associated with indices of metabolic syndrome and oxidative damage. We evaluated the pattern of 24-h ambulatory blood pressure (BP) monitoring (ABPM) in T1D families and its relationship with clinical parameters and oxidative biomarkers.

Methods: A cross-sectional study was conducted in 25 control subjects (46±12 y; BMI 24±3), 21 T1D (45±10; 25±4) and 21 non-diabetic siblings of T1D (46±10; 26±5, p< 0.05 vs controls) using an oscillometric device. In addition to routine laboratory investigations, we measured the rate of oxidant-induced erythrocyte electron transfer to extracellular ferricyanide (RBC vfcy) that supplies electrons (from intracellular electron donors) to reduce extracellular oxidants.

Results: Twenty-four hour systolic BP differed among groups: 121±7 mmHg in controls, 134±12 in T1D, and 127±13 in siblings (p< 0.001). Daytime systolic BP was higher in T1D (137±13 mmHg) and siblings (132±13) than in controls (125±7, p< 0.001), whereas nighttime systolic BP was increased only in T1D 122±17 (107±10 in controls and 109±15 in siblings, p< 0.01). Daytime systolic BP of non-diabetic subjects was positively correlated with BMI and RBC vfcy (r 0.62, p< 0.001).

Conclusions: ABPM data confirm that non-diabetic siblings of T1D patients have abnormal systolic blood pressure during daytime. An index of fat body mass (BMI) and erythrocyte plasma membrane oxidoreductases seem to be important contributors to the development of borderline systolic BP in relatives of T1D patients.

LEFT VENTRICLE MASS AND FUNCTION IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES AND CO-EXISTING METABOLIC SYNDROME

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Type 1 diabetes (T1DM) can result in macroangiopathy, co-existing metabolic syndrome (MS) can be additional risk factor for developing cardiovascular diseases in adulthood.

The aim of the study was to assess the mass and function of left ventricle in patients with type 1 diabetes and metabolic syndrome (with the presence of 2 or 3 risk factors) comparing to the healthy subjects.

Material and methods: Fifty five patients with type 1 diabetes and co-existing metabolic syndrome were enrolled into the study (aged 14-22 years). The control group consisted of 26 patients with no evidence of risk factors for cardiovascular diseases. Left ventricle (LV) mass was calculated according to the formula: LV=1.05 (5/6 A1(L+t)-5/6 A2L)). The systolic function of left ventricle was assessed according to the ejection fraction (EF) and percentage of shortening fraction (SF%) with the use of echocardiograph Hewlett Packard Sonos 4500.

Results: In the group of patients with T1DM and MS we noted the significantly higher left ventricle mass ($p< 0.05$). The highest LV mass, shortening fraction and ejection fraction were observed in patients with T1DM and MS with coexistence of hypertension, obesity and insulin resistance.

Conclusions: Patients with T1DM and MS showed higher left ventricle mass and disturbances in its function. The adolescents and young adults with T1DM, MS and coexistance of subclinical disturbances in cardiovascular system need urgent preventive and therapeutical interventions.

PREVALENCE AND ASSOCIATIONS OF ABNORMAL LIVER ENZYMES IN TYPE 1 DIABETES

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The recognition of non-alcoholic fatty liver disease (NAFLD) as a component of metabolic syndrome (MetS) led to the characterisation of abnormal liver enzymes (LFT) in Type 2 diabetes (T2D). Abnormal LFTs Type 1 diabetes (T1D), however, has received little attention. We wish to establish the prevalence of abnormal LFT in T1D and determine its association with markers of MetS.

Methods: Retrospective study included all T1D patients currently attending diabetes outpatient clinics (n=1044). Data were derived from the latest annual review. Definition of abnormal LFT: alanine transaminase (ALT) >50U/L and/or γ-glutamyl transferase (γ-GT) (>35U/L (women), >55U/L (men). Data expressed as mean (SD).

Results: A total of 180 out of 1044 patients (16.7%) had abnormal LFT. Excluding those with unrecorded alcohol consumption or intake of >14unit/week, 119 out of 713 patients (16.6%) had abnormal LFT and were further analysed (men: 44.5%, n=53). Those with abnormal LFT were older (mean age 52.7 (1.4) vs 46.8 (0.6) years; P=0.0002), had higher; BMI (29.7 (6.8) vs 27.1 (4.8) kg/m^2; $p< 0.0001$), triglyceride (1.7 (1.3) vs 1.3 (1.0) mmol/L; $p< 0.0001$) and daily insulin requirement (1.08 (3.3) vs 0.48 (1.6) unit/kg; p=0.028) when compared with normal LFT group. Those with abnormal LFT were likely to have features of MetS (35.3% vs 13.8%; $p< 0.0001$).

Conclusion: The prevalence of abnormal LFT in T1D in this study was lower than previously reported in T2D. Similar to T2D, abnormal LFT were associated with markers of MetS. It is unclear whether this reflects the presence of NAFLD in T1D.

PREVALENCE OF METABOLIC SYNDROME AND HYPOGONADISM IN MEN WITH TYPE 1 DIABETES (T1D)

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Background and aims: The term "Metabolic Syndrome" is generally used to indicate a clinical situation in which different degrees of hypertension, impaired glucose tolerance, atherogenic dyslipidemia, central fat accumulation, insulin resistance, as well as prothrombotic and proinflammatory states cluster together in the same individual.

Several studies have shown that there is a high prevalence of low testosterone levels in men with the metabolic syndrome. Large longitudinal studies have revealed that a low testosterone level is a independent risk factor for the later onset of the metabolic syndrome. The purpose of this study was to estimate the prevalence of Metabolic Syndrome and of Hypogonadism in Men with Type 1 Diabetes.

Methods: 68 male with diabetes insulino-dependent were recruited for this study. The subjects were between 27 and 53 years of age and had a evolution of diabetes between 5 and 12 years. Anthropometric, biochemical and endocrine parameters were assessed.

Results: The prevalence of metabolic syndrome in patients with insulin dependent diabetes was 32.35%. There were significant differences in the recorded parameters in patients with diabetes and metabolic syndrome versus the diabetic-only patients.

The prevalence of hypogonadism in men with diabetes and metabolic syndrome was 27.27% and 11.36% in diabetic-only patients.

Conclusion: We conclude that the metabolic syndrome is frequent in patients with type I diabetes mellitus (32.35%). There was significant difference between the prevalence of hypogonadism in men with diabetes and metabolic syndrome compared with diabetic-only patients.

EFFECT OFIMPROVED GLYCAEMIC CONTROL ON LEFT VENTRICULAR MASS IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Aim: Diabetes Mellitus is associated with abnormalities in cardiac function and left ventricular(LV)hypertrophy. The beneficial effects of antihypertensive therapy on cardiac structure and function are known. Those for strict glycaemic control on LV mass and parameters of systolic and diastolic function were prospectively evaluated.

Method: 20 pts.with a mean age of 40 and long standing type 1 diabetes mellitus(mean-3o yrs.) with strict glycaemic control were included.Glycaemic control was monitored by Hb A1c levels. Improvement was considered to be more than 15 reduction of HbA1c.2D Echo and ambulatory 24 hr blood pressures were taken at baseline and at 1 year follow up. The left ventricular mass was evaluated by the area-length method.

Results: In 10 pts. with improved glycaemic control, HbA1c dropped from 10% to 8% ($p< .0001$), interventricular septal thickness decreased from 10.0 to 9.0 mm ($p< .05$) and LV mass decreased from 200 to 185 g ($p< .05$) Septal thickness and LVmass remained unchanged in pts. who did not achieve improvement in glycaemic control.LV internal diameters, posterior wall thickness, fractional shortening, E/A ratio of mitral inflow, E-wave deceleration time,and ambulatory 24-hour blood pressures had no significant changes during 1 year of follow up in either group.

Conclusion: Improved glycaemic control in pts. with type1 diabetes is associated with regression of septal thickness and LV mass without significant effect on systolic or diastolic function,in the absence of significant changes in ambulatory 24-hour blood pressures.

TROGLITAZONE ATTENUATES EFFECT OF BETA$_3$ ADRENERGIC STIMULATED NO PRODUCTION THROUGH AMPK IN PRIMARY CULTURE OF VISCERAL ADIPOCYTES

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Background and aims: While lipolysis as antiobesity approach is mainly mediated in adrenergic pathway in visceral adipocytes, antidiabetic drugs targeted to visceral adipocytes are based in PPARgamma pathway. We try to shed light on the relationship between PPARgamma, beta$_3$ adrenergic signaling, lipolysis, adiponectin and NO release.

Methods: Epididymal rat adipocytes were cultivated together with troglitazone, SR202 (selective PPARgamma antagonist), BRL-37344 (beta$_3$ agonist) alone and in combinations. After 24, 48 and 72 hours, culture media were analyzed via ELISA for adiponectin. Glycerol (lipolysis product) and NO_2^- (NO oxidative product) levels were assessed.

Results: Lipolysis was decreased after glitazone and SR-202 and the beta$_3$ agonist-induced lipolysis (BRL-37344) was blocked by glitazone/glitazone +SR-202 application. Adiponectin level was paradoxically decreased after 24 hours but increased more than control after 48 hours. NO exhibited increasing trend after troglitazone/SR-202 alone and in combination with BRL-37344. The BRL-37344 effect on NO was partially attenuated by addition of glitazone/SR-202. All the effect of troglitazone on BRL triggered NO production and lipolysis was completely attenuated when adding AMPK blocker P5499 to the mixture in the first 24 hours of cultivation.

Conclusions: The effect of PPARgamma agonist/antagonist and beta$_3$ agonist signaling on NO release and lipolysis is probably mediated through nonPPARgamma but AMPK pathway in first 24 hours while later-on increased production of adiponectin after glitazone is based on PPARgamma activation.

Aknowledgement: IGA MZ NR/9379-3/2007, VZ MSM 0021620807

TREATMENT WITH GLIMEPIRIDE, BUT NOT MITIGLINIDE AND SHORT-ACTING INSULIN, RESISTS BODY WEIGHT AND ABDOMINAL FAT REDUCTION UNDER DIETARY ENERGY-RESTRICTION

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Object: In the present, we investigate that the combination of calorie restriction with mitiglinide, glimepiride and short-acting insulin reduced abdominal fat area and body weight.

Subjects: 17 participants (10male and 7female) among 229 type 2 diabetic patients from 12 hospitals performed on the meal replacement study in 2006 in Japan supported by Sunny Health (Nagano, Japan).

Research design: After treatment with micro diet (MD) with glimepiride, we divided three groups calorie restriction (mitiglinide, glimepiride and short-acting insulin treatment). Abdominal fat area was analyzed by computed tomography (CT) scans of the abdomen were acquired using an electron beam CT scanner.

Results: In the meal replacement study with 229 diabetic patients, MD treatment reduced body weight by 4.7%. In the 17 subjects analyzed in the present study, the body weight decrease was greater (-7.7%). Eight weeks after the start of the meal replacement study, the 12 patients treated with glimepiride improved glycemic control and, among them, the seven patients switched from glimepiride to mitiglinide. There was no deterioration of glycemic control during the study period. BMI was reduced in the mitiglinide and the low- dose insulin-treated groups, but not in the glimepiride group after 6-month treatment with MD. Abdominal fat area decreased by approximately 20% in the mitiglinide group and by 24% in the low-dose insulin group.

Conclusion: These findings suggest that combined use of mitiglinide with calorie-restriction is warranted, and that short-acting oral hyperglycemic agents and exogenous short-acting insulin are useful for those who receiving instruction in lifestyle change.

PREVALENCE OF PEOPLE AT HIGH RISK OF TYPE 2 DIABETES IN TWO POPULATION SETTINGS IN MADRID, SPAIN 2007

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Objectives: To assess the prevalence of people at high risk of type 2 diabetes (T2D) in two different data sets of people in Madrid as well as to identify new cases of type 2 diabetes (NT2D) and other glucose metabolism disorders.

Methods: Data from 4229 participants 30-74 years-of-age (52.2% women) from two population-based studies conducted in Madrid were analyzed. The first data set consisted of a random sample of 2.268 people from a census registry (PREDIMERC study). The second data set was a random sample of 1.961 patients from six primary health-care registries (DE-PLAN study).

All study participants filled in the FINDIRSC questionnaire (Finnish Diabetes Risk Score).

Results: In the first data set representing a true population sample, 18% of the people (17% men versus 20% women: p-value for difference < 0.05) were at high risk of T2D (> 14 FINDRISC points). In the patients of the primary health-care register the prevalence of people at high risk of T2D was 28% (25% men versus 34% women; p-value for difference < 0.01). The difference in high risk of T2D prevalence between the two study samples was statistically significant (p-value < 0.01). The FINDRISC questionnaire identified 7% new cases of T2D in the general population and 10% in primary health-care patients. In people at high risk of T2D, NT2D accounted for 17%, whereas 34% had IGT or IFG.

Discussion: The FINDRISC questionnaire may be a practical tool to detect people at high risk of T2D who already have IGT or IFG.

BLOOD 25 OH-VITAMIN D3 CONCENTRATION PREDICTS BONE LOSS, BLOOD GLUCOSE AND THE ERYTHROCYTE SEDIMENTATION RATE (ESR) IN A GROUP OF HEALTHY POST-MENOPAUSAL WOMEN

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Aims: Increasing blood sugar in the elderly is linked to insulin resistance (IR). The metabolic syndrome (MS) also increases with advancing age. IR. MS and type 2 diabetes have all been associated with hypovitaminosis D.

Vitamin D modulates the immune system switching th1 responses to th2. Atheroma formation and rupture are linked to th1 activity as is osteoporosis. Here we examine the importance of vitamin D levels in a group of healthy elderly women in the Scottish Borders.

Subjects: 121 healthy elderly female volunteers, age range 62-91 years (mean 73 years).

Methods: Random blood glucose (BS) and other blood parameters were measured along with 25 OH VitD3, 1,25 OH VitD3, intact parathyroid hormone, urinary N-telopeptides, BMI and bone ultrasound (nBUA). Descriptive statistics and regression analysis were performed.

Results: 3% had type 2 diabetes (>=11.1 mmol/l) with a range of BS from 3.3 to 14.7 mmol/l. Only 16% had a 25 OHVitD3 level above 70nmol/l. Bone loss (N-telopeptides) was predicted by 25 OHVitD3, PTH and nBUA. nBUA by age, BMI and N-telopeptides. BS by 25 OHVitD3 independent of any other variable. ESR was predicted by haemoglobin, albumin and PTH independent of age.

Conclusions: Vitamin D levels in healthy elderly women predict bone loss, insulin resistance and inflammation. A low UV index may be responsible for the increased incidence of insulin resistance, metabolic syndrome, vascular disease and osteoporosis in Scotland.

THE OPTIMAL FASTING PLASMA GLUCOSE LEVEL FOR DIAGNOSIS OF DIABETES IN A SINGAPOREAN POPULATION IS LOWER THAN THE STANDARD WHO RECOMMENDATION

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Aim: Diabetes mellitus is defined by the World Health Organization (WHO) as fasting plasma glucose (FPG) ≥ 7.0 mmol/liter (mM,) or 2-hour post-load glucose (2HPG) ≥ 11.1 mM in the 75-gram oral glucose tolerance test (OGTT). However, reported FPG cut-off levels that correspond to this 2HPG level are below 7.0 mM in Asian studies. Our study aims to find the optimal FPG cut-off for the diagnosis of diabetes in a Singaporean population.

Methods: 787 subjects were screened for diabetes with a 75-gram OGTT at the outpatient clinics of a Singapore hospital from 2001-2007. Regression models and receiver operating characteristic (ROC) curves in SPSS 16.0 were used to define the optimal FPG cut-off.

Results: The mean age of our patients (393 males, 49.9%) was 50.0 ± 15.4 years (range 14-93). Their average FPG was 6.5 ± 2.8 mM (range 3.0-24.5), and mean 2HPG was 11.0 ± 5.6 mM (range 3.2-36.4). Exponential regression models were the best fit (highest R^2 value) for the whole population. The FPG level corresponding to 2HPG 11.1 mM using the exponential model was 6.1 mM. Patients aged 50 years and above had lower FPG cut-off (6.1 mM) corresponding to 2HPG 11.1 mM than younger patients (6.2 mM), but both had FPG cut-off 6.0 mM in ROC analyses. The FPG cut-off derived from ROC analysis of the whole population was 6.0 mM (sensitivity 81.5%, specificity 82.0%, area under curve 0.90).

Conclusion: The FPG cut-off for diagnosis of diabetes in our Asian population is lower than current WHO criteria.

ACARBOSE DECREASES URINARY 8-HYDROXYDEOXYGUANOSINE IN TYPE 2 DIABETIC PATIENTS

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Aims: Much attention has been focused on postprandial hyperglycemia that may play an important role in cardiovascular disease. Urinary 8-hydroxydeoxyguanosine (8-OHdG) is a biomarker of oxidative DNA damage, and elevated level of urinary 8-OHdG is associated with hyperglycemia and vascular complications in diabetic patients. We studied the effect of acarbose, an alpha-glucosidase inhibitor that specifically reduces postprandial glucose excursion, on urinary 8-OHdG in patients with type 2 diabetes.

Methods: The study comprised 21 Japanese patients with type 2 diabetes (14 men and 7 women, mean age ± SD: 55 ± 14 years). All patients were treated with 300 mg/day acarbose for 3 months, and blood and urine samples were obtained at baseline and after 3 months of acarbose treatment. The urinary 8-OHdG level was measured using an enzyme-linked immunosorbent assay (Japan Institute for the Control of Aging, Shizuoka, Japan).

Results: Significant decreases in postprandial plasma glucose (12.6 ± 2.6 to 8.8 ± 2.0 mmol/l, $P< 0.0001$) and HbA1C levels (7.8 ± 1.1 to 6.9 ± 1.0 %, $P< 0.0001$) were detected after 3 months of treatment, although body mass index and serum lipid levels did not change. During the study period, urinary 8-OHdG levels also decreased significantly (7.9 ± 2.7 to 6.3 ± 2.5 ng/mg·Cr, $P< 0.005$).

Conclusions: Increased oxidative stress has been considered to be one of the common pathogenic factors of diabetic complications. Our data suggest that acarbose may reduce oxidative DNA damage through an improvement of postprandial hyperglycemia in diabetic patients.

THIAZOLIDINEDIONES EXERT HEPATIC ANTIDIABETIC EFFECTS, NOT MEDIATED BY PPARGAMMA RECEPTOR, BY INHIBITING GLUCOSE-6-PHOSPHATASE ACTIVITY AND STIMULATING PIRUVATE KINASE ACTION IN ISOLATED RAT HEPATOCYTES

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Background: The thiazolidinediones (TZDs) are oral type 2 antidiabetic agents recognized for executing their hypoglycaemic effects mainly through a selective activation of the peroxisome proliferator-activated receptor-gamma (PPARg). We previously reported that these drugs have hepatic DIRECT metabolic effects independently of PPARg activation.

Aim: Investigate the mechanism by which TZDs, pioglitazone (PGZ) and rosiglitazone (RGZ) exert this non-mediated PPARg antidiabetic effects.

Materials and methods: We studied the effect of PGZ or RGZ on liver gluconeogenesis (GNG) and glycolysis (lactate+pyruvate production) by titrating isolated hepatocytes with sub-saturating concentrations of exogenous energetic substrates (dihydroxyacetone -DHA, lactate/pyruvate, glycerol and fructose) in a cell perifusion system. The TZDs effect on glucose-6-phosphatase (G6Pase) and pyruvate kinase (PK) activities and kinetics parameters were also determined.

Results: In perifused hepatocytes, both, PGZ and RGZ, inhibited hepatic glucose production by about 40% and 65%, respectively when the DHA was the energetic substrate. Similar inhibition of GNG was found with the other 3 substrates. Moreover, PGZ and RGZ, stimulated hepatic glycolysis in a similar manner (12%) whatever the substrate used. With regard to this, we showed that PGZ and RGZ exert a direct inhibition on G6Pase activity by decreasing V_{max} by 31% and 27% respectively, without affecting significantly its K_m. We also demonstrated that both TZDs enhanced the V_{max} of PK by 26 % in case of PGZ and 15,5 % in case of RGZ.

Conclusion: The TZDs, PGZ and RGZ, exert direct and acute hypoglycaemic effects on the liver, at least, through G6Pase inhibition and PK activation.

RISK OF DIABETES TYPE 2 ACCORDING TO FINNISH DIABETES RISK SCORE (FINDRISK) CRITERIA IN POLISH POPULATION (HAPIEE STUDY)

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Aim: The aim of the study was to assess the use of the FINDRISK criteria for elevated blood glucose detection.

Sample and methods: The studied population was 1960 men and women aged 45-64, randomly selected from the population of Krakow. The persons with known diabetes were excluded from the analysis. The relation between the blood glucose categories and the FINDRISK categories were assessed by the chi square test. For assessment the best FINDRISK cutoff point for detection elevated glucose Receiver-Operator Curves were used.

Results: The frequency of persons with FINDRISK categories in groups of elevated blood glucose is presented in the table:

	Glucose >5,6 mmol/l	Glucose >6,1 mmol/l	Glucose > 7,0 mmol/l
<7	14,4%	1,3%	0 %
8-11	25,9%	9,0%	2,1%
12-15	30,6%	13,9%	48,8%
>15	61,2%	47,8%	18,0%

The best FINDRISK cut off point for detection of blood glucose higher than 5.6mmol/l was 9 (66% sensitivity and 61% specificity), for detection of blood glucose higher than 6,1mmol/l was 12 (68% sensitivity and 81% specificity), and for detection of blood glucose higher than 7,0mmol/l was 13 (73% sensitivity and 83% specificity).

Conclusion: People with increased risk of diabetes according to FINDRISK had 36-15 times higher prevalence of elevated blood glucose categories than people with low FINDRISK. FINDRISK already validated in several European populations seems to be an important tool for prediction of diabetes also in Polish population.

DIFFERENT ROLES OF ACTIVE GHRELIN AND THE ASSOCIATION WITH METABOLIC VARIABLES INCLUDING LEPTIN IN TYPE 2 DIABETES

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To explore the effects of two well known hormones related to the obesity and glucose metabolism in type 2 diabetes and find out the relationship between those hormones and metabolic variables. We examined demographic, anthropometric and biochemical variables in 63 type 2 diabetes and analyzed the association with ghrelin and leptin. Mean age and diabetic duration of subjects were 57.0 ± 9.2 and 9.2 ± 6.8 years. BMI (24.3 ± 3.0 vs. 26.1 ± 3.9 kg/m^2, p< 0.05) and lepin (1401 ± 616 vs. 3808 ± 684 pg/mL, p< 0.001) were well correlated each other and significantly higher in females (n=31) than males (n=32). Prevalence of diabetic neuropathy, retinopathy, nephropathy and cardiovascular disease in study patients were 28.6, 20.6, 4.8 and 1.6%, respectively. At the time of study, 58.1, 69.4, 9.7, 29.0, 30.6 and 9.7% of patients were receiving metformin, sulfonylureas, meglitinides, a-glucosidase inhibitors, TZD and insulin treatment, respectively. As a consequence of the data from Pearson correlation analysis, plasma ghrelin showed positive correlation with HDL-cholesterol, TZD, age and duration of diabetes. Ghrelin was negatively correlated with waist circumference, pp2hr fasting glucose and c-peptide. In contrast, leptin was all positively correlated with total-cholesterol, triglyceride, LDL-cholesterol, HbA1c, fasting insulin, HOMA IR, BMI, diabetic retinopathy and nephropathy. Our data demonstrates that the clinical characteristics, several representative metabolic markers for CVD and biochemical profiles of glucose metabolism may differently affect the plasma level of ghrelin to compare with leptin and non-diabetic populations, and these findings can be useful indices for progress of diabetes.

PARAOXONASE1 (PON1) AND ARYLESTERASE ACTIVITY IN TYPE 2 DIABETIC EGYPTIAN PATIENTS WITH AND WITHOUT NEPHROPATHY

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Objectives: Pparaoxonase (PON) has been recognized as an antioxidant enzyme that hydrolyzes lipid peroxides. Experimental and epidemiologic studies have shown that oxygen-free radicals are elevated because antioxidant enzyme activities are altered in uncontrolled DM. The current study was undertaken to compare the activity of serum PON1 and Arylesterase in Type II Diabetic patients, with and without diabetic nephropathy.

Methods: 70 subjects were included in the study: 30 as control, 20 with type II diabetes mellitus with nephropathy , 20 type II diabetes mellitus without nehropathy. All studied groups are subjected to the following laboratory investigations after their consents: Fasting and postprandial blood sugars, Serum paraoxonase I activity level, Serum Arylesterase, srum malondialdhyde, Serum glutathione reductase activity.

Results: Serum paraoxonase and arylesterase activity towards paraoxon and phenylacetate,respectively, showed significant decrease in both type 2 diabetic patients without (groupI) and with nephropathy (groupII) when compared to the control group, with significant decrease in its activity in groupII in comparison to groupI.

Conclusions: Further researches is strongly recommended to study genetic polymorphism distribution in large Egyptian population to achieve a compact overview that could explain variability in PON1 activity and its relationship with the other factors that associate the disease and its complications.

EXENATIDE WAS ASSOCIATED WITH BODY WEIGHT REDUCTION AND NORMALISATION OF IMPAIRED GLUCOSE TOLERANCE IN NON-DIABETIC, OBESE PATIENTS

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Objectives: This double-blind, placebo-controlled study assessed the effect of exenatide on weight and glucose normalisation in non-diabetic, obese patients with and without impaired glucose tolerance (IGT).

Methods: Patients (N=152; age 46±12 years, female 82%, 108.6±23.0 kg, BMI 39.6±7.0 kg/m^2, IGT 25%; mean±SD) were randomly assigned to

receive twice-daily exenatide (n=73) or placebo (n=79), along with lifestyle modification, for 24 weeks.

Results: Exenatide-treated patients lost 5.06 (0.49) kg from baseline ($p< 0.0001$). A between-group difference in weight reduction (exenatide - placebo) was observed at Week 8 (-1.56 [0.48] kg, $p=0.0013$) and continued until study end (-3.45 [0.52] kg, $p< 0.0001$). At 24 weeks, significantly more exenatide-treated patients experienced ≥5% weight reduction compared with placebo (31.5% [n=23] vs. 16.5% [n=13], respectively, $p=0.0393$). Most patients with IGT demonstrated normalisation of glucose at endpoint (exenatide, 77% [13/17]; placebo 56% [9/16]). Weight reduction was similar between patients who normalised glucose tolerance (-4.42 [1.11] kg) and those who remained glucose intolerant (-3.04 [1.59] kg). Five patients (3 exenatide, 2 placebo) developed type 2 diabetes during the study; 3 of these (2 exenatide, 1 placebo) had IGT at baseline. The most common adverse events with exenatide were mild-to-moderate nausea (25%, 18/73) and diarrhoea (14%, 10/73). No hypoglycemia was reported. Weight reduction with exenatide was independent of having experienced nausea.

Conclusions: Exenatide was associated with greater weight reduction (5.06 vs. 1.61 kg) compared with placebo. An improvement in glucose tolerance was observed in the majority (67%) of patients with IGT at baseline.

ACUTE TREATMENT WITH ATENOLOL DECREASES ACYLATION STIMULATING PROTEIN IN TYPE 2 DIABETIC MEN

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Introduction: Atenolol is a specific beta-1 adrenergic receptor blocker commonly prescribed for the treatment of hypertension. Weight gain and hyperglycemia are common side-effects which are partially mediated through alteration of adipose tissue metabolism. These side-effects are particularly concerning for populations, such as type 2 diabetics.

Objective: We sought to determine how atenolol affects adipose tissue function in type 2 diabetic men during exercise. Specifically, we evaluated how atenolol affects adipose tissue secreted hormones such as acylation stimulating protein (ASP) which plays a role in adipose tissue fatty acid metabolism.

Methods: Ten type two diabetic men underwent a one-hour exercise session at 60% of their $V0_{2max}$ under four different conditions: 1) fasting after one week treatment with atenolol or 2) with placebo; and 3) two hours postprandial with placebo or 4) after one week treatment with atenolol. In addition, we also evaluated the direct effects of atenolol on adipocyte function using the 3T3-L1 murine adipocyte cell model.

Results: Atenolol treatment decreased circulating ASP in type 2 diabetic men; however, ASP did not change as a result of exercise or under postprandial versus fasting conditions. In addition, we tested if atenolol directly or indirectly affected ASP production. After 48 hours treatment with 10nM atenolol, there was no change in ASP production by 3T3-L1 adipocytes but there was a partial prevention of epinephrine-mediated decreases in ASP production.

Conclusion: Atenolol treatment decreased ASP in type 2 diabetic men potentially via an indirect mechanism on adipocyte fatty acid metabolism.

TEA MADE FROM *RAUVOLFIA VOMITORIA* AND *CITRUS AURANTIUM* REDUCES THE SYMPTOMS OF TYPE II DIABETES IN MAN: A PILOT RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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Background: A combination of calorie restriction and chronic treatment of genetic diabetic (BKS-*db*) mice with tea made from *Rauvolfia vomitoria* and *Citrus aurantium* (*R-C* tea) lead to normalization of blood glucose and protection of the BKS-*db* "brittle" pancreas.

Objective: The aim of this study was to find out if *R-C* tea reduces the symptoms of type II diabetes (T2D) in man.

Methods: Twenty two T2D patients were enrolled in the study. Twelve patients (7 men and 5 women) were treated with *R-C* tea for four months, while nine patients (6 men and 3 women) got placebo, alongside their prescribed oral diabetic and hypertension medication. Before inclusion in the study, all participants were subjected to liver and kidney function tests, analysis of T2D metabolic parameters, and given advice by a dietician on suitable calorie-restricted diets. In addition, they each got a diary, blood-pressure and blood-glucose measuring apparatus with instructions to record their daily measurements. Skeletal muscle biopsies were also taken before and after the treatment phase for the analysis of their fatty acid profiles. The laboratory analyses were repeated at half way and at the end of the treatment phase. The Data were analyzed on the basis of intention to treat.

Results & conclusions: As with the BKS-*db* mice, application of the *R-C* tea led to significant reduction in HgA1C and fasting blood glucose levels in man. In one of the *R-C* tea-treated patients, glucose intolerance was completely abolished. No compromising side effects were experienced during the study.

UNDIAGNOSED DIABETES AMONG ADULT MOROCCAN SAHRAOUI WOMEN: PREVALENCE AND ASSOCIATED RISK FACTORS

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Objective: The present work aims to examine the prevalence and associated

risk factors of undiagnosed diabetes among urban Moroccan Sahraoui women.

Design and setting: Randomised sample of adult women living in the city of Laayoune in south Morocco who visited public health centres during an immunisation campaign. Body weight, height, waist and hip circumferences, blood pressure, fasting plasma glucose (FPG), triglycerides, dietary intake and physical activity were collected.

Subjects: Data were obtained on 249 urban women aged 15 years and older, who were not pregnant. Only subjects identified as of Sahraoui origin were eligible for this investigation.

Results: The prevalence of impaired fasting glucose (IFG) was 5.5% and that of undiagnosed diabetes 6.4%. Diabetes and IFG were more common among older and obese women as well as among women with hypertension or a family history of diabetes. In addition, sucrose intakes were higher in women with diabetes than in those with normal FPG. Also, physical activity estimated as the time spent in walking was negatively associated with FPG. Regression analyses showed an independent association of age, obesity, family history of diabetes and triglycerides with diabetes.

Conclusion: The high proportion of unknown diabetes suggests the need for increased diabetes awareness in this population. The data suggest also the involvement of obesity in diabetes and the potential importance of intervention strategies to reduce population adiposity for the prevention and management of cardiovascular risk factors.

Keywords: Morocco, Sahraoui ethnic group, Women, Undiagnosed diabetes.

PHYSIOLOGICAL AND PSYCHOLOGICAL RISK FACTORS FOR T2D AMONG PAKISTANI FEMALE IMMIGRANTS: THE INVADIAB-DEPLAN STUDY ON PAKISTANI IMMIGRANT WOMEN LIVING IN OSLO, NORWAY

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Background: Pakistani immigrants living in Oslo, Norway, have a high prevalence of Type 2 diabetes (T2D), but data on the distribution of physiological and psychological risk factors for T2D in this population are scarce.

Aim: To study the distribution of, and association between, physiological and psychological risk factors for T2D in a group of Pakistani women living in Oslo.

Methods: Female Pakistani immigrants (n=198) with increased risk of, or newly diagnosed T2D were interviewed to obtain information on diet, physical activity, and demographic and psychological data. Anthropometric and blood data were also obtained. Additionally, an oral glucose tolerance test was performed, and maximum heart rate and level of physical activity were recorded objectively using SenseWear Armband.

Results: There was a high prevalence of T2D risk factors; 98 % had body mass index (BMI) values higher than WHO's recommendation for South-Asians (BMI >23) and 39% were obese (BMI >/≥30). Impaired glucose tolerance was found in 37.4% and T2D in 12.6%. Objective measurement of physical activity (with SenseWear Armband) revealed low energy expenditure, despite acceptable levels of physical activity. According to the Findrisk and Ramachandran's Indian risk scores, 29% and 89%, respectively, had a high risk of T2D. Subjects with the metabolic syndrome (MetS) reported more pain, reduced physical functioning and more subjective health complaints than those without the MetS.

Conclusions: T2D risk factors are prevalent in young, female Pakistani immigrants in Oslo, Norway. Subjects with impaired glucose tolerance have more subjective health complaints than those without.

DIABETES: CAN WE PREDICT IT IN PRIMARY CARE?

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The Diabetes type 2 (DM2) role in cardiovascular disease etiopathogenesis makes its prediction of high importance in the primary care (PC) set in order to prevent or delay the DM2 onset.

Objectives: To determine a predictor of DM2 applicable in a PC consultation.

Methods: Multicentric, case-control study in patients of 12 files diagnosed with DM2 in the year 2006 and 2007; data gathered from clinical files from two different time periods before the diagnosis: P1 - mean 6,23 years and P2 - mean 2,59 years. Data analysed with SPSS: Total cholesterol (TC), HDL cholesterol (HDL), LDL cholesterol (LDL), triglycerides (TG), fasting glucosis (FG), body mass index (BMI), abdominal circumference (AC) and LDL/HDL,TC/HDL and TG/HDL ratio.

Results: Sample n=122 (55,7% male), mean age 61 years old. Comparing diabetic (D) and control (C) in P1 and P2, statistically significant difference for TG/HDL in P2 (C=3,16±2,25; D=4,41±3,36; p=0,039), for FG in P1 (C=92,46±9,74; D=108,81±16,73; p=0,000), for FG in P2 (C=90,79±12,4; D=113,82±16,1; p=0,000), for TG in P2 (C=152,61±80,26; D= 200,27±139,60; p=0,043) and for BMI in P1 (C=26,93±4,35; D=30,36±3,99; p=0,009). Binary logistic regression defines FG in P2 the future diagnosis predictor variable: each unit above 113 mg/dl, represents 17% of higher risk.

Discussion/ conclusion: Despite having several variables with different values in diabetic and controls, the FG is the one that statistically defines risk of DM2: FG > 113 mg/dl predicts higher risk of developing future DM2. It is essencial to have good quality file notes to be able to gather this kind of data.

A UBIQUITOUS CHRONIC DISEASE CARE SYSTEM USING CELLULAR PHONES AND THE INTERNET

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Background: The rapidly increasing prevalence of chronic diseases represents an important challenge to health care systems worldwide.

Objective: To improve the quality and efficiency of chronic disease care, we investigated the effectiveness and applicability of the Ubiquitous Chronic Disease Care (UCDC) system using cellular phones and the internet for overweight patients with both type 2 diabetes and hypertension.

Research design: We conducted a randomized, controlled clinical trial over 3 months that included 123 patients at a university hospital and a community public health center.

Results: After 12 weeks, there were significant improvements in HbA1c levels of the intervention group (7.6 ± 0.9% to 7.1 ± 0.8%, $P < 0.001$), compared to the control group (7.4 ± 0.9% to 7.6 ± 1.0%, $P = 0.03$). Furthermore, we observed a significant reduction in systolic and diastolic blood pressures, as well as improvement in total cholesterol, low density lipoprotein (LDL) cholesterol, and triglyceride levels in the intervention group. In addition, there was a significant increase in adiponectin levels in the intervention group compared to the control group, although hsCRP and IL-6 levels did not change in either group.

Conclusions: The novel UCDC system presented in this paper improved multiple metabolic parameters simultaneously in overweight patients with both type 2 diabetes and hypertension.

FEMUR LENGTH, SERUM VITAMIN D AND RISK OF TYPE 2 DIABETES AMONG ADULTS

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To examine the relationship between stature components (standing height [SH], femur length [FL], standing height without femur length [SHWFL: SH-FL]), serum levels of vitamin D (VitD), and diabetic risk, we used the NHANES (2001-04) data for this cross-sectional analysis and confined the eligible subjects to 3,549 adults aged 20+ years who were assigned to a morning section, had fasted ≥8 hours and had no missing values of FL, SH and VitD. Individuals were categorized as either diabetes (diagnosed diabetes or fasting plasma glucose (FPG) >125 mg/dL), or impaired fasting glucose (IFG: 100≤ FPG< 126 mg/dL), or normal fasting glucose (NFG: FPG< 100 mg/dL). Each individual was also grouped into a quintile of each height components. The adjusted mean levels of VitD were lower among those with IFG and diabetes in comparison to those with NFG in both sexes. Using multinomial logistic regression, we found that in both sexes, only FL in quintiles were significantly associated with the risk of diabetes; while both SH and SHWFL were not significant. When pooling both sexes together to examine the relationship between FL in quintiles, VitD levels, and diabetic risk, we found that the levels of VitD were lower in those with IFG and diabetes in each quintiles of FL, and that the levels of VitD increased as the FL increase. In summary, the results from this study may shed a light on the observed phenomenon that some components of stature are negatively associated with the risk of type 2 diabetes among adults.

GENE EXPRESSION OF CHROMOGRANIN A IN SALIVA OF DIABETIC PATIENTS

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Aims: Chromogranin A is present in secretion granules of nerve, endocrine and immune cells and is a precursor of several peptides with antibacterial and antifungal properties at micromolar concentrations.

In this prospective, double blind study, our aim was to determine the expression of chromogranin A and its peptides at protein level in saliva of type 2 diabetic patients and thereby to obtain a new non-invasive diagnostic means for the future.

Methods: Saliva was taken from 50 type 2 diabetic patients and 50 healthy individuals at the same time interval in the morning without any oral stimuli. Circadianic periodics in protein productions have been avoided. The presence of chromogranin A and its derived peptides was determined in whole saliva, after centrifugation at 4 degree for 8 min at 14 000rpm, by SDS-PAGE electrophoresis and Immunoblotting (Western Blot). To ensure same protein concentrations Bradford protein quantification assay has been performed before.

Results: For the first time, we have determined an overexpression of chromogranin A in saliva of diabetic patients in 90% of the individuals.

Conclusions: Chromogranin A, a circulating biomarker for epithelial tumours, is also overexpressed in saliva of type 2 diabetic patients. To confirm our results, more studies with a larger amount of patients is necessary.

CARDIAC ABNORMALITIES AND MICROALBUMINURIA IN DIABETIC PATIENTS

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Background: Microalbuminuria correlate with cardiac abnormalities, including left ventricular (LV) dysfunction and hypertrophy, electrocardiographic abnormalities and ischemic heart disease. Albuminuria has been shown to predict cardiovascular disease (CVD) in populations with diabetes mellitus (DM). The mechanism of the association of albuminuria and CVD is unclear.

Objectives: We sought to compare systolic and diastolic function in patients with DM based on albuminuria status.

Methods: We selected 80 adults with type 2 diabetes,47 women and 33 men, mean age 51±14. Diabetes was defined by fasting plasma glucose 126 mg/dl or by specific treatment. BMI was calculated by the standard formula. Albuminuria was measured by fasting random urine specimen on arrival to the clinic, usually in the morning. Echocardiography methods. LV mass index (LVMI) has been evaluated according to the method of Devereux and Reichek. Abnormal diastolic function was defined as E/Aratios of < 1. Abnormal systolic function was defined as abnormal ejection fraction (< 35%).We compared echo-derived indices of LV systolic and diastolic function in three groups of patients with DM based on albuminuria status:

I = no albuminuria (< 30 mg albumin/g creatinine), 27 patients;

II = microalbuminuria (30 to 300 mg/g) 26 patients; and

III = macroalbuminuria (>300 mg/g) 27 patients.

Results: LV systolic function was lower in the groups with albuminuria.Similarfindings were noted in diastolic LV filling with lower mitralE/A ratios in groups with albuminuria. LVMI were highest with macroalbuminuria and lowest without albuminuria.

Conclusions: Albuminuria is independently associated with LV dysfunction in type 2 DM; this may explain in part the relationship of albuminuria to increased CV events in the DM population.

THE RELATIONSHIP BETWEEN BODY MASS INDEX AND METABOLIC CONTROL PARAMETERS, INSULIN SENSITIVITY IN OBESE PATIENTS WITH TYPE 2 DIABETES

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Background and aims: In this study, we investigated whether there was a relationship between body mass index (BMI) and metabolic control parameters, insulin sensitivity in patients with type 2 diabetes or not.

Material and methods: We evaluated 39 type 2 diabetic patients (mean age: 56.6 ± 13.8 years). The insulin sensitivity were assessed using the HOMA index. The study group was divided into two subgroups (Group A=BMI>30 kg/m², Group B= BMI< 30 kg/m²) according BMI.

Results: The study results showed that the mean insulin sensitivity index of study patients was lower than normal ranges (group A: (HOMA-IR: 9.1 ± 5.8), group B: (HOMA-IR: 5.1 ± 4.6), serum fasting insulin levels (group A: (insulin: 22.6 ± 16.0 µU/ml), group B: (insulin: 11.8 ± 7.8 µU/ml) were higher than normal ranges. The correlation analyses (Pearson) have shown that in type 2 diabetic patients, there was a statistically significant correlation between HOMA-IR and BMI (r=0.38, p< 0.05), fasting serum C-peptid (r=0.54, p< 0.001), fasting serum glucose (r=0.45, p< 0.01). The Mann Whitney U test have shown that there was a statistically significant difference between group A and group B subjects according to HOMA-IR (p< 0.05), fasting serum insulin (p< 0.05), BMI (p< 0.05), HbA1c (p< 0.01).

Conclusion: In this study, we showed that there were significant correlation between BMI and fasting serum glucose, insulin, C-peptid, HbA1c. We thought that the weight loss must be an important therapeutic target other than anti-diabetic treatment in obese patients with type 2 diabetes.

INSULIN SENSITIZING ACTIVITY OF XANTHONES DERIVATIVES: PRECLINICAL EVIDENCE

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Background and aim: Xanthones are a class of polyphenolic compounds that commonly occur in plants and have been shown to have extensive biological and pharmacological activities. In this study we examined the glucose-lowering effect of a natural extract containing high amount of xanthones derivatives (NEXD) in differentiated L6-rat skeletal muscle cells and in obese Zucker rats (OZR), as a model of insulin resistance.

Methods: L6 myotubes cells were incubated with NEXD, at different concentrations, for 18hr. Glucose uptake was measured by using 2-[^{3}H]-Deoxy-Glucose (2-DG). The ability to improve whole peripheral insulin sensitivity was also tested in OZR chronically fed with NEXD (dose 0.8 g/kg diet) by using euglycemic-hyperinsulinemic clamp technique. Plasma membranes from L6 and soleus muscle were isolated for determination of glucose transporters 1 and 4 (GLUT1, GLUT4) by Western-blot.

Results: NEXD induced an increase (>45%, $p< 0.05$) in basal 2DG uptake, mediated by a raise (>30%, $p< 0.05$) in the total amount of GLUT4, without changes in GLUT1 protein. Glucose infusion rate was 40% greater in rats fed with NEXD in comparison with control rats, being GLUT4 content in soleus muscle significantly induced by NEXD (>40%, $p< 0.05$).

Conclusion: Our results indicate that xanthones derivatives may exert antidiabetic activity by enhancing whole body tissue sensitivity as a consequence of an increase in the amount of GLUT4 transporter.

CHARACTERIZATION OF PHYSIOLOGICAL FACTORS AND ISLET HORMONES IN ANIMALS PRIOR TO THE ONSET TYPE 2 DIABETES

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Type 2 diabetes (T2D) has become the worldwide health issue. To tackle the future epidemic of T2D, recent researches aim to employ the intervention at prediabetes, also described as metabolic syndrome. However, it could facilitate the intervention approach if pathophysiological factors could be characterized before the onset of diabetes. By employing rats received both high-fat diet and STZ (50 mg/kg, i.p.) administration

(HFSTZ rats), the onset of diabetes (fasting glucose level ≧ 200 mg/dl)

occurred respectively and was approximately within 4 weeks after STZ injection. Body weight and diet/water consumption of animals were measured every 3 days. Serum was prepared for biochemical analysis and intravenous glucose tolerance test (IVGTT) was performed weekly. Our results demonstrated that weight gain, hyperlipidemia, and modest hyperglycemia were observed in HFSTZ rats. During the progress of the diabetes, impaired fasting glucose level resulted in the overall pattern of IVGTT results shifting upwards and the efficiency of glucose utility (% hypoglycemic efficiency) was gradually deteriorated. Another interesting observation was that the level of serum glucagon and insulin become reciprocal fluctuating but the level of both was elevated prior to the onset of T2D. The fluctuating pattern of glucose level was similar with that of insulin. Therefore, such results suggested the dysfunction of islet hormone regulation in pancreas and could be the late warning for the onset of diabetes. In conclusion, further characterization of both physiological changes and endocrine profiles could facilitate for the future monitoring of diabetes pathogenesis and make a better diabetes intervention program.

VITAMIN A, VITAMIN E AND DEGENERATIVE COMPLICATIONS IN A NON INSULIN DEPENDENT DIABETES MELLITUS GROUP

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Aims: We aimed to study the association between some anti oxidant vitamins (Vitamin A and Vitamin E) and degenerative complications in a non insulin dependent diabetes mellitus (NIDDM) group.

Subjects and methods: A total of 48 NIDDM patients were recruited. The diabetic patients were divided into tow groups: group I consisted of 14 patients without complications. Group II, consisted of 34 patients with degenerative complications. Fasting blood samples were obtained from all subjects. Levels of vitamins in serum were measured by high performance liquid chromatography (HPLC).

Results: A statistically significant higher values of vitamin E were observed in diabetic patients without complications compared to patients with degenerative complications ($p=0.004$).Vitamin A levels were not significantly different between the two groups. Glycated hemoglobin ($p=0.001$) and Apo A ($p=0.022$) levels were significantly higher in group II. Vitamin E was significantly correlated to glycated hemoglobin($r=-0.37$; $p=0.046$) and systolic pressure($r=-0.35$; $p=0.037$). Vitamin A was significantly correlated with glycemia ($r=0.35$; $p=0.045$), systolic and diastolic pressures($r=-0.41$; $p=0.019$ and $r=-0.46$;$p=0.009$ respectively).

Conclusion: Hyperglycemia induces the overproduction of oxygen free radicals. Low levels of anti oxidant vitamins such vitamin E seems to be implicated in the development of diabetic complications.

HYPERHOMOCYSTEINEMIA, C677T POLYMORPHISM AND TYPE 2 DIABETES

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Objective: Hyperhomocysteinemia is known a risk factor for the development of cardiovascular diseases which seem to be the main cause of mortality in patients with type 2 diabetes. The C677T polymorphism variation of MTHFR, the key enzyme in Homocystein metabolism, may have a role in Hcy levels. In the present study, we intend to determine whether hyperhomocysteinemia or C677T polymorphism have a highest risk for the development of type 2 diabete.

Methods: We included 149 type 2 diabetic patients and 130 control subjects. Clinical examination and measurements of tHcy, Fol, VitB12, Tchol, HDLc and TG were done in both groups. C677T polymorphism variation was determined for patients and control groups.

Results: Homocystein, folates and VitB12 mean levels were higher in type 2 diabetics than in control subjects ($p=0,05$). In diabetic group 35,4% were hyperhomocysteinemics and 62,2% have CT or TT genotype in comparison with control group 13,1% hyperhomocysteinemics and 29,2% have CT or TT genotype. The risk of developing the disease in hyperhomocysteinemics is higher than those with normal Hcy level (OR=3,6 ; 95% IC : 1,93-6,69. $p< 0,001$). The same result was found for the C677T mutation (OR=2,55 ; 95% IC : 1,36-4,75. $P=0,002$).

Conclusion: Hyperhomocysteinemia seems to enhance the risk of DNID independently of C677T polymorphism.

THE ASSOCIATION BETWEEN HIGH-SENSITIVE C-REACTIVE PROTEIN AND INSULIN RESISTANCE IN IGR FIRST-DEGREE RELATIVES OF TYPE 2 DIABETES

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In 89 impaired glucose tolerance (IGT) first-degree relatives of type 2 diabetes, 34 impaired fasting glucose (IFG) first-degree relatives of type 2 diabetes, and 34 IFG+IGT first-degree relatives of type 2 diabetes, high-sensitive C-reactive protein (CRP) was measured. The result showed that C-reactive protein was increased in first-degree relatives with IGT (1.81±0.45 mg/L) or IFG+IGT (2.05±0.48 mg/L) as compared with normal controls (1.65±0.56 mg/L), and the first-degree relatives with IFG+IGT had higher CRP level than those with IGT or IFG (1.69±0.52 mg/L). First-degree relatives with higher CRP level (more than 1.85 mg/L) had higher body mass index, systolic blood pressure, diastolic blood pressure, wrist hip ratio, circum insulin resistance by HOMA, total cholesterol, triglyceride, low density lipoprotein and lower high density lipoprotein than those with lower CRP level (less than 1.85 mg/L). The analysis of stepwise regression showed that C-reactive protein was correlate with insulin resistance in the first-degree relatives of type 2 diabetes.

Keywords: Diabetes mellitus, type 2; First-degree relatives; H igh-sensitive C-reactive protein; insulin resistance; IFG; IGT.

DEFINING LABORATORY PARAMETERS TO SCREEN INSULIN RESISTANCE SYNDROME IN ADULTS SUSCEPTIBLE TO DEVELOP TYPE 2 DIABETES IN MAURITIUS

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The prevalence of type 2 diabetes is around 20 % in Mauritius.Since metabolic syndrome (MS)precedes type 2 diabetes, an early detection of MS would serve as a good prevention means.

Aims: The main aim of the present study is to assess laboratory procedures for MS screening.

Methods: Participants comprised of four groups ,based on their FBS values: Normal (n = 247), Diabetic(n = 439), Impaired Fasting Glucose (n = 112) and Impaired Glucose Tolerance (n = 109).Homeostasis Model Assessment (HOMA) and Quantitative Insulin Check (QUICK) were calculated for each group.Anthropometric measurements were also taken on the subjects.

Results: The findings are as follow, NormalGroup: Sensitivity is 9.1%, Specificity = 4.3% and the Positive Prevalence of MS is 10%, Mean HOMA: 1.81 ± 1.14, Mean QUICK: 0.38 ± 0.08. For diabetic group: Sensitivity is 63.2%, Specificity = 60.3% and the positive prevalence of MS= 22.2%, Mean HOMA: 4.90 ± 4.6, Mean QUICK: 0.32 ± 0.02. For IGT group: Sensitivity is 30.8%, Specificity = 8.6% and the Positive Prevalence for MS=33.3% Mean HOMA: 2.43 ± 1.43, Mean QUICK: 0.43 ± 0.19. For IFG group: Sensitivity is 50%, Specificity = 10.7% and the Positive Prevalence (MS)= 33.3%, Mean HOMA: 2.55 ± 1.43, Mean QUICK: 0.35 ± 0.06.

Conclusion: The findings indicate that MS tends to more prevalent in the "pre diabetes" group i.e. IGT and IFG than in the affected cases. One can conclude that MS screen has a potential in the early detection of subjects susceptible to type 2 Diabetes.

ONE-YEAR FOLLOW-UP OF BIOLOGIC CORRELATES FOR ARTERIAL BLOOD PRESSURE IN TYPE 2 DIABETES

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Aims: Previous results suggested that blood pressure (BP) response to exercise was significantly correlated with HbA1c levels in healthy normotensive non-diabetic control subjects. Present investigation evaluated the biologic determinants of arterial BP during one-year follow-up in patients with type 2 diabetes (T2D).

Methods: Cardiovascular risk factors were assessed at baseline, 1, 3, 6, 9 and 12 months in 20 T2D (age 60±5 y). Were measured: body mass index (BMI), waist to hip ratio (WHR), mean BP, fasting plasma glucose (FPG), HbA1c, plasma LDL cholesterol, folate and total homocysteine (tHcy), urinary albumin excretion (UAE). Dietary habits were estimated at each visit by administering a 2-d 24-h dietary recall (24HDR).

Results: BMI was 31±5 kg/m2, WHR 0.97±0.06, mean BP 98±10 mm Hg, FPG 159±42 mg/dl, HbA1c 7.4±1.2%, LDL 118±31 mg/dl, folati 8.9±6.6 ng/ml, tHcy 11.5±3.4 µmol/l. UAE ranged from 0 to 2957 µg/min (median 15.8). Multivariate regression analysis of longitudinal data found the following independent variables to be associated with MBP ($|r| = 0.54$, $P < 0.0001$): HbA1c (t-value 5.24), folati (-2.84), and LDL (2.21). Estimated daily intake of folic acid was 286±129 µg/day significantly lower than Recommended Dietary Allowance.

Conclusions: Present study confirms in T2D previous observations in healthy people. There is a significant positive correlation between protein glycosylation and arterial BP. Additional influential factors are plasma folate and LDL cholesterol. These findings strengthen the need for maintaining a strict metabolic control (glycosylation of matrix proteins affect artery compliance) and promoting an adequate dietary intake of folate.

PREVALENCE OF DIABETES MELLITUS TYPE 2 IN NATIVE AND ALIEN POPULATIONS IN REPUBLIC TYVA

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Republic Tyva is the part of Russia with area 168.6 square km. It is situated in the South of the Eastern Siberia in the geographic center of the Asia. The climate is sharply continental. Total population is 308,500 and represented by natives (tyvinians, 77%) and aliens (caucasians, 23%). The native peoples still continue to follow their traditional lifestyle and nutrition. In rural area of Republic live 70% natives and 30% aliens.The aim of the study is to compare the prevalence of diagnosed diabetes mellitus type 2 (DM2) in native and alien populations from Tyva. The State register of DM2 for Republic was used.According by WHO (1999) criteria 843 subjects (378 natives and 465 aliens) with DM2 were registered in Tyva in 2005. The DM2 prevalence for native population with age 20+ was 2.67 (95%CI: 2.63-2.71) /1,000 and for aliens was 11.52 (10.50-11.52)/1,000 (ð< 0,0001). For males in natives the DM2 prevalence was 1,25 (1,21-1,29)/1,000 and in aliens - 5,49 (4,94-6,04)/1000 (ð< 0,0001). For females in natives the DM2 prevalence was 3,87 (3,78-3,96)/1,000, in aliens - 15,66 (14,34-16,98)/1,000 (ð< 0,0001). There was not a difference in DM2 prevalence in rural and urban natives. In aliens the DM2 prevalence was higher among urban males than rural males. The DM2 incidence for native population was 0,61 (0.48-0,74)/1,000 and for alien population - 1,56 (1,18-1,94)/1,000 (ð< 0,0001). These data indicates that DM2 among native population is lower tan among alien population in Republic Tyva. The maintenance of particular lifestyle protects native population from DM2.

ANTIPLATELET DRUG USE IN PATIENTS WITH TYPE 2 DIABETES

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Aims: Diabetic patients are at increased risk for macrovascular complications. While antiplatelet treatment in patients with established large-vessel disease is unquestionably beneficial, the indications for such treatment without macrovascular disease are less certain. Recently, US guidelines (American Diabetes Association) recommend aspirin for diabetic patients over 40 years of age, or under 40 years with additional risk factors. The aim of our study was to investigate the use of antiplatelet drugs in diabetics.

Methods: We examined the case-notes of 439 patients (216 males) of mean±SD age 64.7±9.6 years, and HbA1c 8.3±1.9%, who visited consecutively the outpatient diabetes department in a primary care setting.

Results: 433 patients should be on aspirin treatment according to ADA recommendations. Antiplatelet drugs, however, were being taken by 135 (31.2%) patients only. Antiplatelet drug use was more common in patients with a history of cardiovascular events such as ischaemic heart disease, cerebrovascular disease and peripheral vascular disease (67.7% vs. 21.2% in patients with no history of macrovascular disease, $p< 0.01$). Of the 298 untreated patients, only 53 patients (18%) had contraindications to antiplatelet treatment.

Conclusions: Under-use of antiplatelet drugs has been reported in diabetics in our study since practically only patients with established large-vessel disease were on such treatment. It seems that most doctors prescribe aspirin in diabetics only for secondary prevention instead for primary, fact which indicates a mistrust of the current guidelines and the urgent need for evidence-based indications.

DETERMINANTS OF CAROTID ATHEROSCLEROSIS IN PATIENTS WITH TYPE 2 DIABETES AND METABOLIC SYNDROME

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Aims: The increased incidence of atherosclerotic macrovascular disease in type 2 diabetic patients is associated both with diabetes specific factors and coexisting classic cardiovascular risk factors as components of the metabolic syndrome. The aim of this study was to investigate the association between carotid atherosclerosis with metabolic parameters in type 2 diabetics with metabolic syndrome.

Methods: 174 type 2 diabetic patients (mean age: 64.6±9.6 years, 79 males), with metabolic syndrome according to IDF criteria, were included in the analysis. The intima-media thickness (IMT) of the common carotid artery was measured bilaterally using B-mode ultrasound imaging, and averages were calculated. Multiple regression analysis was performed in order to determine variables associated with increased IMT. Age, gender, duration of diabetes, HbA1c, smoking status, systolic and diastolic blood pressure (SBP and DBP respectively), LDL- and HDL- cholesterol, triglycerides were used as independent variables in the regression model.

Results: Mean values±SD of the main metabolic parameters were as follows: BMI: 30.6±4.9 kg/m^2, HbA1c: 8.2±1.5%, SBP: 149.1±17.6 mmHg, DBP: 87.6±8.9 mmHg, HDL: 46.6±14.7 mg/dl, LDL: 153.5±35.2 mg/dl, TG: 161.8±82.8 mg/dl, IMT: 0.83±0.32 mm. On multiple regression analysis only LDL-cholesterol levels were found to be associated with increased IMT values (B=0.003±0.001, p=0.03).

Conclusions: LDL-cholesterol levels in patients with type 2 diabetes and metabolic syndrome are associated with increased IMT values independently of glycaemic control as well as of other cardiovascular risk factors.

CONTROL OF MULTIPLE CARDIOVASCULAR RISK FACTORS AMONG PATIENTS WITH TYPE 2 DIABETES

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Aims: Guidelines recommend multifactorial intervention on cardiometabolic parameters in patients with type 2 diabetes in order to reduce morbidity and mortality. The aim of our study was to evaluate the efficacy of such interventions in diabetic patients during a 2-year period.

Methods: The sample consisted of 191 men and women (100/91) diagnosed with type 2 diabetes who visited the diabetes outpatient department. All patients received treatment according to the recent recommendations for the control of their cardiovascular risk factors and were followed up for a period of 2 years.

Results: At baseline the prevalence of the risk factors was: HbA1 $\geq$ 7% 76%, body mass index (BMI) $\geq$ 30 kg/m^2 39%, blood pressure (BP) $\geq$ 130/80 mmHg 82%, LDL-cholesterol $\geq$ 100 mg/dl (or 70 for those with coronary artery disease) 80%. After 2 years the respective prevalences were as follows: HbA1 $\geq$ 7% 46% ($p< 0.001$ vs. baseline), BMI $\geq$ 30 kg/m^2 43% (p= non significant vs. baseline), BP $\geq$ 130/80 mmHg 68% (p=0.002 vs. baseline), LDL-cholesterol $\geq$ 100 or 70 mg/dl 65% (p=0.003 vs. baseline).

Conclusions: In long term clinical practice the multifactorial intervention for the control of major risk factors in diabetic patients proved to be effective for all the factors except weight loss. However, it should be noted that despite the observed differences (reductions) during the 2-year period, the prevalence of major risk factors still remains high.

MANAGEMENT OF PAINFUL DIABETIC NEUROPATHY WITH GABAPENTHIN

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Background: The commonest cause of peripheral neuropathy is diabetes and pain occurs in approximately 30% of diabetic patients with neuropathy. Anticonvulsant drugs have been used in the management of pain since the 1960s. The clinical impression is that they are useful for chronic neuropathic pain, especially when the pain is lancinating or burning.

Objectives: To evaluate the analgesic effectiveness and adverse effects of gabapentin for management of painful diabetic neuropathy.

Material and methods: A total of 86 subjects were randomized. A 4-week titration period to a maximum dosage of 900 mg/d of gabapentin. Treatment was maintained for another 12 week. The primary efficacy measure was

change in the average daily pain score based on an 11-point Likert scale (0, no pain; 10, worst possible pain) from baseline week to the final week of therapy. Secondary measure included Short-Form McGill Pain.

Results: Subjects receiving gabapentin had a statistically significant reduction in average daily pain score from 7.8 to 5.2 points (P< .001). Secondary measures of pain showed improvement with gabapentin (P< .001). Somnolence, dizziness, were present in 10 patients, but there were no withdrawals because of the side effects.

Conclusions: Gabapentin is effective in the treatment of associated with PHN. This evidence, combined with its favourable side-effect profile in various patient groups (including the elderly) and lack of drug interactions, makes it an attractive agent. Therefore, gabapentin should be considered an important drug in the management of neuropathic pain syndromes.

ASSOCIATION OF *THR54* ALLELE OF FATTY-ACID BINDING PROTEIN 2 GENE WITH OBESITY AND TYPE 2 DIABETES MELLITUS IN A CAUCASIAN POPULATION

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Aims: The fatty acid-binding protein 2 (*FABP2*) *A54T* polymorphism has been associated with type 2 diabetes mellitus (T2DM) and obesity in many but not all studies. Our aim was to investigate possible associations of *FABP2 A54T* polymorphism with T2DM and/or obesity in a Greek Caucasian population.

Methods: 242 subjects with T2DM and 188 control subjects were genotyped for the *FABP2 A54T* polymorphism using polymerase chain reaction-restriction fragment length polymorphism method. Of the total subjects included in both groups, 172 were classified as obese (BMI>30 kg/m^2) and 258 were classified as nonobese (BMI< 30 kg/m^2).

Results: In the whole population, 218 subjects (50.7%) were genotyped as AA, 175 subjects (40.7%) as AT, and 37 subjects (8.6%) as TT for the *FABP2 A54T* polymorphism. According to the dominant model, the frequency of AA genotype was significantly lower in obese than in nonobese subjects (43.0% vs 55.8%, p=0.009). No significant difference was observed either in genotypes or alleles between diabetic and nondiabetic subjects. According to the additive model, the presence of TT genotype was significantly associated with obesity after adjusting for age, sex, and the presence of T2DM (OR 2.32, p=0.028).

Conclusion: *FABP2 A54T* polymorphism may help identify Caucasian subjects at risk for obesity.

THE EFFICACY OF PIOGLITAZONE ON THE PLASMA ADIPONECTIN LEVEL AND GLUCOSE CONTROL IN PATIENTS WITH STEROID-INDUCED DIABETES

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Aims: We investigated the efficacy of pioglitazone in patients with steroid-induced diabetes.

Methods: Nine outpatients with steroid-induced diabetes at Niigata University Hospital were enrolled, whose blood glucose control had been interfered during maintenance steroid treatment (HbA1C≥6.5%) and who had been on either diet therapy or α-glucosidase inhibitor, sulfonylurea or rapid-insulin secretion inducer medication. We excluded patients who were under insulin or biguanide medication, had heart failure, or severe liver or kidney dysfunction. Given 15 mg/day pioglitazone for 24 weeks, we monitored the participants' body weight, blood pressure, FPG, HbA1C and liver function parameters every 4 weeks, and waist circumference, IRI, creatinine, adiponectin, leptin, total cholesterol, HDL-C, triglyceride levels every 12 weeks. The dosage was maintained throughout the study if no obvious side effects were observed, and if HbA1C improved since the beginning of the study at week 12. If HbA1C did not improve at week 12, the dosage was doubled to 30 mg/day, which was determined to be the maximum of a daily dosage.

Results: No obvious side effects such as edema or liver dysfunction were observed at week 24. The dosage was increased to 30 mg/day for one participant for no improvement on HbA1C. The parameters that changed with statistical significance are: body weight (58.2±10.6kg→59.5±11.6kg), BMI (23.4±3.7kg/m²→23.9±4.9kg/m²), HbA1C (7.8±0.8%→6.9±0.4%), adiponectin (10.2±4.0μg/ml→24.9±15.6μg/ml). The parameters that showed no significant differences are: waist circumference, lipid, blood pressure, FPG, IRI, HOMA-IR and leptin.

Conclusion: Pioglitazone promoted increase in adiponectin level in the steroid-induced diabetic patients and improvement on their blood glucose control.

PREVALENCE AND RISK FACTORS OF POOR BLOOD GLUCOSE CONTROL IN THE ABSENCE OF DIAGNOSED DIABETES IN AN URBAN, DEVELOPING AFRICAN COMMUNITY

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We determined the prevalence and determinants of poor blood glucose control in an urban, developing African population.

We assessed demographic characteristics, lifestyle factors, blood pressure, lipids, C-reactive protein (CRP) concentrations and glycated hemoglobin (HbA_{1c}) in 621 randomly selected subjects >16 years of age in an urban population sample of African ancestry.

Seventy-five percent of women and 51% of men were overweight or obese and, 139 (22.5%) participants had a HbA_{1c}>6.1% of whom 95 had no known diabetes mellitus. In multivariable analysis in the 540 subjects without known diabetes, one SD increase in adiposity indices (body mass index, waist circumference or waist-to-height ratio) and one SD decrease in physical activity spent in walking were associated with a 2-fold increase (P< 0.0001) and a 50% reduction (P≤ 0.03) in the prevalence of a HbA_{1c}>6.1%, respectively. An interaction between adiposity and age in subjects without known diabetes also explained an elevated HbA_{1c} (P< 0.05), and age predicted poor blood glucose control in overweight or obese but not in normal weight subjects. CRP concentrations were 3.8-fold higher in subjects with poor glucose control but this relationship was explained by adiposity indices. Poor blood glucose control in undiagnosed participants was further independently associated with atherogenic dyslipidemia (P=0.0003) and hypertension (P=0.02).

Poor blood glucose control was present in as much as 22.5% of subjects, more than two thirds of whom had no known diabetes. Excess adiposity, a synergism between adiposity and age, and physical inactivity were important potential determinants of this preclinical state.

BENEFICIAL EFFECTS OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND THIAZOLIDINEDIONS ON ATYPICAL ANTIPSYCHOTIC-INDUCED INSULIN

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Aims: To investigate the pharmacological suggestibility of atypical antipsychotics-induced weight gain (WG) and insulin resistance (IR) on obese and diabetic Otsuka Long Evans Tokushima Fatty (OLETF) rats.

Methods: The OLETF rats and their lean littermates (LETO) rats were treated either clozapine (10 mg/kg), captopril (50 mg/kg) or combination of both. Rosigliazone treatment (3 mg/kg) served as positive control while control group was treated with tap water. All treatment schedules were once a day oral dose of the selected drug/vehicle and the treatment period lasted over 5 weeks. The IR was determined by means of hyperinsulinaemic euglycaemic glucose clamping, metabolic variables by metabolic cages, plasma insulin by RIA, and CCK-1 (CCK-1R), CCK-2 (CCK-2R) receptor mRNA in the hypothalamus by RT-PCR.

Results: Clozapine monotherapy caused IR and WG both in LETO and OLETF rats. Captopril monotherapy had opposite effect on the IR and body WG. When combinatory therapy was applied in OLETF rats the IR improved but there was no significant change in the WG as compared with the clozapin treated OLETF rats, whereas the combination had effect neither the IR nor the WG in LETO rats. Roziglitazone improved the IR but caused a slight, non-significant WG. Clozapine-induced an elevation on CCK-1R and CCK-2R on LETO rats, but opposite effect was seen in OLETF rats regarding CCK-2R.

Conclusions: Clozapine-induced IR and WG occurs when functionally intact CCK-1 is lacking. Captopril treatment restores the clozapine-induced metabolic changes in OLETF rats and this effect could be explained by the altered expression of CCK-receptors.

THE COMPONENTS OF METABOLIC SYNDROME IN KETOSIS PRONE TYPE 2 DIABETES MELLITUS

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Background and aims: The clinical presentation is commonly reported in African and African-American persons, also observed in Hispanic persons and now in Russians. The aim of the study was to investigate the presence of metabolic syndrome (MS) in ketosis prone type 2 diabetes mellitus (KPDM).

Materials and methods: 10 patients (all men) with KPDM was investigated. 6 of them - retrospectively.

We measured β-cell function after resolution of ketoacidosis and at normoglycemic remission.Analyses of relative frequencies of HLA alleles was made. ICA, IAA and GADA were measured. All participants underwent ECG, measurement of height, weight, waist and hips circumference, BMI, blood pressure, blood lipids.2 control groups consist of 10 obese patients with type 2 diabetes mellitus and 10 healthy men.

Results: MS was verified in all respondents with KPDM. The most common MS components were arterial hypertension, abdominal obesity, hypertriglyceridemia. Mean BMI was 34±2 kg/m^2. HOMA-IR was 7±1,5%. All patients have no autoimmune markers. An association with HLA susceptibility alleles (HLA-DR3) found in 2 patients.

During normoglycemic remission patients with KPDM had substantial improvement in basal and stimulated C-peptid levels.

Conclusion: In spite of acute initial presentation with severe hyperglycemia and diabetic ketosis this variant must be referred to type 2 diabetes (KPDM).

MS is common feature of KPDM.

DIABETES MELLITUS IN PATIENTS WITH SLEEP APNEA SYNDROME

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Aim: The purpose of this study was to estimate the prevalence of diabetes mellitus type 2 or glucose levels higher than 100mg/dl (DM-2) in patients with obstructive sleep apnea syndrome (OSAS), upper airway resistance syndrome (UARS) or snorers (SN) according to their medical history (A) and to glucose levels reevaluated after polysomnography (B).

Material and methods: A total of 3384 consecutive patients (2653 men and 731 women) were studied. A specific questionnaire for sleep apnea was completed for each patient. The medical history and the reevaluated glucose levels measurements were used to estimate the DM-2 prevalence in these patients. 2511 patients was found to suffer from OSAS (Group I), 568 patients from UARS (Group II), while 306 were habitual snorers (Group III).

Results: In Group I the prevalence of DM-2 was 5.9% and 38.7% according to their medical history (A) and after reevaluation (B) respectively , significantly higher than in Groups II or III ($p< 0.02$ and 0.001respectively). In each group significantly higher was the proportion who ignore the presence of DM-2 ($p< 0.001$ to 0.02).

Conclusion: In patients with OSAS the prevalence of DM-2 was 38.7%, significantly higher than in UARS or snorers. The glucose measurements after sleep study revealed that a great proportion of our patients ignore the presence or the risk of DM-2 development.

CARBOHYDRATE METABOLIC DISORDERS IN PATIENTS WITH ADRENAL TUMORS

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Introduction: Adrenal hormones cause carbohydrate metabolic disorders.

Aim of the study was to assess the frequency of the metabolic syndrome in patients with adrenal tumors.

Materials and methods: In patients hospitalized because of adrenal tumors , in Endocrinology and Diabetology Ward of District Hospital in Olsztyn in years 2000-2007, hormonal activity and features of the metabolic syndrome were assess. Body mass, height, blood pressure, lipid profile, fasting gliceamia and/or gliceamia in oral glucose tolerance test were measured.

Results: 106 patients - 68 women (64,2%), 38 men (35,8%), in mean age ± 56,04 =/- 12,7 years, with mean tumor size 32,5 ± 21 mm; hormonal active tumors (Cushing Syndrome and Pre-Cushing Syndrome, Conne Syndrom, pheochromocytoma) were diagnosed in 31 patients (29%).

Carbohydrate metabolic disorders were found in 34 patients (32,1%), abdominal obesity in 62 patients (58,5%), arterial hypertension in 71 patients (67%), dyslipidemia in 62 patients (58,8%). Metabolic syndrome were diagnosed in 37 patients (34,9%). 11 patients (10,4%) had hormonal disorders and fullfiled criteria of the metabolic syndrome simultaneously.

Conclusions: In patients with adrenal tumor diagnostics of carbohydrate metabolic disorders and of the metabolic syndrome should be performed.

THE RELATION BETWEEN SOCIOECONOMICAL POSITION AND GLYCAEMIA AND RISK OF DIABETES TYPE 2 ESTIMATED BY FINNISH DIABETES RISK SCORE CRITERIA IN POLISH POPULATION (HAPIEE STUDY)

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Aim: The aim was to study the relation of socioeconomic position with glycaemia levels and the risk of diabetes type 2 according to FINDRISK criteria.

Sample and methods: The studied population was 1960 men and women aged 45-64, randomly selected from the population of Krakow. The relation between socioeconomic position and FINDRISK categories and elevated blood glucose was assessed by Chi square test.

Results: 33.2% men and 25,9% women (p< 0,05) had FINDRISK below 7, and 11,8% men and 15,6% women (p< 0,05) had FINDRISK between 15-20. The prevalence of FINDRISK higher than 15 and elevated blood glucose in education categories are presented in the table. There was no association of FINDRISK and elevated blood glucose with marital status, economical position and position at work in both sexes.

		Elementary and high school	University completed
FINDRISK score >15	Men	14,1%	9,9%
	Women*	17,5%	11,0%
Glucose > 6,1 mmol/l	Men	16,9%	16,8%
	Women*	11,0%	6,0%
Glucose > 7,0 mmol/l	Men	4,5%	4,8%
	Women*	3,8%	0,9%

Conclusion: The higher education was related to lower risk of type 2 diabetes according to FINDRISK and elevated blood glucose in women but not in men. This analysis confirm influence of education on lifestyle factors associated with development of diabetes in women presented in previous studies.

ANGIOTENSIN-CONVERTING ENZYME GENE AND GENETIC SUSCEPTIBILITY TO TUNISIAN TYPE 2 DIABETES PATIENTS

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Background: Despite studies suggesting a substantial genetic contribution to the susceptibility of type 2 diabetes mellitus (DM), no major susceptibility genes have been identified so far. ACE, a key enzyme, catalyzes the conversion of angiotensin I to II and inactivates bradykinin in many tissues.

Aim was to investigate the distribution of ACE genotypes and to evaluate the role of serum ACE activity and their effects on DM.

Methods: 115 DM patients were compared to 165 healthy controls. The ACE polymorphism was determined by PCR-RFLP.

Results: The ACE D-allele was significantly more frequent in the DM patients than controls (p< 0.001) and the OR was highly significant at 6.75. So, the ACE I/D polymorphism was significantly associated with DM (p< 0.001). The DD genotype have significantly higher serum ACE activity than ID and II (P< 0.001). A significant association between the DD genotype and diabetes [ACE DD *vs*. ID and II; OR=5.99 (95% CI, 3.49-10.28; p < 0.001)] and a significant association between II genotype and decreased risk of diabetes [II vs. DD and ID, OR= 0.09 (95% CI, 0.03-0.23; p < 0.001)]. II genotype may have a protective effect against diabetes. On the other hand, the mean serum ACE activity were significantly lower in women compared to men (132.71±43.83 *vs* 108.45±38.02; p < 0.05).

Conclusion: The current investigation could provide new evidence regarding the role of the ACE gene in the pathogenesis of DM, which may have significant clinical implications.

THREE YEAR INCIDENCE OF TYPE 2 DIABETES MELLITUS AMONG CARDIOVASCULAR DISEASE

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Objective: We evaluated the 3-year incidence of diabetes in an adult population from Greece.

Research design and methods: 1521 individuals (>18 years), free of cardiovascular disease, participated in the baseline examination (during 2001-2002). Of this sample, 506 men and 517 women were found alive at the time of follow-up, while 32 (2.1%) men and 22 (1.4%) women died during this period. The rest were lost to follow-up. Incidence of type 2 diabetes mellitus was evaluated in 903 participants who did not have diabetes at baseline.

Results: The age-adjusted 5-year incidence of diabetes was 5.5% (men, 5.8%; women, 5.2%). A linear trend was observed between diabetes incidence and age (5.6% increases in incidence per 1-year difference in age, p< 0.001). Multiple logistic regression analysis revealed that age (OR per 1 yr=1.04, 95% CI 1.02-1.06), waist (OR per 1 cm=1.02, 95% CI 1.01-1.003), physical activity (OR=0.62, 95% CI 0.35-1.02) and family history of diabetes (OR=2.65, 95% CI 1.58-4.53), as well as fasting glucose levels (OR per 1 mg/dl=1.05, 95% CI 1.03-1.07), were the most significant baseline predictors for diabetes, after adjusting for various potential confounders. Additionally, presence of metabolic syndrome at baseline evaluation 2.95-fold the risk of diabetes (95% CI 1.89-4.61), and showed better classification ability than the model that contained the components of the syndrome (ie, correct classification rate: 94.5% vs. 92.3%).

Conclusion: Our findings show that a 5.5% incidence rate of diabetes within a 5-year period, which suggests that the prevalence of this disorder in Greece is rising.

ASSOCIATIONS OF LIPOPROTEIN PARAMETERS AND CHRONIC INFLAMMATION MARKERS WITH THE STAGE OF INSULIN RESISTANCE IN TYPE 2 DIABETES MELLITUS PATIENTS

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The aim of the study was to reveal associations of inflammatory markers, lipoprotein parameters and remodeling proteins with the stage of insulin resistance.

In the 162 T2DM patients clinical and lifestyle characteristics and also cardiovascular complications were registered; BMI and WHR were calculated. Cardiovascular complications were proven angiographically. Fasting serum glucose, insulin, inflammatory markers, lipoprotein parameters and remodeling proteins were measured, HOMA -IR was calculated.

All measured variables were compared in the HOMA-IR tertiles. In the third tertile of HOMA-IR BMI and WHR were higher and myocardial infarction was diagnosed earlier than in patients of the first tertile. hsCRP and SAA were marginally higher in the third tertile compared with the first one. A significant influence of HOMA-IR on hsCRP value was confirmed by one-way analysis of variance (p=0,009). The differences between tertiles were remarkable in the lipoprotein parameters, TG/HDLC and ApoB/ApoA-I ratio ($p < 0.05$). In multiple linear regression analysis among T2DM patients HOMA-IR correlated independently and positively with Apo E polymorphism, TG/HDLC ratio, WHR, occurence of cardiovascular complications and gender. Association of HOMA-IR with inflammatory markers was not confirmed in the multifactorial analysis.

We did not find any difference in PLTP and CETP activity in HOMA-IR tertile groups.

The results suggest a strong association of carbohydrate metabolism indices with typical dyslipidemia and abdominal obesity in T2DM patients; the relationship with inflammatory markers was not so strongly expressed.

INFLUENCE OF TRANSFORMING GROWTH FACTOR-BETA 1 ON CARDIAC REMODELING IN 2ND TYPE DIABETES MELLITUS PATIENTS

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Aim: To investigate the serum concentration of transforming growth factor beta 1 (TGF-beta 1) and his role in development of left ventricular hypertrophy (LVH) of patients with arterial hypertension in combination with 2nd type diabetes mellitus (DM) and also of patients without DM.

Methods: The study population consisted of 50 patients with arterial hypertension [30 patients with DM (first group) and 20 patients without DM (second group)] and 30 healthy subjects.

Results: We determined that serum concentration of TGF-beta1 (ELISA method) was compounded 35.17±2.76 ng/ml in first group, 32.13±0.95 ng/ml in second group that are differed significantly from control group - (19.9±6,85 ng/ml; $p < 0.001$ for all cases). Analysis of the serum concentration of TGF-beta 1 against geometric type of left ventricle allowed to determine that from patients with arterial hypertension important differences the level of TGF-beta 1 were revealed from patient with CLVH and ELVH as compared to NGLV and CLVR as well as control group. Even dynamics of studied characteristic were preserved in principal group but changes of the level of TGF-beta 1 in case of CLVH and ELVH were more manifested and were differed statistically significantly between groups in case of development of CLVH.

Conclusions: Increase of the blood level of TGF-beta1 is observed from patients with arterial hypertension and this change more expressed in combination with 2nd type DM. TGF-beta1 level may be considered as indicating about his influence on the mechanisms of forming adverse types of LV geometry in DM patient population.

HEALTH TECHNOLOGIES FOR MONITORING DIABETES AND REDUCING CARDIOVASCULAR COMPLICATIONS: A SYSTEMATIC REVIEW

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Objective: Diabetes self-monitoring technologies help patients manage their disease and may assist in the prevention of developing cardiovascular complications (CVCs). This review aimed to determine the strength of evidence for the effectiveness of interventions with self-monitoring technologies for individuals with type 1 (T1D) or type 2 diabetes (T2D) at risk for developing CVCs. A secondary objective was to explore issues of feasibility and compliance according to patients and providers.

Methods: Study criteria included: adults ≥18 and youth (7-14) years with T1D or T2D, intervention with a self-monitoring device, assessment of clinical outcomes with the device, and ≥ 10 participants. Relevant published literature was searched from 1985 to 2008. Randomized controlled trials and observational studies were included. Data was extracted from clinical outcomes, feasibility, and compliance methods and results. Selected studies were independently evaluated with a validated instrument.

Results: Thirty trials were selected. Predominant types of device interventions included self-monitoring of blood glucose, pedometers, and wireless technologies. Feasibility and compliance were measured in the majority of studies. Self-monitoring of blood glucose devices remain the cornerstone of diabetes self-care. Pedometers are effective lifestyle modification tools and cell phones (wireless technologies) may offer increased accessibility for diabetes self-management. The results of this review indicate a need for additional controlled trial research on existing and novel technologies for diabetes self-monitoring, on health outcomes associated with diabetes and cardiovascular complications, and device feasibility and compliance.

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ACTIVATION OF AMPK BY NATURAL PRODUCTS

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For centuries, cultures throughout the world have made use of plant-based remedies to treat diabetes, and from these, hundreds of compounds with antihyperglycemic activity have since been isolated. There is emerging evidence that the AMP-activated protein kinase (AMPK) is often the mediator of the activity of these products and that AMPK is activated secondarily to the metabolic stress induced by a transient disruption of mitochondrial oxidative phosphorylation (OxPhos). Our lab has determined that this mechanism, which is similar to that of Metformin, is responsible for the effects of important Mediterranean, African, and native North American antidiabetic plant products. Recently, we have identified several naturally-occurring compounds of the flavonoid family that either inhibit or uncouple OxPhos to stimulate AMPK, resulting in increased skeletal muscle glucose uptake and in inhibition of hepatic glucose-6-phosphatase activity, in-vitro. Most of these compounds induce only small and transient changes in ATP concentration or in reliance on anaerobic metabolism, suggesting that they are easily metabolized and may be attractive alternatives to alkaloid-based or nitro-substituted compounds. Plant-sourced compounds that can uncouple OxPhos appear to be surprisingly common; this activity can be well-predicted from structure-derived physicochemical parameters, thereby facilitating the design of derivatives and the identification of natural products that should be consumed with vigilance.

These findings not only raise awareness of the efficacy of traditional antidiabetic remedies but suggest that naturally-occurring compounds have the potential to yield alternatives to the biguanides as well as safe uncoupling drugs for the treatment of obesity. Supported by CIHR Canada.

THE PREVALENCE OF HAEMOSTATIC AND FIBRINOLYTIC FACTORS IN MEN WITH ERECTILE DYSFUNCTION. A CONTROLLED STUDY

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Introduction & objectives: There is some evidence that erectile dysfunction (ED) is an early predictor of cardiovascular diseases. Recent studies highlight the relationship between ED and metabolic syndrome (MS). We assessed the prevalence of MS looking in particular into haemostatic and fibrinolytic markers in a group of men with ED versus a control group of men with normal potency.

Material & methods: 110 consecutive men with ED (ED group) and an age-matched control group of 118 potent men (potent group) were recruited. The revised National Cholesterol Education Programme (NCEP) and International Diabetic Federation (IDF) criteria were used to identify MS. ED was assessed with International Index of Erectile Function (IIEF). The following markers were measured; fibrinogen, D-Dimer, PAI-1, hs-CRP and insulin.

Results: Mean age for the ED group was 58.4yrs and 57.8yrs for the potent group. NCEP definition reveled MS in 19% of men in the ED group and 11% in the potent group. The IDF identified MS in 49% and 33% in the ED group and the potent group respectively. The plasma circulating level of D-Dimer was significantly raised in the ED group (mean 103ng/ml) vs (76ng/ml) in the potent group ($p< 0.005$). Insulin was marginally raised in the ED group. There was no difference between groups in fibrinogen, hs-CRP and PAI-1.

Conclusions: It has been suggested that men with ED are at increased cardiovascular risk. However, our study didn´t reveal strong evidence of increased prevalence of MS in ED group in comparison to potent controls.

ASSOCIATION BETWEEN SERUM URIC ACID AND THE METABOLIC SYNDROME IN TYPE 2 DIABETIC PATIENTS

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Aims: Metabolic syndrome (MetS) is defined as a cluster of interrelated metabolic disorders. Hyperuricemia is associated with hypertension, insulin resistance, obesity and hyperlipidemia, but the association with MetS is still under debate. Therefore we examined the associations of serum uric acid (UA) with MetS components and the sex-differences of these associations in T2DM patients with MetS (ATP III criteria).

Methods: The study is cross-sectional comprising 310 in-patients with T2DM and MetS (194 w/116 m). Different components of MetS were compared by quartiles of UA, and also mean UA levels among 3 groups defined on number of MetS components. Student's t-test, Pearson correlation were used.

Results: 26.77% (24.74% w; 30.17% m) of patients presented hyperuricemia. Analyzing data for the number of MetS components fulfilled, in those with 5 criteria hyperuricemia was more frequent 37.23% vs. 20.59% in those with 3 criteria, but the mean UA value was significantly higher only in women (5.74 vs. 4.23; $p< 0.0001$). UA levels correlated best with waist circumference and body weight ($r=0.3$). Analyzing data for UA quartiles, significant statistical differences were recorded between the first and the last quartile for: waist circumference, body weight ($p< 0.0001$), BMI ($p=0.0003$), HbA1c ($p=0.0014$), total cholesterol ($p=0.006$), number of ATP III criteria that were fulfilled ($p=0.03$), LDL-cholesterol ($p=0.02$), SBP ($p=0.01$) and diabetes duration ($p=0.018$).

Conclusions: Hyperuricemia is frequent in patients with T2DM and MetS. Women fulfilling all MetS criteria were most likely to have hyperuricemia. Hyperuricemia is strongly correlated with metabolic and hemodynamic disorders found in T2DM and MetS.

MOMORDICA CHARANTIA, AN ANTIDIABETIC PLANT, INHIBITS APOPTOSIS OF INSULINOMA CELLS VIA INHIBITION OF MAPK PATHWAY

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Although traditional plants have been reported to have antidiabetic effects, the molecular targets of such plants have not been revealed, and a careful analysis of their mode of action in diabetic models has not been undertaken. In the present study, we have focused on the unripe fruit of *Momordica charantia* (MC) because it has been shown to have antidiabetic properties, although its mechanism of action is not fully known. Apoptosis, programmed cell death, is the main form of beta-cell death in both type 1 and type 2 diabetes. The inhibitory effect of the extract from the unripe fruit of MC on cytokine-induced apoptosis was investigated in insulinoma MIN6N8 cells. MC extract inhibited cytokine-mediated apoptosis. The effect was mediated through the suppression of phosphorylations of P38 mitogen-activated protein kinase (MAPK), P44/42 MAPK, stress-activated protein kinase (SAPK), and c-Jun N-terminal kinase (JNK). This study suggested that MC extract may have therapeutic potential in modulating beta-cell survival in diabetes. Acknowledgments for Korea Research Foundation (the grant No. F00017).

ATTITUDE TOWARDS GLYCAEMIC CONTROL STRATEGIES AMONG ADULT PATIENTS WITH TYPE 2 DIABETES MELLITUS IN SUB-SAHARAN AFRICA: WHERE IS THE GAP?

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Objectives: To assess attitude towards glycaemic control strategies among adult

type 2 Diabetes patients attending diabetes clinics in Dar es Salaam, Tanzania.

Methods: A cross-sectional survey that consisted of 400 randomly sampled diabetics was done between July - Sept 2007. Semi-structured questionnaires were the main tools used. Variables included 10 likert items that were used to estimate attitudes on exercise, lifestyle modifications and oral hypoglycaemics. Data analysis was done using Epi-info version 3.3.2. Statistical significance tests included the usage of P-values < 0.05 to rule out the role of chance and X^2-test to check for the association between variables. Chronbach´s alpha coefficient was used for internal consistency reliability test.

Results: Among respondents surveyed, 136 (34%) were males. Mean chronbach´s alpha score (r) was 0.725. Almost all (92.5%) respondents declared oral hypoglycaemics to be very expensive (r=0.86%). About a quarter (22%) revealed skipping meals to be an option in maintaining their blood sugar levels in a euglycaemic state (r = 0.68). Significant amount (36.5%) perceived regular exercise to have a limited/no role once a

desirable body weight has been achieved (r= 0.71). About a third (33.75%) declared weight gain to be acceptable once a euglycaemic state has been achieved (r= 0.66). The usage of traditional medicaments was inversely related to the level of education of the respondent (P=0.0001).

Conclusion: Costs of oral hypoglycaemics were perceived to be very high in this study population. The usage of traditional medicaments may have an impact in the current morbidity and early mortality among diabetics surveyed.

THE PREVALENCE OF METABOLIC SYNDROME AT NEWLY DIAGNOSED PATIENTS WITH T2DM AND T1DM, COHORT 2008

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Metabolic syndrome is defined of interrelated metabolic disorders more frequently at patients with insulinoresistence or hyperinsulinemia and represents an increased risk for cardiovascular disease or type 2 diabetes mellitus (T2DM) - if not already present.

Aims: To describe prevalence and particular aspects of MS at T2DM patients, using International Diabetes Federation definition criteria.

Material and methods: We analyzed 2314 patients with T2DM (1115 w /1199 m), aged 40 to 79 years, having the characteristics shown in the table.

Parameters	T1DM Mean (min - max)	T2DM Mean (min - max)	P for difference between T1 and T2
BMI (kg/m2)	25 (14.88 - 38.87)	30.5 (14.3 - 68.3)	P = 0.0001
Fasting blood glucose (mg/dl)	395 (103 - 1200)	212.84 (55 - 1240)	P = 0.0001
HbA1c (%)	11.67 (5.80 - 17.40)	8.37 (4.5 - 17,9)	P = 0.0001
Cholesterol (mg/dl)	201.85 (106 - 322)	224.71 (26 - 705)	P = 0.0001
HDL-c (mg/dl)	44.12 (17 - 70)	45.81 (18 - 172)	NS
Triglycerides	290.36 (66 - 1695)	235.01 (30 - 3000)	NS

Results: Metabolic syndrome prevalence was higher for men. The most frequent component of MS was decreased HDLc, followed by high blood pressure, low triglycerides with the same pattern for both sexes. Most T2DM patients fulfilled four criteria for the diagnosis of MS.

Conclusions: Prevalence of MS in T2DM patients is very high (our data are comparable with those described in literature). Due to this high prevalence is imperative to actively search for all MS components at newly discovered patients with T2DM and to aggressively treat all cardiovascular risk factors in this patients.

CHRONIC COMPLICATIONS AT NEWLY DIAGNOSED T1DM AND T2DM, COHORT 2008

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Background and aims: Diabetes mellitus usually is asymptomatic at diagnosed, but sometimes micro- and macrovascular complications might be present. The aim of this study was to evaluate the prevalence of chronic diabetes complications in newly diagnosed diabetic patients registered in the outpatient Department of Institute N. Paulescu in 2008.

Material and methods: A cohort of 2314 diabetic patients was analyzed between January - October, 2008 : 1199 (51.81 %) man, 1115 (48.19%) woman; average age :57.8 years; BMI average:30.49 Kg/m2. The two groups 56 (2.4%) T1DM, 34 (60.71%) man and 22 (39.29%) woman, 2134 (%) T2DM 1199 (51.81%) man and 1115 (48.19%) woman were studied depending on present/absent of diabetic complications. The statistic program was SPSS 15.0; we used Chi-Square tests with statistical significant $p \leq 0.05$, Spearman's .

	Total patients	Retinopathy	Neuropathy	Arteropathy	Ischaemic heart disease	Myocardial infarction	Stroke
T1DM	56 (2,4%)	0	0	0	0	0	0
T2DM	2314 (92.7 %)	4 (0,2%)	1	10 (0,4%)	136 (5,9%)	47 (2%)	64 (2.8 %)
Total	2370 (100%)	4 (0,2%)	1	10 (0,4%)	136 (5,9%)	47 (2%)	64 (2.8 %)

Conclusions: At diagnosis T1DM patients and T2DM patients are mostly free of complications, but if they have it, the most common ones are macrovascular complications in T2DM patients Most frequent diabetic macrovascular complications affects only one vascular territory, this is the cerebral territory or peripheral territories, affected 4 times more frequent than coronaries territory. Newly diagnosed chronic complications are higher in T2DM than in T1DM patients due to a longer pre - diagnosis period.

ARE ELECTRONIC MEDICAL RECORDS AN EFFECTIVE TOOL FOR MONITORING THE QUALITY OF DIABETES CARE AND PREVENTION IN PRACTICE-BASED RESEARCH?

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Background: Electronic medical records (EMRs) can provide clinic-level information on strengths and deficits of diabetes care and prevention. Yet research shows that improvements in quality of care do not necessarily follow the implementation of EMRs.

We evaluated the usefulness of EMRs for practice-based research on the quality of diabetes care and prevention in an underserviced island population in Canada where diabetes rates are the highest in the province.

Methods: We extracted anonymized health information in four medical practices involving 14 physicians and four different EMR software. We audited 998 patient records and the services they received over a 15 month period.

Results: EMRs were successfully used to assess the quality of diabetes care at the population level. Results were compared to practice guidelines and national benchmarks. Monitoring prediabetes however was not possible at

this point. A shared definition of prediabetes is required in order to effectively monitor interventions such as CV risk factor modification with EMRs.

Conclusion: The usefulness of EMR software to monitor the quality of diabetes care and prevention varied. We found that EMRs built on a problem-orientated software architecture were most effective in rapidly examining patient records. However, all records had to be exported to additional software in order to perform the complete set of analyses. There is tremendous potential for physicians to monitor prediabetes and diabetes care within their patient population with the help of EMRs. Software vendors need to develop EMRs that go beyond warehousing of health information to enable user-friendly, clinically-relevant analysis of care.

CARDIOVASCULAR AUTONOMIC DYSFUNCTION AND RECENTLY DIAGNOSED TYPE 2 DIABETES

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Aim/ hypothesis: Cardiovascular autonomic dysfunction (CAD) is a serious complication and carries a high risk of mortality. We studied the prevalence of CAN in asymptomatic recently diagnosed type 2 diabetes mellitus (DM), without other chronic complications.

Patients and methods: Twelve patients and ten gender- and age-matched healthy control subjects were studied at rest and during active ortostatism. Autonomic function was assessed using five standard tests, and subjects with total score of ≥ 2 were considered to have autonomic neuropathy. Power spectral analysis of heart rate applied to 24-hour ECG recordings, and R-R interval variability was calculated through, time domain SDNN (SD normal-to-normal RR intervals), rMSSD (mean square difference of successive NN intervals) and frequency domain analysis, very-low-frequency power (VLF), low-frequency power (LF), high-frequency power (HF) and low-frequency/High-frequency (LF/HF) power.

Results: Cardiovascular standard tests have shown the presence of parasympathetic dysfunction, all three tests were positive in 8 of 12 patients (75%), without significant difference for sympathetic response (hand-grip test and head-up tilt test). Power spectral analysis have shown that spontaneous HRV was almost significantly reduced in patients in comparing to controls, for SDNN (125.00±21.07 vs. 130.55±31.00, p= 0.05), and not significantly reduced for HF power (32.9± 22.00 vs. 40.70 ±16.60, p= NS).

Conclusion: The prevalence of autonomic dysfunction, with predominance of reduced parasympathetic activity, is high in patients with short duration of Type 2 DM. This study suggests that early diagnosis of CAN can lead to the deployement of strategy to improve outcome in Type 2 DM.

EFFECT OF SIX-WEEKS METFORMIN TREATMENT ON SERUM LEPTIN CONCENTRATION AND SELECTED METABOLIC PARAMETERS IN IMPAIRED GLUCOSE TOLERANCE PERSONS

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Prediabetic state is a risk factor for type 2 diabetes and cardiovascular disease. Metformin can reduce body weight in nondiabetic, obese patients.

Aim: The aim of the study was to evaluate effect of six-weeks metformin treatment on serum leptin concentration and selected metabolic parameters in impaired glucose tolerance (IGT), obese persons.

Methods: 47 patients (30 women and 17 men; mean age 51,0) with central obesity (mean BMI 38,07± 7,5 kg/m2) were qualified for OGTT. During OGTT fasting (G 0') and 2h-glycemia (G 120') were estimated (bioMérieux, UV-160A Shimadzu). Fasting T-CH, HDL-CH, LDL-CH and TAG concentrations in serum (bioMérieux, UV-160A Shimadzu) were measured. Leptin fasting serum concentration was determined in duplicate by ELISA kit (R&D Systems and Sunrise Tecan reader). OGTT results allowed to express normal glucose tolerance group (n=16; mean BMI 34,5± 4,8 kg/m2) - treated only by lifestyle modification and IGT group (n=31; mean BMI 39,0 ± 8,2 kg/m2) treated by diet and 6-weeks regimen of metformin (1000 mg per day).

Results:

1. After 6-weeks in both groups significant decreased of BMI, fat content, waist circumference were observed, but there were no differences between metformin and diet groups.
2. No significant differences in leptin concentration before and after lifestyle/metformin intervention in both groups were observed.
3. In IGT group the positive correlations between G 120' and leptin were counted.
4. Metformin was well tolerated and decreased significant fasting glucose level.

Conclusion: Six-month treatment of metformin reduces weight but not leptin concentration in prediabetic state.

THE EFFECT OF WEIGHT REDUCTION AFTER DIET AND PHYSICAL ACTIVITY INTERVENTION BY OBESE MEN WITH DIABETES MELLITUS OF SECOND TYPE

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Introduction: Diabetes mellitus is growing problem in many countries all over the world and its role in cardiovascular disease has recently drawn increased attention.The associated risks are dependent of fitness, family history of disease and sedentary lifestyle.

Aim: The aim of our study was examined the role of the level of physical activity and lifestyle education in concentrations and changes in the glucose ,lipids and insulin concentrations in the obese diabetes men.

Methods: Patients - 12 men (mean age, 48 ±15 yrs; body weight, 146 ± 33,5 kg; BMI range 41- 51,5 kg/m2) with abdominal obesity were examinated . 6 patients with insulin treatment with oral hypoglycemic agents and 6 patients only with oral hypoglycemic agents (biquanides, sulfonylureas, thiazolidindiones) were included.

Results: After intervention were decreased BMI ,glycemia,total cholesterol, LDL cholesterol. After weight reduction 6 patients are without insulin treatment and in rest 6 patients is reduced oral hypoglycemic agents.

Conclusion: This study was proved changes in glucose and lipid metabolism after weight reduction after diet and physical activity intervention by obese diabetic patiens.

HBA_{1c} AS A MARKER TO REDUCE LOWER LIMB AMPUTATION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background and objective: One of the most common complications of diabetes in the lower extremity is the diabetic foot ulcer. The objective of this case- control study was exploiting HbA_{1c} as a predictive monitoring test of choice to reduce complications of diabetes mainly septic foot in type 2 diabetic patients.

Subjects and method: Forty type 2 diabetes cases with septic foot (group 1 cases), 40 type 2 diabetes cases without septic foot (group 2 cases), and 40 healthy controls participated in this study. Their ages ranged between 50 to 70 years. Serum HbA_{1c} levels were estimated by affinity chromatography method.

Results: The level of HbA_{1c} was 9.947±1.40%, 7.908±0.45% and 6.462±0.07% in group 1, group 2, and the healthy control respectively. There was significant increase in percentage level of HbA_{1c} in group 1 cases compared to group 2 cases and to healthy control ($p = 0.002$, 0.001 respectively). We found very low correlation between fasting blood sugar and HbA_{1c} in group 1 cases ($r = + 0.331$; $p=0.042$).

Conclusion: This study indicates that the progression to the complication of foot ulcer in type 2 diabetic patients was correlated to the level of HbA_{1c}. These data may suggest a beneficial effect of considering measurement of HbA_{1c} as a routine test especially for elderly diabetic patients with diabetes for long period. This may help to maintain blood glucose levels in the normal or near normal range and to provide an opportunity for patients to live out their normal life expectancies with minimal complications.

DIABETIC SEPTIC FOOT IN TEACHING HOSPITAL KHARTOUM STATES- SUDAN

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Patients with diabetes are more predisposed to infection [1-3]. Elderly patients were most common develop skin ulceration. Diabetes mellitus is growing health problem in Sudanese population these individual are predisposed to foot infection.

Aim: The aim of this study is to isolation and identification of aerobic and anaerobic organisms in patients with diabetic septic foot and to select appropriate antibiotic. This study was descriptive study.

Method and study design: 158 patients, invasive diagnostic technique should be consider for deeply sampling with deeply ulcers in foot specimen was collected by rotating sterile swab deeply, transportation to lab for culture anaerobically and selective. This study was carried out in -Sudan. The study was perspective all regards to incidences of age, sex, History, duration, duration of sepsis, type of sepsis [neuropathic, clinical presentation and.

Result: Poly microbial was most common mixture of aerobic gram positive microorganisms was common foot. MRSA take high prevalence [23.9%] in this study which was sensitive to clindamycine, Other isolates take part, By using statistic analysis RV/O.

Discussion: During this study Methicillin resistant s.aureus was associated with 23.9%out of all isolates in patients with diabetic septic foot this incidence was high than that reported in Denamark by Schberget al 1991in surgical wound sepsis.

Conclusion: From our study we beloved that surgical patients should be separated from each others and doctors wash their hand sufficiently Moisten Floors must be dried to Reduce infection, because moist area favorable condition for Growing.

PREVALENCE OF KIDNEY HYPERFILTRATION AT CARDIOLOGICAL PATIENTS IN MOSCOW

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The level of kidney dysfunction determines cardiological patients life prognosis and quantity of fatal outcomes. Glomerular hyperfiltration (GH) takes central place in investigations of B. Brenner, H. Hostetter et al. And is included to classification of diabetic nephropathy by C.E. Mogensen. GH is more early marker of kidney damage than microalbuminuria. Today there is no data on prevalence of GH in cardiological patients. The aim of our study was to determine the prevalence of GH in cardiological patients and its correlation with basic demographic, clinical and laboratory data.

We analyzed 1160 case histories of outpatients and 1070 of in-patients for age, sex, diagnosis, anamnesis of stoke and myocardial infarction, heart rate, blood pressure, obesity, patients medical treatment, smoking habits, results of ultrasonic cardiography, general and biochemical blood and urine tests, etc. Then we calculated Glomerular Filtration Rate (GFR) with 4-variable equation from the Modification of Diet in Renal Disease Study.

Mean GFR was 73,66± 23,22 ml**/min/1,73 m^2 at outpatients and** 65,79 ±22,45 - at in-patients (the difference was significant (SD), $p< 0,008$). GH was found in 152 outpatients (13,1%) and 50 in-patients (4,67%). Thus prevalence of GH is higher in outpatients ($\rho< 0,001$). Among outpatients we didn't observe GFR less than 30 ml/min. In the group of GH there were more men ($\rho< 0, 01$), patients were younger ($\rho< 0,001$), hemoglobin level was higher ($\rho< 0,001$). Thus GH is typical for outpatients, and it is "a must" to detect the earliest stages of renal impairment and start treatment in time.

PREVALENCE OF DIABETES AND ITS RISK FACTORS AMONG GOVT. OFFICIALS

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Introduction: Globally diabetes is on rise and highest among Indians. Prevalence of diabetes in India is 10 - 15%.

Objective: The study was done to know the prevalence of diabetes and its risk factors in urban government officials.

Study desgin: Cross sectional study.

Setting: Sachivalaya of Gandhinagar city, Gujarat, India.

SAMPLE SIZE 590

Method: A pre-tested semi structured proforma administered to the participants. Investigation was done for diagnosing diabetes using FBS & PP2BS.

Results: Overall prevalence rate of diabetes among study population was 13.4% with higher rate in males (13.7%) than in females (11.1 %). Prevalence of diabetes was highest (19%) in class I cadre and lowest (8.2%) in lower most cadres. The association between WHR and diabetes prevalence among male employees was found statically significant in cadre. I, cadre III, cadre IV and all cadre combined. Prevalence rate of diabetes in low income group was found to be 10.60% , in middle-income group to be 14.69% and in high-income group to be 15.04% . The family history was positive in 49.36% among diabetic compare to 17.61% among non-diabetic

and the difference was statistically significant. The prevalence of hypertension was 48.1% in diabetic compare to 30.7% in non-diabetic and the association between hypertension and diabetes has been found statically highly significant.

Conclusion: Overall prevalence of diabetes is high overall particularly in males. High income group, positive family history, hypertension, BMI and sedentary life style were contributing factor for it.

Keywords: Yoga.

THERAPEUTIC AND PREVENTIVE EFFECTS OF AMILORIDE ON EDEMA INDUCED BY TIAZOLIDINEDIONES

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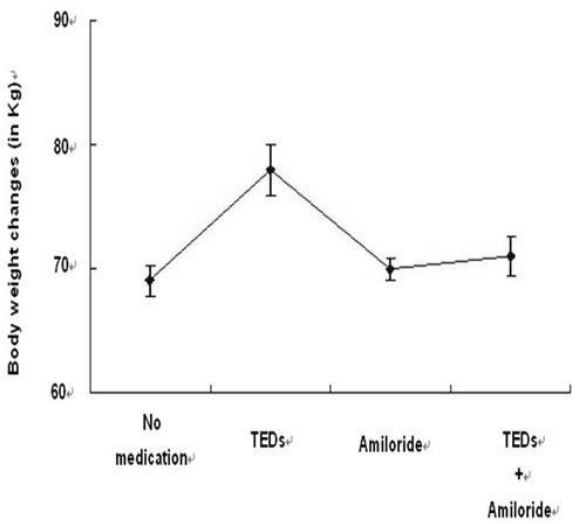
Insulin resistance as a cause of metabolic syndrome, for which, the antihyperglycemic effect of thiazolidinediones(TZDs) is well documented. In clinical experience 15% of patients received TZDs developed edema.The objective of this study is to evaluate the therapeutic and preventive effects of amiloride on edema induced by TZDs. Eleven patients with metabolic syndrome developed edema while receiving either piglitazone or rosiglitazone participated in this study. They were asked to record the body weight while getting up, and were watched in the OPD.

Results: Edema in the limbs in 8 patients, in the eyelids in 2 and in the hands only in1.The changes in body weights are shown in figure 1. The edema completely disappeared while receiving amiloride 5mg QD after discontinuing TZDs. When TZDs need to restart plus Amiloride 2.5m no edema developed. It has shown that the TZDs enhance sodium absorption in connecting duct due to increased PPARr receptors, which is specifically blocked by amiloride.

Conclusion: Amiloride is effective in treating and prevent edema induced by TZDs.



[Body weight changes]

EVALUATING THE EFFECT OF SUGAR BEET FIBER ON SERUM FASTING BLOOD SUGAR AND LIPID PROFILE OF TYPE II DIABETES PATIENTS

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Aims: Dietary soluble fibers have beneficial effects in reducing serum glucose and lipid levels. Sugar beet is a dietary soluble fiber. Contradictory results have been reported about its consumption on serum glucose and lipid levels. The present study was performed to assess its effect on type II diabetes patients.

Methods: A cross-over, single-blind clinical trial was done on 30 type II diabetics with FBS>7.8 mmol/L and an HbA_1C of 5-9% while being treated with Glibenclamide tablets twice daily.

Sugar beet fibers were refined, dried, ground and packed into 10-gram sachets. The individuals were randomly divided into two groups; one receiving 20 grams of sugar beet fiber, blended with yoghurt at lunch and dinner for 4 weeks, while the other group receiving 20-grams starch powder instead. The participants had another 4-week round of trial for cross-over study after a 2-week washout period.

Blood samples were taken for FBS and serum lipids at the beginning of study and five more at 2-week intervals. Paired t-tests and t-tests were used for statistical analysis. A p-value < 0.05 was considered significant.

Results: Consumption of sugar beet fibers resulted in the reduction of 33% (P< 0.001), 13% (P< 0.01), 11% (P< 0.05), 30% (P< 0.02) and 15% (P< 0.05) in serum FBS, T-Cholesterol, LDL-C, Triglyceride and T-Cholesterol/HDL ratio respectively but it did not have any statistically significant effect on HDL-C levels.

Conclusions: Consumption of Sugar beet fiber, as a glucose and lipid lowering agent, is recommended for type II diabetes patients.

THE RELATIONSHIP BETWEEN BODY MASS INDEX- LEFT VENTRICLE MASS INDEX-MYOCARDIAL PERFUSION INDEX IN TYPE 2 DIABETES

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Introduction: Diabetes mellitus(DM) has been associated with abnormalities of cardiac function and left ventricular hypertrophy. Diabetic individuals, particularly women,had higher heart rates, greater left ventricular wall thicknesses,greater cardiac mass than unaffected subjects. We aimed to investigate association between waist circumference-body mass index(BMI) and left ventricle mass (LVM)-left ventricle mass index (LVMI),left ventricle myocardial perfusion index (MPI) in patients with type 2 DM and without known cardiac disease.

Methods: The patients with type 2 DM were examined with tissue doppler imaging echocardiography to detect MPI. LVM was calculated by the Penn Convention formula.

LVMI was calculated.Waist circumference was measured, BMI was calculated. The exclusion criterias; known cardiac diseases, pulmonary diseases, endocrine diseases except DM, anemia, angina pectoris,dyspnea,peripheral edema, serum creatinine level> 1,5 mg/dl,

ejection fraction (EF)< 50%. The GraphPad Prisma V.3 package program was used for statistical analyses.

Results: A total of 42 patients, men(40.5%) and women (59.5%) aged 37-57 years were included. In all patients; There were significant correlations between waist circumference and LVM; between BMI and LVM; between BMI and LVMI. Looking at the results according to sex; there were significant relations between BMI and LVM(p:0,r:0.685), BMI and LVMI(p:0.007,r:0.528) in women. This parameters were not associated in men.There was significant correlation between BMI and MPI (p:0.026,r:-0.537) in only men.

Conclusion: BMI associated with increasing LVM and LVMI, is an important risk factor in expecially women for diabetic heart disease. The MPI, a new doppler index of global cardiac function, has limited importance in type 2 diabetes without clinical cardiac disease and is more important in men.

COMPARISON THE EFFECTIVENESS OF COGNITIVE-BEHAVIORAL STRESS MANAGEMENT TRAINING AND RELAXATION PROGRAM ON GLYCEMIC CONTROL TYPE 2 DIABETES MELLITUS

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Aims: To determine and comparison the effectiveness of cognitive-behavioral stress management training program and relaxation program on glycemic control and altering some indications of mental health (ie. Depression, anxiety and stress) in patients with type 2 diabetes mellitus.

Method: In an experimental design, 60 patients with type 2 diabetes mellitus were selected. Participants were randomized to cognitive-behavioral group (n=20), relaxation training group (n=20) and control group (n=20). . To evaluate the effects of intervention, HbAC test were administered before and 3 mounth after interventions. And Depression Anxiety, Stress Scale (DASS) were administered before, after, and 3 mounth after interventions. Data were analyzed using variance analysis for repeated measures and covariance analysis.

Results: The differences between experimental groups and control in post test were significant about HbAC. the effects of interventions in reduction of depression, anxiety and stress, were significant and this effects remains in 3 mounth follow up.

Conclusion: Stress management training can improve glycemic control and some indices of mental health in patients with type 2 diabetes mellitus.

BUSCHKE´S SCLEREDEMA AND DIABETES MELLITUS: A REPORT OF THREE CASES

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Introduction: The Scleredema of Buschcke (SB) is an uncommon dermatosis of unknown etiology. It has been associated with long-standing and poorly controlled diabetes mellitus, monoclonal gammapathies and some infections as streptococcicals. We present two cases of our unit on its first year program.

Materials and methods: We studied three patients with poorly controlled diabetes mellitus and clinical diagnosis of scleredema confirmed with histopathological study. We reviewed associated diseases, clinical and histopathological characteristics, evolution and response to treatment.

Results: See attached board.

Discussion: Scleredema of Buschke (SB) appear in a 3% of diabetics type II, between 40 to 60 years, with obesity. It's characterized by indurated skin with progressive hardening, predominantly the upper trunk. Sometimes quickly involves face, neck and upper abdomen, but hands and toes are free. The most of cases are associated with diabetes mellitus. The diagnosis are clinical though can make a biopsia of skin. Histopathological characteristics are mucin deposits among collagen fibers of unknown etiology with a thickening of the dermis and growes producing hardening of the skin. In the differencial diagnosis have to be considered some diseases like sclerodermia, dermatomyositis, rheumatic fever and other disorders with general hard edema. It hasn't specific treatment and a torpid evolution with little response to several treatments. Some authors speak about take measures with the HbA1c maybe improve evolution.

GOP THERAPY, A MIXTURE OF JAPANESE GINSENG, GANODERMA LUCIDUM AND CORIOLUS VERSICOLOR, LOWERS BLOOD GLUCOSE, C-PEPTIDE AND LDL CHOLESTEROL

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Objective: The aim of double-blind, randomized, cross-over trial was to test if GOP, a mixture of Japanese Ginseng (JG), Ganoderma Lucidum (GL) and Coriolus Versicolor (CV), or any of the three materials given as single therapy, would improve glucose metabolism or lower lipid fractions.

Methods: The study enrolled 16 NIDDM patients, who in turn were given either JG 3 g , GL 10 g and CV 5 g, as GOP therapy, or each of the three different components as single therapy. Each treatment period was 28 days. Between each of the four treatment periods, there was always a wash out period of 28 days. Blood glucose, C-peptide and cholesterol fractions were measured at the beginning and at the end of each treatment period, using normal laboratory routine.

Result: As compared to pre-treatment respectively, GOP therapy showed lowering blood glucose 10.4%($p< 0.02$), C-peptide 10%($p< 0.011$), LDL-cholesterol 18.0%($p< 0.002$). GL therapy showed lowering C-peptide 17%($p< 0.001$), Insulin 21%($p< 0.014$), and LDL-cholesterol 2.5%, while blood glucose did not change significantly. CV therapy showed lowering C-peptide 2.3%, LDL-cholesterol 4.7% while blood glucose did not change significantly. JG therapy did not significantly lower blood glucose, but reducing C-peptide 14% ($p< 0.004$) and LDL-cholesterol ($p< 0.002$).

Conclusion: The present data shows that reduction of blood glucose, LDL-cholesterol and C-peptide were observed only in GOP therapy. Thus, GOP can be utilized as a possible therapy against prediabetes and metabolic syndrome.

GENDER DIFFERENCES IN SIGNIFICANCE OF TYPE 2 DIABETES MELLITUS RISK FACTORS FOR RURAL POPULATION OF UKRAINE

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Objective: For an appropriate of preventive activity planning gender peculiarities of type 2 diabetes mellitus (DM2) risk factors (RF) structure in rural population were determined.

Methods: 16 DM2 RF in residents of Kharkiv rural region aged 45 and more years in context of asymptome DM2 screening were registered. Such as: overburdened heredity on DM (1), and another endocrine pathology (2), increase of waist circumference (3) and index of waist/hips circumference (4), surplus of body weight (5), adiposity of I (6), II (7) and III (8) extent,

arterial hypertension (9), transmitted stroke (10) and myocardial infarction (11), parodontosis (12), diabetic complaints (13), inclination to pustular infections (14), overburden obstetrical anamnesis (15) and polycystic ovaries syndrome (16) for women. Were used artificial neural networks (ANN) methods to determine the significance of each RF with accounting of their combinations in the normo- and hyperglycemia. 461 men and 601 women, which were enrolled, at the first time hyperglycemia was revealed in 7,16% and 6,49%.

Results: 88,9% men and 94,3% women with normoglycemia had some of above mentioned RF. More then 3 FR had 26,0% and 39,0% (P< 0,001). In the groups with hyperglycemia: 26,6% men and 91,3% women had more then 3 FR (P< 0,001). ANN analysis let to form decreasing rows of RF significance: for men - 1,7,8,3,4,6,12,10,9,13,5,2,11,14; for women - 1,9,15,13,6,4,11,10,14,16,3,7,2,5,12,8.

Conclusion: It has been shown the gender differences in DM2 RF significance. Overburdened DM heredity is the most significant RF both for men and women, the significance of other RF has gender specific.

DIABETES AND CHRONIC KIDNEY DISEASE IN THAI ADULTS: THE CROSS SECTIONAL HEALTH SURVEY IN A COMMUNITY-BASED POPULATION

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Objective: To determine the prevalence of chronic kidney disease (CKD) and the causes of CKD in Thai adults from National Health Examination Survey in 2004.

Material and method: Data from a nationally representative sample of 3,117 individuals aged 15 years and older was collected using questionnaires, physical examination and blood samples. GFR was estimated using the Chinese modified Modification of Diet in Renal Disease Study equation. Chronic kidney Disease stages were classified based on kidney Disease Outcome Quality Initiative (K/DOQI).

Results: The prevalence of CKD in Thai adults weighted to the 2004 Thai population by stage was 4.47% for stage 3, 0.11% and 0.11% for stage 4 and 5 respectively. Compared to non-CKD, individuals with CKD were older, having higher level of cholesterol, and blood pressure. The prevalence of cardiovascular risk factors were more common in those with CKD (stage 3-5) than those without, including hypertension (48.8% vs 15.4%), diabetes (18.6% vs 4.9%) and overweight (BMI > -25 kg/m^2, 24.0% vs 22.9% respectively). The prevalence of diabetes was significantly high in the group with CKD comparing with the non-CKD group (18.6% vs 4.9%, $P < 0.001$).

Conclusions: The prevalence of CKD (stage3, 4, 5) in Thailand was 4.69%. The prevalence of diabetes in these CKD patients was very high. Therefore, the identification of diabetes should be evaluated and monitored for the appropriate treatments in order to prevent the progression of diabetic CKD.

COPPER, ZINC AND VASCULAR COMPLICATIONS IN NON INSULIN DEPENDENT DIABETES MELLITUS

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Introduction: Hyperglycaemia is considered a primary cause of diabetic vascular complications and it is associated with impaired trace element metabolism abnormalities.

Aims: In this study we intend to evaluate copper and zinc levels in a non insulin dependent diabetes mellitus group and to investigate the relationship between the presence of complications in diabetics and these trace elements.

Subjects and methods: A total of 49 non insulin dependent diabetes mellitus (13 NIDDM with macro vascular complications, 19 NIDDM with micro vascular complications and 17 NIDDM without any complications) and 50 healthy controls were recruited in this study.

Copper and zinc were measured in plasma for all subjects by atomic absorption.

Results: Diabetic subjects have significantly reduced mean values of Zn but higher mean values of Cu when compared to control subjects ($p < 0.05$). Diabetics with macro vascular complications have the highest Cu values when compared to diabetic without complications (0.70 ± 0.18 ml/l versus 0.91 ± 0.25 mg/l; $p = 0.04$).

Conclusion: These results can confirm the role of impaired trace element status in the development of diabetes mellitus and vascular complications.

HYPERTENSION CONTROL AMONG PATIENTS WITH TYPE 2 DIABETES

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Aims: Hypertension is quite common among subjects with type 2 diabetes and contributes to their morbidity and mortality. This study aimed to determine hypertension prevalence as well as treatment and control rates among diabetic patients.

Methods: The sample consisted of 191 men and women (100/91) diagnosed with type 2 diabetes who visited the diabetes outpatient department. Semi-structured interviews were conducted with all participants. Controlled hypertension definition was based on having a systolic blood pressure (BP) of < 130 mmHg and diastolic BP of < 80 mmHg in subjects taking antihypertensive medications.

Results: The mean±SD systolic and diastolic BP was 140.4±21.1 mmHg and 82.5±11.4 mmHg, respectively. The overall prevalence of hypertension was 176/191 (92.1%). In total, 22% of the patients (42/191) were not aware of having hypertension. Of those who were aware of having hypertension (n=134, 70.1%), all were treated. Among those treated, only 20 persons (20/134, 15%) had systolic BP < 130 mmHg and diastolic BP < 80 mmHg. 86.6% (116/134) of the patients treated, were on treatment with an ACE inhibitor or AT2 antagonist.

Conclusions: Although all of the diagnosed hypertensive patients (n= 134) received antihypertensive drug therapy, in only 15% the treatment was effective (BP < 130/80 mmHg). Translating our findings into clinical practice, there is a need for aggressive treatment of hypertension, as well as regular surveillance to detect developing hypertension in diabetic patients.

PREVALENCE AND DETERMINANTS OF MACROVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES

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Aims: In addition to being a risk factor for cardiovascular disease in its own right, diabetes mellitus is associated with a higher prevalence of other risk factors such as hypertension and dyslipidaemia, which, in turn, have a more harmful effect in the presence of diabetes. The aim of this study was to assess the prevalence of macrovascular complications in a sample of patients with type 2 diabetes and to determine their predictors.

Methods: The study included 245 patients (118 males) of mean±SD age 64.8±9.9 years, and HbA1c 8.3±1.7% who visited the outpatient diabetes department. All patients were subjected to interview and assessment of their metabolic parameters.

Results: Overall, 63 of the patients (25.7%) were found to have established cardiovascular disease: 24% with coronary artery disease, 14% with peripheral vascular disease and 3% with cerebrovascular disease (in the whole sample). On binary logistic regression analysis, increasing levels of systolic blood pressure (odds ratio 1.2, p=0.005), and LDL-cholesterol (odds ratio 1.1, p=0.042) were found to be predictive of the presence of macrovascular disease, while HbA1c only tended to be associated with macrovascular complications without reaching statistical significance (p=0.07).

Conclusions: Our data revealed a significant association between elevated systolic blood pressure and LDL-cholesterol values with the presence of cardiovascular disease among diabetic patients. On the contrary, no relationship between glycaemic control and macrovascular disease was observed.

GLOMERULAR HYPERFILTRATION, METABOLIC CARDIOVASCULAR RISK AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Glomerular hyperfiltration is a marker of metabolic cardiovascular disease (CVD) risk in apparently young healthy men. Rheumatoid arthritis (RA) patients experience a 2-fold increased risk of CVD. We assessed renal function in RA subjects that were free of chronic kidney disease and diagnosed CVD.

We estimated the creatinine clearance by the Cockroft-Gault equation, categorized metabolic risk factors as recommended by the NCEP guidelines and calculated RA disease activity using the Simple Disease Activity Index (SDAI) in 510 patients with RA of which 83.5% were women. Statistical associations were adjusted for age and gender.

One or more metabolic risk factors were present in 81.8% of subjects. NCEP defined MetSyn was found in 22.2% of all subjects and associated with a 3.5-fold increase in odds ratio of hyperfiltration (95% CI=1.3-3.4). Increased waist circumference and elevated blood pressure (but not elevated plasma glucose and dyslipidemia) increased the odds ratio of hyperfiltration to 16.7 (95% CI=3.5-80.4) and 3.6 (95% CI=1.2-10.7) respectively. One log unit increase in SDAI increased the odds ratio of glomerular hyperfiltration to 3.3 (95% CI=1.0-10.7), a value that was not materially altered after further adjustment for abdominal obesity (4.7 (95% CI=1.2-18.2)). The use of antihypertensive agents, non-steroidal antiinflammatory agents, glucocorticoids and disease modifying agents were not associated with glomerular hyperfiltration.

Glomerular hyperfiltration is associated with metabolic atherosclerotic CVD risk and disease activity in patients with RA prior to diagnosed CVD. The potential role of adipokines and inflamed joint derived cytokines in glomerular hyperfiltration in RA deserves exploration.

NEW APPROACH TO TYPE 2 DIABETES MELLITUS EDUCATION AMONG LOW SOCIAL ECONOMIC STATUS TANZANIAN PATIENTS: A QUALITY IMPROVEMENT APPROACH

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Healthcare systems in Sub-Saharan Africa are not equipped to diagnose and treat diabetes because HIV/AIDS and other infectious diseases dominate the healthcare agenda. The chronic nature of diabetes makes it an unattractive investment. Even with investments, patients remains undiagnosed as they prefer treatment from traditional healers over biomedical care. Currently there is little hope of slowing down the spread of morbidity and mortality associated with untreated diabetes. We propose creation of a new environment of diabetes prevention. We expect our simple quality improvement (QI) intervention to build locally relevant knowledge on prevention, which can then be disseminated to other stake holders. The global aim is to reduce the incidence of Type 2 diabetes in Tanzania's urban population. Specifically, we propose the implementation in the primary care clinics. We reflect on how to induce effective change with the following QI equation: Generalizable scientific knowledge + Particular context → Measured performance improvement. In this intervention, scientific knowledge pertains to the evidence on diabetes prevention programs, nursing education programs and cultural disease models. We provide a rich description of the clinic's context in Tanzania including its interdependence with hospital staff, political institutions and the patient community. We select and adapt a patient education strategy from the literature that focuses on physical activity and nutritional intake. We measure change over time with operationalized metrics, which can be displayed to the stake holders. The transparency of these results ainable improvement through collaboration. This intervention is different from most QI initiatives in developing countries.

SERUM TOTAL NUCLEIC ACIDS LEVEL AT THE DIABETES MELLITUS

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Background and aim: Type 2 Diabetes mellitus (DM2) are complex disease and involve many parts of tissue damage in pathogenesis. Serum total nucleic acids (SNA) are detected in very small amount in healthy subjects and may increase at the different disorders. The level of SNA in DM2 patients and relationship with glycemic control presented the interest of this investigation.

Materials and methods: In 32 DM2 patients and 9 healthy subject SNA, fasting (FG) and 2 hour after breakfast (2HG) glycemia, HbA1c, serum nitrites and nitrates (NN) level, CRP, erythrocytes sialidase activity (ESA) were measured and HOMA were calculated as (FG x fasting insulin) : 22.5.

Results shown that SNA level were increased in 2.3 time ($P < 0.05$) than in healthy subjects, whereas FG and 2HG were increased in 1.9 2.1 time and HbA1c level was increased in 1.7 time, HOMA was increased in 2.7 time and suggested about poor glycemic control and insulinresistance in observed patients. ESA was increased in 9.1 time and indicate cell plasma membrane destabilization and CRP level was increased in 1.6 times which suggest presenting of tissue damage and inflammation. NN levels were

decreased in 2.1 time and indicated endothelium dysfunction in observed patients. Increasing the SNA level shown positive correlation with FG (r=0.4) and 2HG (r=0.48), HbA1c (r=0.3) level and had linkage with HOMA, ESA, NN.

Conclusion: SNA level are increased in 2DM and shown positive correlation with glycemia indexes and had linkage with HOMA, NN, ESA and reflected tissue damage at the 2DM.

TREATMENT BELIEFS IN DIABETIC PATIENTS

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Introduction: Beliefs in chronic illness are known to be an influential part of treatment outcomes. Diabetes is a condition that due to its treatment peculiarity has many conditioning beliefs associated.

Objective: To analyse treatment beliefs in type 1 diabetic patients.

Patients and methods: We gathered a sample of 52 type 1 diabetic subjects, 50% males, 50 % females, with a mean age of 30,8 ± 11,9 (17-64) years. To accomplish our work we applied a couple of instruments: a general biographical questionnaire and the Experience of Treatment Benefits and Barriers (ETBB). This instrument is based on the Leventhal's model of beliefs.

Results: In this sample we found that patients had more benefit beliefs than barrier beliefs about diabetes treatment. Relatively to gender, man had significantly higher benefit beliefs about treatment than women (32,6 ± 3,7 vs 29,1 ± 3,8; p = 0,002). We also found a significant association between treatment barriers perceptions and number of glucose checks per day (r= 0,36; p= 0,007). We observed a significant difference, mostly in terms of barrier perceptions, between subjects with the 1st grade educational level and subjects with the 9th grade or higher.

Conclusions: The analysis of the cost/benefit ratio tell us that, in this sample, the positive perceptions of this treatment are greater than the barrier beliefs, especially in man. On the other hand, some beliefs clearly affect the patients' daily routines mainly in social contexts.

HYPERINSULINEMIA IS A PREDICTOR OF NEW CARDIOVASCULAR EVENTS IN COLOMBIAN PATIENTS WITH A FIRST MYOCARDIAL INFARCTION

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Background: Acute Myocardial infarction (AMI) is one of the main causes of mortality and disability in Colombia. The factors associated to a new event in surviving subjects to a first AMI have not been well identified yet.

Methods: Two hundred and ninety five surviving subjects to a first AMI (58.8±12.6 years) were included in a prospective cohort study between 2000 and 2006. Lipid profile, glycemia and plasma insulin levels were measured. Deaths of cardiovascular origin, a new AMI, unstable angina, heart failure, stroke, new myocardial revascularization or angioplasty were considered as new cardiovascular events.

Results: The study included 61 (20.6%) women and 236 (79.4%) men. The mean follow up time was 50±30 months with a 38.85% incidence of new events. Insulin levels ≥ 10 mUI and total cholesterol > 200 mg/dl were higher in subjects who presented a new event. Bi-varied analysis identified as risk factors for new cardiovascular events the presence of: hypertension (HT), anterior descending coronary artery stenosis, intrahospitalary cardiac failure, age over 55, low income, lack of education, Killip III-IV, heart rate over 76 bpm, pulse pressure over 80 mm Hg, total cholesterol over 200 mg/dL and insulin over 10 IU/mL. After the logistic regression analyses, insulin over 10 UI/ml remains as a significant predictor for new cardiovascular events.

Conclusions: Hyperinsulinism was the most important factor associated to the presentation of new cardiovascular events in Colombian patients with AMI, which emphasizes the importance of insulin resistance in the causal relationship between metabolic alterations and cardiovascular diseases.

THE IMPAIRMENT OF THE ARTERIAL BARORELEX-MEDIATED MICROCIRCULATORY CONTROL, A POSSIBLE MECHANISM OF INSULIN RESISTANCE, POTENTIAL WAYS OF TREATMENT

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Objectives: Increasing evidence suggests impairment in baroreflex-mediated autonomic cardiovascular modulation in prediabetes. We studied less explored baroreflex microcirculatory control mechanism after sinocarotid baroreceptor stimulation by static magnetic field (SMF) with regard to potential implementation in diabetic microcirculatory disturbances.

Methods: Mean femoral artery blood pressure (MAP), heart rate (HR), and ear lobe skin microcirculatory blood flow, measured by microphotoelectric plethysmogram (MPPG), were simultaneously recorded in conscious rabbits before and after a 40 min local exposure of the sinocarotid baroreceptors to 350 mT intensity SMF, generated by Nd-Fe-B alloy magnets (n = 14) or sham magnets (n = 10, control series). Arterial baroreflex sensitivity (BRS) was estimated from HR/MAP response to intravenous bolus injections of nitroprusside and phenylephrine.

Results: SMF significantly decreased MAP (-6.2%). A positive correlation between

SMF-induced significant increase in BRS ($\Delta BRS = BRS_{afterSMF} - BRS_{priorSMF}$) and in microcirculatory blood flow ($\Delta MPPG = MPPG_{afterSMF} - MPPG_{priorSMF}$) ($r = 0.66$, $p < 0.009$) indicates arterial baroreflex participation in microcirculatory control and its enhancement after SMF exposure.

Conclusion: Clinical trials should be performed to support our hypothesis, but it is likely that in prediabetes, along with dyslipidemia and arterial hypertension, impaired baroreflex-mediated autonomic microvascular control worsens sophisticated "heartbeat-to-heartbeat" sensitive regulation of the microcirculatory blood flow, tightly adjusted to tissues´ actual metabolic demands, contributing therefore to the development of insulin resistance. Sinocarotid baroreceptor stimulation by SMF may be a potential method how to improve dysregulation of the autonomic makro- and microcirculatory control, tissue perfusion and insulin resistance in prediabetic and diabetic conditions.

ASSOCIATION OF A DIABETES RISK SCORE WITH RISK OF MYOCARDIAL INFARCTION, STROKE, SPECIFIC TYPES OF CANCER, AND MORTALITY: A PROSPECTIVE STUDY IN THE EPIC-POTSDAM COHORT

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Objective: To evaluate the impact of a recently developed, non-invasive risk score predictive for type 2 diabetes on the incidence and mortality of cardiovascular diseases and of specific types of cancer.

Methods: A total of 23,455 participants from the population-based, prospective EPIC-Potsdam study aged 35-65 years and free of diabetes and major chronic diseases at baseline (1994-98) were followed through 2006 for incident myocardial infarction, stroke, types of cancer, and death. Risk score points were assigned to each participant based on age, waist circumference, height, physical activity, history of hypertension, smoking, alcohol consumption, and intake of red meat, whole-grain bread, and coffee. Relative risks (RRs) were estimated by Cox regression models.

Results: In age- and sex-adjusted analyses, participants with a high risk score (5-year probability to develop diabetes ≥ 10%) had significantly higher risks of myocardial infarction (RR 2.7, 95% CI 1.5-5.0) and stroke (1.9, 1.0-3.6), but not of colon, breast or prostate cancer incidence, than those with a low score (5-year probability < 1%). In addition, participants with a high risk score had considerably higher risks of cardiovascular (RR 4.6, 95% CI 2.3-9.4), cancer (1.7, 1.1-2.7), and total mortality (2.4, 1.8-3.4), the latter being equivalent to a difference in life expectancy of 13 years.

Conclusions: These data indicate that a risk score predictive for type 2 diabetes is also related to elevated risks of myocardial infarction, stroke, and premature death in apparently healthy individuals and emphasize the need for early intervention in high-risk individuals.

THE ASSOCIATION OF BRACHIAL-ANKLE PULSE WAVE VELOCITY WITH 30-MINUTE POST-CHALLENGE PLASMA GLUCOSE LEVELS IN KOREAN ADULTS WITH FASTING HYPERGLYCEMIA

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We analyzed the relationship of brachial-ankle pulse wave velocity (baPWV) with fasting and post-challenge plasma glucose levels in the oral glucose tolerance test. In 664 subjects with fasting hyperglycemia, 75g OGTT were performed to confirm the glucose tolerant status, and fasting, post-challenge 30-minute and 120-minute glucose levels were measured. Anthropometric measurements were done, and fasting lipid profiles were measured. baPWV were measured in all subjects and the relationship between fasting, 30- and 120-minute post-challenge glucose levels and baPWV were analyzed. Mean age was 47.38 years and mean body mass index was 25.3 kg/m^2. Among the plasma glucose levels measured during 75g OGTT, mean values for fasting, post-challenge 30-minute and 120-minute were, 119.0±18.6, 186.07±34.0, and 162.76±56.7 mg/dL. Fasting plasma glucose level showed significantly negative correlation with HDL-C level and post-challenge 30-minute plasma glucose level showed significantly positive correlation with LDL-C, and 120-minute plasma glucose level showed significantly positive correlation with total cholesterol, LDL-C levels, and negative correlation with HDL-C level. baPWV values showed significant positive correlations with post-challenge plasma glucose at both 30- and 120-minutes, but not with fasting plasma glucose levels. In linear regression analyses with baPWV as the dependent variable with only OGTT glucose levels and age as the independent variables, age and post-challenge 30-minute plasma glucose level were the significant determinants for baPWV values. Among the plasma glucose values in 75g OGTT, post-challenge 30-minute plasma glucose level showed mostly significant correlation with baPWV in subjects with fasting hyperglycemia.

THE QUOTIENT FASTING PLASMA GLUCOSE/BMI PREDICTS MAJOR CARDIOVASCULAR EVENTS AND TOTAL MORTALITY AMONG WOMEN BUT NOT AMONG MEN IN 75-YEAR-OLDS

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We determined the predictive ability of fasting plasma glucose (FPG) and body mass index (BMI) on major cardiovascular events (MCVE) and all-cause mortality in 75-year-olds during a ten-year follow-up. In view of previously reported higher impact of diabetes on mortality among women sex-specific analyses were performed.

Study population: Ten years follow-up of MCVE and all-cause mortality in relation to FPG and BMI in a cohort of 210 men and 222 women and comprising 70% of a random sample of all 75-year-olds living in the Swedish city Västerås. Eight percent were previously known diabetics. Cox regression survival analysis was used.

Results: During the follow-up 35% of men and 19% of women experienced a MCVE. All-cause mortality was 46% for men and 27% for women. The relative risk of MCVE per 1 mmol/L FPG was for men 0.98 (P=0.727), women 1.20(P=0.016); all-cause mortality men RR 1.08 (P=0.054), women 1.24 (P< 0.001).Relative risk of MCVE per unit BMI was for men 1.04 (P=0.332), women 0.92: (P=0.039); all-cause mortality men 1.03 (P=0.377), women 0.95 (P=0.148). Thus, high BMI in women implied better prognosis.Relative risk of MCVE per 0.1 unit of the quotient FPG (mmol/L) / BMI was for men 0.87(P=0.490), women 1.85 (P< 0.001); all-cause mortality men 1.20 (P=0.098), women 1.90 (P< 0.001).The sex difference in prognostic ability of the quotient FPG/BMI was significant: MCVE (P=0.003) and all-cause death (P=0.006).

Main conclusions: High FPG in combination with low BMI signifies dismal prognosis in 75-years-old women. There is a significant sex disparity in this prognostic ability.

SEX DISPARITY OF CARDIOVASCULAR DISEASE INCIDENCE REFLECTS DIFFERENCES IN WAIST/HIP RATIO

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Excessive waist circumference is a key component of the metabolic syndrome. This syndrome is closely related to cardiovascular disease. The incidence of cardiovascular disease is higher among men than among women. Sex disparity in waist/hip ratio (WHR) is a conspicuous sexual characteristic. We examined the relationship the importance of sex and WHR for cardiovascular disease incidence by Cox regression analysis and the sex disparity in incidence of cardiovascular disease.

Study population: A population-based cohort (n=33601; men 48,0%, women 52.0%) were subjected to a health survey in the years 1990-1999 in the county of Västmanland, Sweden. 45.5% of the patients were 40 and 54.5% 50 years of age. The cohort comprised 50% of persons invited to the

survey. The patients were followed for major cardiovascular events, MCVE (hospitalisation or death by myocardial infarction, stroke or ruptured abdominal aortic aneurysm) until 2006-12-31.

Results: The median (interquartile range) of WHR was for men: 0.902(0.868-0.939), for women 0.778(0.740-0.820). The MCVE rate was 5.1% for men and 2.3% for women ($p< 0.001$). Relative risk by univariable Cox regression of WHR was 1.85 (1.74-1.96; 95 CI) per 0.1 unit WHR; after adjustment for sex 1.81 (1.68-1.94). Sex adjusted for WHR was non-significant.

Conclusion: The strong sex disparity in incidence of cardiovascular events reflects sex disparity of waist/hip ratio. Alternativt Waist/hip ratio is such a strong risk factor for cardiovascular events that it rules out sex as a risk factor.

DIETARY BEHAVIOUR, THE METABOLIC SYNDROME, AND CORONARY ATHEROSCLEROSIS

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Aims: Hardly any data on the association of self-reported dietary behaviour with the metabolic syndrome (MetS) and with angiographically determined coronary artery disease (CAD) are available. We aimed at investigating the association of self-reported dietary behaviour with the MetS in the clinically important population of angiographied coronary patients.

Methods: The standardized FEG questionnaire was performed in 197 patients undergoing coronary angiography for the evaluation of CAD.

Results: When compared to subjects without the MetS, patients with the MetS (NCEP ATP-III definition, n = 86) had lower FEG scores for being content with their eating behaviour (0.88 ± 1.52 vs. 1.80 ± 1.21; $p < 0.001$) and higher scores for having meals in an inconstant manner (3.67 ± 0.44 vs. 3.82 ± 0.36; $p = 0.014$) and for consuming meals in order to compensate frustration (1.67 ± 0.92 vs. 1.45 ± 0.85; $p = 0.044$). Concordantly, patients with the MetS had higher scores for the wish to change their eating behaviour (3.20 ± 1.06 vs. 2.51 ± 1.03; $p < 0.001$). However, scores also were higher for having difficulties in achieving this aim (3.3 ± 1.15 vs. 2.78 ± 1.13; $p = 0.010$). In contrast to these results for the MetS, no association of FEG scores with the presence of significant stenoses at angiography was observed.

Conclusions: Among angiographied coronary patients, dietary habits are strongly and significantly associated with the MetS but not with angiographically determined CAD. Specific dietary counselling should be provided for coronary patients with the MetS.

ALTERED VASCULAR ACTIVITY AFTER A HIGH-FAT MEAL IN FIRST-DEGREE RELATIVES OF SUBJECTS WITH TYPE 2 DIABETES

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Background: High-fat (HF) meal is known to impair endothelial function in normal subjects and in patients with type 2 diabetes (T2DM). The aim of this study was to assess the effect of a high-fat meal on endothelial function in young and healthy, normal glucose tolerant first-degree relatives of subjects with T2DM as no such data is available.

Methods: Fifty FDRS were matched for age (25.3 ± 4.5 years), sex and BMI with 20 subjects without the family history of T2DM. Flow mediated vasodilation (FMD) as a parameter for endothelial function was measured after an overnight fast and 2 hours after a HF meal (Egg McMuffin, Sausage McMuffin, 2 hash brown patties - 900 calories, 50 g of fat, 225 mg cholesterol; McDonald's Corporation). Blood was collected at fasting and post-prandial stages for the determination of glucose, CRP and lipid profile.

Results: In FDRs, FMD was significantly lower ($4.2 \pm 8.3\%$ vs $12.9 \pm 4.1\%$; $p< 0.0001$) than controls before the HF meal. However, vasoactivity increased after the meal when compared to baseline levels ($6.7 \pm 9.1\%$ vs $4.2 \pm 8.3\%$) in FDRs. It was associated with significant changes in the levels of post-prandial glucose (4.4 ± 0.8 vs 5.0 ± 1.1 mmol/L; $P< 0.0001$), TGL (1.3 ± 1.2 vs 2.2 ± 1.6mmol/L) and HDL (1.3 ± 0.3 vs 1.2 ± 0.3 mmol/L).

Conclusion: Prolonged hyperglycemia in FDRs suggests altered glucose metabolism. Paradoxical vasodilation after a fatty meal may be an early sign of altered vascular activity in FDRs.

COMPREHENSIVE EVALUATION OF CORONARY ARTERY IN ASYMPTOMATIC METABOLIC SYNDROME BY MULTIDETECTOR-ROW CARDIAC COMPUTED TOMOGRAPHY

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Objective: Early detection of atherosclerosis in metabolic syndrome is demanding nowadays because of high association with cardiovascular disease. We performed multidetector-row computed tomography (MDCT) in asymptomatic individuals to investigate the status of coronary artery stenosis and plaque characteristics depending on the presence of metabolic syndrome (MS).

Methods and results: The plaque burden, severity of stenosis, plaques characteristics, and coronary artery calcium score (CACS) were assessed by MDCT in 1,043 asymptomatic individuals. Anthropometric parameters and metabolic profiles were also acquired. 8.8 percents of subjects had MS. Subjects with MS had a greater plaque burden, more coronary stenosis (>50% of diameter stenosis) and higher CACS than normal subjects (all, $P< 0.01$). Severe coronary stenosis (>75% of diameter stenosis) and left main coronary artery disease are significantly higher in MS. After adjustment for confounding factors, the presence of metabolic syndrome was strongly associated with vulnerable plaque burden.

Conclusions: More significant coronary stenosis and multivessel involvement, higher CACS, and greater plaque burden were founded in subject with MS by MDCT, even they are asymptomatic. The proactive screening and treatment for atherosclerosis are needed in MS subjects with high risk factors.

METABOLIC SYNDROME DOES NOT PREDICT AN INCREASED RISK OF CORONARY DISEASE IN PATIENTS WITH TRADITIONAL RISK FACTORS REFERRED FOR STRESS TESTING

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Aims: To evaluate the impact of metabolic syndrome (MS) on the prediction of coronary disease (CAD) in subjects with multiple traditional risk factors.

Methods: We enrolled 2626 consecutive subjects who underwent clinically indicated stress imaging using echocardiography or SPECT myocardial perfusion. Patients with known CAD were excluded leaving 1256 subjects. MS was defined by National Cholesterol Education Program- ATP III criteria. The number of traditional risk factors and the presence of MS were compared with the results of stress imaging. Logistic regression analysis was used to assess the impact of MS on CAD prevalence in subjects with limited (≤2) traditional risk factors and multiple (≥ 3) risk factors.

Results: MS was present in 540 (43%) of subjects. Presence of MS was associated with a non-significant 3%-4% increase in overall prevalence of CAD. MS did not increase the prevalence of CAD in those with multiple (≥ 3) traditional risk factors (MS 25% vs no MS 21%, p=0.62) or in those with limited (≤2) risk factors (MS 19% versus no MS 16%, p=0.13). The presence of limited vs multiple risk factors had poor accuracy for prediction of CAD with area under the receiver operating curve (ROC)=0.52. Information on the presence or absence of MS did not improve identification of CAD, ROC area of 0.54, p=NS. None of the 5 components of MS showed significant association with CAD.

Conclusions: The addition of MS to traditional risk factors does not increase the prevalence of CAD determined by stress imaging.

STATIN USE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND NEWLY-DIAGNOSED ABNORMAL GLUCOSE TOLERANCE IS ASSOCIATED WITH IMPROVED CLINICAL OUTCOMES

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Background: Recent studies have demonstrated that newly-diagnosed abnormal glucose tolerance (AGT) is common among the patients with acute myocardial infarction (AMI), and is a critical risk factor for future cardiovascular events. Statin treatment may have a great impact on the long-term prognosis after AMI in patients with newly-diagnosed AGT.

Methods: A total of 190 consecutive patients with AMI and without previously diagnosed diabetes were enrolled to this prospective study. We tried to manage the patients to achieve LDL-C level less than 120mg/dL according to a recommendation by the domestic guideline in the latter 1990s. Patients were divided into four groups based on the statin use during hospitalizations and the result of 75g oral glucose tolerance test at discharge; 22 patients with normal glucose tolerance (NGT)/statin+, 58 patients with NGT/statin-, 46 patients with AGT/statin+, and 64 patients with AGT/statin-. The incidence of major adverse cardiovascular events (MACE) during the follow-up was compared among the groups.

Results: LDL-C level at admission was higher in patients with statin use than those without statin use (142.7±29.4 vs 121.9±21.2 mg/dl; p< 0.0001). The Kaplan-Meier survival curves showed that the AGT/statin+ group was better than the AGT/statin- and equivalent to both the NGT groups in prognosis. The age-adjusted relative risks for future MACE in NGT/statin+, NGT/statin-, AGT/statin+, and AGT/statin- groups were 1.0 (referent), 1.07 (95%CI 0.29-3.98), 1.75 (0.47-6.45), and 3.34 (1.01-11.07; p< 0.05), respectively.

Conclusions: Statin use was associated with better clinical outcomes in AMI patients with newly-diagnosed AGT, regardless of higher LDL-C level.

EFFECT OF ALPHA-GLUCOSIDASE INHIBITORS ON CARDIOVASCULAR EVENTS IN TYPE 2 DIABETES COULD BE EXPLAINED BY THE INCREASE OF HYDROGEN GAS IN INTESTINAL TRACT?

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Postprandial hyperglycemia has an important role in the development of cardiovascular disease. The STOP-NIDDM trial demonstrated that alpha-glucosidase inhibitors may interfere with the development of macrovascular diseases through an additional mechanism(s) beyond expected effects on glycaemic control.

Alpha-glucosidase inhibitors increases hydrogen gas in excretory breath after the meal, because undigested carbohydrate enters the large intestine where it is digested by colonic bacteria with resulting gas formation.

We reported that highly diffusible hydrogen selectively scavenges hydroxyl radicals, and inhaled hydrogen protects brain, liver and heart. Regarding the heart, we reported recently that inhaled hydrogen gas is rapidly transported and reaches 'at risk' ischemic myocardium before reestablishment of coronary blood flow of the occluded infarct-related artery. The cardioprotectional effect of increased hydrogen gas, evaluated by measuring infarct size after left anterior descending coronary artery occlusion and reperfusion, showed that inhalation of hydrogen gas (2%) before reperfusion significantly reduces oxidative stress-induced myocardial injury and infarct size without affecting hemodynamic parameters, and thereby prevents deleterious left ventricle remodeling. This result indicates that diffusible hydrogen caused by increased hydrogen gas limits the extent of myocardial infarction in rat models of ischemic-reperfusion injury.

Based on this observation, we suggest that the prevention effect of alpha-glucosidase inhibitors of cardiovascular protective effect can at least partially be attributed to their ability to neutralize vascular oxidative stress via an increased production of hydrogen in gastrointestinal tract.

INFLUNCE OF GENDER ON THE ASSOCIATION BETWWEN LEFT VENTRICULAR HYPERTROPHY AND METABOLIC SYNDROME IN HYPERTENSIVE PATIENTS

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Several studies documented an association between metabolic syndrome (MetS) and left ventricular hypertrophy, independently from various confounding factors, such as blood pressure values and age. However, some studies detected this association only in female gender.

The aim of our study was to verify, in a wide sample of essential hypertensive patients, the influence of gender, if any, on the relationship between left ventricular mass (LVM) and MetS.

We enrolled 475 nondiabetic subjects (mean age: 46 ± 11 years), with mild-to-moderate essential hypertension, of whom 40% had MetS, defined on the basis of ATPIII criteria.

All the patients underwent a 24-h ambulatory blood pressure monitoring and an echocardiogram. In female subjects (n = 180) LVM indexed for height$^{2.7}$ (LVMH$^{2.7}$) was significantly ($p < 0.001$) higher in women with MetS than in those without it (54 ± 17 vs 42 ± 11 g/m$^{2.7}$). However, a slightly lower difference in LVMH$^{2.7}$, but equally significant ($p < 0.001$),

was documented between the two groups with and without MetS (51 ± 14 vs 43 ± 11 g/m$^{2.7}$), also in male gender (n = 295). The relationship between MetS and LVMH$^{2.7}$ remained statistically significant ($p < 0.001$) in both sexes, in a linear multiple regression analysis, even after adjustment for 24-h systolic blood pressure, age and duration of hypertension.

Our results seem to suggest that the relationship between MetS e LVMH$^{2.7}$ is only in part affected by gender, being LVMH$^{2.7}$ significantly increased in both hypertensive women and men with MetS.

TRIGLYCERIDE/HDL-CHOLESTEROL RATIO IS AN INDEPENDENT PREDICTOR FOR CORONARY HEART DISEASE IN IRANIAN MEN POPULATION

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Aims: To determine if triglyceride/high density lipoprotein cholesterol ratio (TG/HDL-C), which has been shown as an indicator of metabolic syndrome (MetS) and insulin resistance, can predict coronary heart disease (CHD) independent of total cholesterol (TC) and other risk factors in Iranian population with high prevalence of MetS and low HDL-C.

Methods: Between February 1999 to August 2001, 1,824 men ≥ 40 years old, free of clinical cardiovascular diseases at baseline, were followed. Baseline measurements included serum level of TC, HDL-C, TG, and risk factors of CHD including age, systolic and diastolic blood pressure, body mass index, waist circumference, diabetes, smoking and family history of premature cardiovascular diseases.

Results: During a median follow up of 6.5 years until March 2007 (11,316 person-years at risk), a total of 163 new CHD events (27 fatal and 136 nonfatal) occurred. The prevalence of MetS in subjects with TG/HDL-C ³ 6.9 (top quartile) reached to 63.6% versus 3.0% in those with TG/HDL-C < 2.8 (low quartile). According to a stepwise Cox proportional hazard model, including TG and TG/HDL-C quartiles, with TC and other risk factors, men in the top quartile of TG/HDL-C relative to first quartile had a significant hazard ratio (HR) of 1.75 (95% CI, 1.02-3.00), while TG was not remained in the model.

Conclusion: The evaluation of TG/HDL-C ratio should be considered for CHD risk prediction in our male population with high prevalence of MetS.

THE IMPACT OF SOCIODEMOGRAPHIC DISADVANTAGE ON ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RISK AMONG AFRICANS WITH RHEUMATOID ARTHRITIS

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We performed a case-control study among Africans with established rheumatoid arthritis (RA) seen in a public care setting to investigate its association with atherosclerotic cardiovascular disease (CVD) risk.

We assessed modifiable conventional and non-conventional CVD risk factors in 653 RA subjects, 451 public care and 202 private care patients. Statistical comparisons were adjusted for age and gender.

Public care patients were more frequently of African ancestry (66.5 versus 4.5%, p< 0.0001) and less frequently European (14.2 versus 83.2%, p< 0.0001). Overall, 57.9% were hypertensive, 19.3% dyslipidemic (cholesterol/HDL cholesterol >4), 11.2% smoked and 9.5% had diabetes. The proportion of patients with one or more of these modifiable risk factors was higher in public care patients (72.3 versus 62.4%, p=0.02). Public care was associated with hypertension (OR [95% CI]=1.63 [1.15-2.31], reduced HDL cholesterol (OR [95% CI]=1.77 [1.14-2.74]) and current smoking status (OR [95% CI]=0.60 [0.36-1.00]). Abdominal obesity and the metabolic syndrome were more often encountered in public care patients (61.8 versus 49.5%, p=0.007 and 24.8 versus 12.4%, p< 0.0001, respectively). Additionally, public care patients had higher C-reactive protein concentrations (mean [95% CI]=7.8 [7.0-8.8] versus 3.9 [3.2-4.6], p< 0.0001), less frequent RA remission (12.4 versus 38.1%, p< 0.0001) and higher numbers of deformed joints (9.9 [9.0-10.8] versus 5.2 [4.1-6.3], p< 0.0001). In further multivariate models, a higher inflammatory burden and reduced alcohol intake (but not obesity) explained the association of public care with reduced HDL cholesterol.

Sociodemographic disadvantage is associated with enhanced atherosclerotic CVD risk in Africans with RA.

CURRENT CHOLESTEROL GUIDELINES AND CLINICAL REALITY: A COMPARISON OF CORONARY ARTERY DISEASE PATIENTS FROM NOW AND FROM SEVEN YEARS AGO

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Aims: Current guidelines recommend serum LDL cholesterol < 100 mg/dl for patients with coronary artery disease (CAD) and < 70 mg/dl for the very high risk patients with CAD plus type 2 diabetes (T2DM). We aimed to investigate the patients who achieve these current guidelines.

Methods: We obtained lipid panels in two cohort of patients who were referred to coronary angiography for the evaluation of previously (>1 month) established CAD in 1999-2000 (n = 349) and in 2005-2007 (n = 656), respectively.

Results: The prevalence of diabetes was 24.9% in the first and 26.9% in the second cohort. Overall, 59.3% and 64.6% of diabetic patients (p = 0.408) and 50.8% and 58.5% of non-diabetic patients (p = 0.043) were on statins in the first and in the second cohort, respectively. Among non-diabetic patients with CAD, the proportion of subjects with LDL cholesterol < 100 mg was 23.5% in the first cohort and 28.9% in the second cohort (p = 0.182); among patients with CAD plus T2DM 36.0% and 40.6% (p = 0.481) and 8.1% and 9.1% (p = 0.788) had LDL cholesterol < 100mg/dl and < 70 mg/dl in the first and second cohorts, respectively.

Conclusions: The proportion of CAD patients meeting current lipid treatment goals is low and has only marginally improved during the last 7 years. This in particular holds true for the very high risk patients with CAD plus diabetes. Targeted programs to improve the lipid management of CAD patients in current clinical pratice are necessary.

ETHNIC DIFFERENCES IN PERIPHERAL AND CENTRAL ARTERIAL STIFFNESS WITH AGING

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Background: Arteries stiffen with advancing age. In Africans arterial stiffness is even more increased and their arteries seem to function differently from Caucasians. We compared the age-related changes in arterial stiffness of the muscular arteries with two more central segments of the arterial tree in normotensive (NT) and hypertensive (HT) African and Caucasian individuals from South Africa.

Methods: Apparently healthy African (N=374) and Caucasian (N=376) subjects took part in this cross-sectional study (aged 20-70 years). Subjects were divided into four age-groups: 20-30; 31-40; 41-55 and 56-70 years. Carotid-radial (C-R) and carotid-dorsalis pedis (C-DP) pulse wave velocity (PWV) were determined with the Complior SP. Aortic input impedance (Zao) was derived from a 5 minute continuous cardiovascular recording with the Finometer device.

Results: NT and HT Caucasians indicated increased trends of C-R PWV with aging (p=0.029 and 0.067, respectively), not seen in the African groups (p=0.122 and p=0.526). C-DP and Zao showed significant increases with aging for both ethnic groups. HT Africans had significantly higher stiffness than HT Caucasians for almost all age groups, and for all three measures of stiffness (C-R and C-DP PWV, Zao). In the NT groups similar results were seen in the younger age groups. C-R PWV of Africans (NT and HT) correlated significantly with blood pressure, but not with age. Opposite results were observed for Caucasians.

Conclusion: Significant differences in the rate of age-related deterioration in peripheral and central arteries of NT and HT Africans were shown, compared to Caucasians, possibly due to differences in vascular remodelling.

DIABETIC MELLITUS IS THE MOST IMPORTANT RISK FACTOR FOR MYOCARDIAL INFARCTION IN IRANIAN ADULTS: A POPULATION BASE STUDY

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Aims: To investigate the association of diabetic mellitus with the risk of myocardial infarction (MI) in man and female 30 years and over.

Methods: In the Tehran Lipid and Clucose study(TLGS) included 5187 Iranian adults at Tehran city aged 30 to 90 years at baseline. The mean duration of follow up was 6.2 years. Analysis was done using Cox proportional hazard regression.

Results: The TGLS cohort had 83 MI. The age and sex adjusted relative risk of MI in patients with FBS>126 at baseline was 5.4(95% CI: 3.4 to 8.4) times compared with FBS < 126 .Attribute risk fraction for exposed group(FBS>126) was 85.4% and attribute risk fraction for population was 37.1%; it means with control FBS 37.1 MI events decrease in population. The relative risk for FBS was height compared with others risk factors such as total cholesterol, LDL, HDL, BMI, SBP, DBP.

Conclusions: FBS remains as an important and independed risk factor for MI in men and women aged 30 years and older.

IS THERE ANY CORRELATION BETWEEN ENDOTHELIAL DISFUNCTION MEASURED BY NONINVASIVE TECHNIQUES AND INTIMA MEDIA THICKNESS IN DIABETES AND PREDIABETES?

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Background: Endothelial vasodilator dysfunction and carotid intima-media thickening (IMT) are two indicators of subclinical cardiovascular disease. We examined their correlation and interaction with biological markers (IL6, IL8, TNF alfa, PCR us) in patients with diabetes mellitus and prediabetes.

Methods: This is an prospectiv study on 29 patients, hospitalized in the Internal Medicine Department. Endothelial disfunction was investigated using Ultrasound Doppler of the brachial artery. The variation of the vassel diameter due to reactiv hiperemia was recorded. The second noninvasive parameter investigated was intima media thickness (IMT) at the carotide artery level. Statistical analysis used the Microsoft Office Excel (student t-test; Chi-square test, Fisher test). The results are presented as mean ± standard deviation. P value < 0.05 was considered statisticaly significant.

Results: General characteristics of the studied group were: age 62.4 ± 11.11 years old; weist circumference 111 ± 11.5 cm; BMI 30.16 ± 4.66 Kg/m^2. Seventeen (59%) were women and 12 (41%) were men. Most of the patients were non-smokers (78%). Eighteen patients (62.1%) from the study group had diabetes and 11 (37.9%) had prediabetes (impared fasting blood glucose or impared glucose tolerance). In the diabetic patients group 89% had impared endothelium-dependent brachial artery flow-mediated dilatation and 78% had increase carotid artery IMT. On the other hand, in prediabets group, only 34% of the patients had impared flow-mediated dilatation and 28% had increased IMT. This findings were correlated with increased biological markers of endothelial disfuction: Il-6, Il-8, TNFα and CRP.

RESTING HEART RATE IS ASSOCIATED WITH THE METABOLIC SYNDROME - AN ADDITIONAL CONNECTION BETWEEN RESTING HEART RATE AND CARDIOVASCULAR DISEASE

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Background: To explore the possibility that increased resting heart rate (RHR) is associated with the prevalence of the metabolic syndrome (MetS) in a sample of apparently healthy individuals and those with atherothrombotic risk.

Methods: A cross-sectional analysis in a large sample of apparently healthy individuals who attended a general health screening program.

Results: In a sample of 4515 men and 2316 women, with 13.8% men and 9.3% women with MetS, the multi-adjusted odds for the presence of the MetS increased gradually from an arbitrarily defined figure of 1.0 in the lowest RHR quintile (< 60 beats per minute (BPM) in men and < 64 BPM in women) to 4.77 and 4.22 in men and women respectively in the highest one (≥80 BPM in men and ≥82 BPM in women).

Conclusion: Raised resting heart rate is significantly associated with the presence of MetS in a group of apparently healthy individuals and those with an atherothrombotic risk. The strength of this association supports the potential presence of one or more shared pathophysiological mechanisms for both RHR and the MetS.

PREDIABETES AND RESPONSE TO CLOPIDOGREL AMONG PATIENTS UNDERGOING ELECTIVE INTRACORONARY STENT IMPLANTATION

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Aim of this study was to determine influence of elevated fasting glucose levels on response to antiplatelet therapy among patients undergoing elective intracoronary stent implantation.

Methodology: Study population was 103 patients undergoing elective PCI treated with dual antiplatelet drugs (aspirin 100mg daily and clopiodgrel

75mg daily at least 7 days prior to PCI). Patients were divided in three groups according to standard criteria for prediabetes/diabetes mellitus (group I without glucose metabolism disorders, group II with prediabetes and group III with diabetes mellitus). Also, for all the patients flow cytometric analysis of platelet reactivity index (PRI) was performed, and according to cut off of PRI>50% patients were determined as non responders to clopidogrel.

Results: In whole study population there were 70 patients (67,96%) in group I, 14 patients (13,59%) in group II and 19 (18,44%) patients in group III. In group I the majority of patients were responders to antiplatelet therapy (50 pts) vs. 20 pts non responders, in group III there was similar ratio of responder/non responder (15 pts vs. 4 pts), respectively, but in II group with prediabetes, the majority of patients were non responders 6 pts vs.8 pts responders.

Conclusion: This pilot study indicates that patients with prediabetes mellitus undergoing elective PCI may be considered for increasing dose of standard antiplatelet therapy in order to protect them adequately from thrombotic events.

ALANINE AMINOTRANSFERASE CONCENTRATION, EVEN WITHIN THE REFERENCE RANGE, IS ASSOCIATED WITH CAROTID ATHEROSCLEROSIS AND METABOLIC SYNDROME

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Aims: To investigate whether alanine aminotransferase (ALT), even within the reference range, is associated with atherosclerotic burden in apparently healthy adults.

Methods: Eight hundred thirty healthy individuals with normal ALT concentration (≤ 40 U/L) and who did not consume excessive alcohol participated in this study. A standard interview, anthropometrics, biochemical studies, and abdominal ultrasonography were conducted for each participant. Atherosclerotic burden was assessed by carotid arterial intima-media thickness (IMT). All subjects were divided according to the quartile based on their ALT concentrations.

Results: Despite all subjects having a normal ALT concentration, ultrasonographic liver steatosis was observed in 48.4% and 36.7% of men and women, respectively. In both genders, subjects in the highest quartile of ALT concentration had a significantly higher waist circumference, triglyceride concentration, HOMA-IR, a higher prevalence of metabolic syndrome, and a greater severity of ultrasonographic liver steatosis than did those in the lower quartiles. In women, the carotid IMT increased significantly with increasing quartiles of ALT concentration (0.62±0.14, 0.66±0.15, 0.69±0.15, vs. 0.72±0.24 mm; P for trend < 0.001). Based on multivariate regression analysis, the serum ALT, even within the normal range, was associated with the carotid IMT in both men and women, and independently of traditional cardiovascular risk factors.

Conclusions: ALT concentrations, albeit within the reference range, were associated with atherosclerotic burden and metabolic syndrome in healthy adults. Therefore, people with high normal ALT activity should be closely observed and further investigated for cardiovascular and metabolic diseases.

BODY MASS INDEX, CARDIOVASCULAR RISK FACTORS, METABOLIC SYNDROME AND GLOBAL CARDIOVASCULAR RISK

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Objective: To assess the relation between body mass index (BMI), vascular risk factors (VRF), metabolic syndrome (MS), and global cardiovascular risk (VR).

Methodology: Cross-sectional and observational study. 1,085,237 workers (72.8% males, mean age 36.7 years), who underwent a routine medical checkup between May 2004 and November 2007, were included in the study. According to (BMI), subjects were classified as normal weight (Nw: < 25 kg/m2), overweight (Ow: 25-29.9 kg/m2) and obese (Ob: ≥30 kg/m2). The Adult Treatment Panel III (ATPIII) definition for MS and estimated SCORE for VR were used. Previous diagnosis of vascular disease (PVD): stroke, coronary or peripheral arterial disease.

Results: Prevalence (%) of risk factors in subjects (Nw / Ow / Ob) was: Smoking (50.0, 44.7, 44.8%); Blood pressure ≥140/90 mmHg (10.8, 25.8; 42.9); Dyslipidemia (42.0, 61.6, 70.6); Fasting glucose ≥126 mg / dl. (0.8, 2.4, 6.0); Fasting glucose > 110 and < 126 mg / dl. (1.1, 3.3, 6.2); Alcohol consumption standard drink units ≥2 / day (2.6, 3.7, 4.1); Previous diagnosis of type 1 diabetes (0.3, 0.3, 0.3) and type 2 diabetes (0.3, 1.3, 2.9); Waist circumference > 88 cm -female - (2.2, 29.9, 84.3) and >102 cm -male-(0.3, 8.6, 67.0); MS (0.9, 7.0, 32.0); moderate VR (0.4, 1.2, 1.6) and high VR (2 , 3, 6.8, 12.1). PVD (0.3, 0.7, 1.2)

Conclusions: Except for smoking (attributable to the increased prevalence of young smokers), workers with Ow and Ob showed higher prevalence of risk factors, MS and moderate and high VR and PVD.

ROLE OF THE INTERLEUKIN 10 POLYMORPHISMS IN THE GENETIC SUSCEPTIBILITY TO ACUTE CORONARY SYNDROME

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Proinflammatory cytokines, like IL-6 and TNF-alpha, are implicated in the development of acute coronary syndrome. The role of anti-inflammatory cytokines, like IL-10, is largely unknown. Considering that cytokines play a crucial role in the pathogenesis of acute coronary syndrome, the aim of the present study was to evaluate the role of *IL-10* gene polymorphisms as susceptibility markers for this syndrome in a group of Mexican patients. Promoter polymorphisms (positions *-592*, *-819* and *-1082*) of the *IL-10* gene were analyzed by 5' exonuclease TaqMan assays in a group of 301 patients with acute coronary syndrome (191 with myocardial infarction and 110 with unstable angina) (mean age=57.9±12.0 years) and 248 healthy unrelated controls (mean age=55.9±4.24 years). Allele and genotype distribution of the polymorphisms in patients and controls was evaluated using chi-square, Fisher's exact test, and Woolf method for odds ratio (OR). Distribution of the three polymorphisms was similar in the whole group of patients and healthy controls. However, when patients with myocardial infarction, unstable angina and healthy controls were compared, some differences were observed in the *-1082* polymorphism. Patients with myocardial infarction showed increased frequencies of *-1082 A* allele and *AA* genotype when compared to patients with unstable angina (p=0.03, OR=1.49 and p=0.01, OR=1.79, respectively). Also, patients with

myocardial infarction showed increased frequency of -1082 *AA* genotype when compared to healthy controls (p=0.03, OR=1.52). The preliminary results suggest that *-1082* polymorphism of the *IL-10* gene could be involved in the risk of developing myocardial infarction in Mexican individuals.

ABNORMAL GLUCOSE METABOLISM IN PATIENTS WITH ACUTE CORONARY EVENTS

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Aims: Insulin resistance and abnormal glucose metabolism are associated with an increased risk for cardiovascular events. Our aim was to determine the prevalence of impaired glucose metabolism in patients with acute coronary event but without diagnosed diabetes.

Methods: We performed a prospective study, in which we enrolled 80 consecutive patients (mean age: 59.8±0.9 years old, 75 males) admitted to the coronary care unit with acute coronary event and with no previous diagnosis of diabetes. All patients were subjected to a 2-hour oral glucose tolerance test (with 75gr of glucose) 2-3 weeks after their discharge.

Results: The mean glucose plasma concentration before the administration of glucose (baseline value) was 112±1.4 mg/dl, while the mean 2-hour postload concentration was 176.1±6 mg/dl. 11 patients (14%) were identified as having impaired fasting glucose only (baseline glucose ≥100 mg/dl), 29 (36%) as impaired glucose tolerance (2-h glucose between 140 and 200 mg/dl) (with or without impaired fasting glucose) and 28 (35%) as type 2 diabetes (2-h glucose ≥200 mg/dl).

Conclusions: Previously undiagnosed diabetes and impaired glucose tolerance are quite common in patients with an acute coronary event. These abnormalities can be detected early in the post-event period. Our results suggest that oral glucose tolerance test should be performed in all diabetes-undiagnosed patients with coronary artery disease.

NONDIPPING STATUS AND CARDIOVASCULAR REMODELING IN GEORGIAN OBESE HYPERTENSIVE SUBJECTS

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Purpose: Taking into consideration prevalence of *AH* and the higher incidence of "nondipping" status in obese patients, we studied influence of blunted nocturnal decline in *BP* on cardiovascular remodeling and examined differences in target-organ injury (left ventricular hypertrophy (*LVH*) and carotid artery intima-media thickness (*IMT*) in Georgian obese "dipper" and "nondipper" hypertensive patients.

Methods: We studied 156 patients with mild to moderate *AH* (88males/68females, mean age 50,5±1,2years, *BMI* 30,8±2,8kg/m^2, duration of *AH* 6,1±1,4years). Examination included 24-hour BP monitoring (*ABPM*), ultrasound evaluation of left ventricular mass index (*LVMMI*), carotid artery *IMT*. 86 "nondipper" patients were assigned to group 1 and 70 "dipper" to group 2.

Results: The groups were comparable by the age, *BMI*, duration of *AH*, daytime mean *BP* values. Mean values of nocturnal *BP* (136±2,6/94±4,4vs128±1,5/91±3,2 mmHg), *LVMMI* (146,3±10,8vs141,1±9,7gr/m) and carotid artery *IMT* (1,07±0,03vs1,04±0,02mm) were certainly increased in "nondipper" patients compared with "dipper" ones ($p< 0,05$). Occurrence of *LVH* was higher in gr1 (concentric type: 55vs48%; eccentric type: 32vs24 %) ($p< 0,01$), of concentric remodeling and normal geometry in gr2 (18vs8% and 10vs5%, respectively) ($p< 0,05$).

Conclusions: Thus, in Georgian obese hypertensive subjects with "nondipper" circadian *BP* profile we detected more pronounced and frequent target-organ injury (*LVH*, enhanced *IMT*) comparing with patients with normal nocturnal decline in *BP*. Data of our study demonstrate importance of *ABPM* and more profound examination of cardiovascular system in obese hypertensive patients with blunted nocturnal decline in blood pressure.

SHORTER INHERITED TELOMERE LENGTH DOES NOT PREDISPOSE SUBJECTS TO ATHEROSCLEROSIS: RESULTS FROM THE ASKLEPIOS STUDY

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Aims: Telomeres, the nucleoprotein complexes capping chromosomal ends, shorten with each cell division, potentially leading to replicative senescence. Although largely genetically determined, systemic telomere length (TL) is featured by an age-dependent attrition and therefore considered as a marker for biological aging. Shorter telomeres have been found in subjects with cardiovascular disease and a causal effect of shorter TL at birth on cardiovascular risk has been suggested. On the other hand, oxidative stress and inflammation have been associated with both atherosclerosis and an accelerated telomere attrition, providing an alternative explanation. Here, we evaluated whether shorter inherited TL predisposes subjects to atherosclerosis.

Methods: Systemic (peripheral blood leukocyte, PBL) TL was measured by telomere restriction fragment analysis in 2509 subjects from the Asklepios Study cohort (~35-55 years old). All subjects were free from overt cardiovascular disease. Intima media thickness (IMT) and presence of plaque were evaluated by ultrasonography.

Results: In both sexes, PBL-TL was not significant as an independent determinant of IMT (P>0.3) or presence of plaque (P>0.05) for both carotid and femoral arteries separately. When considering general presence of plaque (carotid and/or femoral), PBL-TL was a significant - but weak - independent determinant in women (P=0.03), but not in men (P>0.4). TL in women was longer than in men, independent of presence of plaque, suggesting no effect of shorter TL as such.

Conclusions: These results indicate that shorter inherited TL does not predispose subjects to atherosclerosis and that the possible effects of an accelerated telomere attrition in cardiovascular disease should be evaluated.

INTENSIVE LIFE STYLE MODIFICATION IMPROVES GLUCOMETABOLIC STATUS AFTER CORONARY INTERVENTION IN PATIENTS WITH NEWLY-DIAGNOSED ABNORMAL GLUCOSE TOLERANCE

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Aim: Recent studies have demonstrated that newly-diagnosed abnormal glucose tolerance (AGT) is common among the patients with coronary artery disease and is a risk factor for future cardiovascular events. Thus, aggressive therapeutic strategy is necessary for secondary prevention of

future cardiovascular events. The aim of this study was to investigate whether intensive lifestyle modification can improve their glucometabolic status after coronary stenting in patients with newly-diagnosed AGT.

Methods: The study patients consisted of 38 consecutive patients without previously known diabetes mellitus who underwent coronary stenting and revealed to have AGT according to a 75g oral glucose tolerance test (OGTT). Nineteen patients were assigned to an intensive program of lifestyle modification (group A), and the remaining 19 patients who denied entering the program were followed in general outpatient clinic (Group B). All patients underwent 75g OGTT at baseline and 9-months follow up. We compared the reduction of 2-hour post-load plasma glucose concentration (2hPG) and plasma immunoreactive insulin (IRI) between 2 groups.

Results: There were no significant changes in glucometabolic status in Group B. However, in Group A, lifestyle modification for 9 months resulted in significant decreases in 2hPG (10.2±1.6 to 8.4±1.3 mmol/L, p=0.0015), fasting IRI (9.2±4.6 to 6.5±4.6 μU/ml, p=0.0189) and 2hIRI (108.1±58.9 to 53.1±47.1μU/ml, p< 0.0001).

Conclusions: Life style modification is effective for reducing post-load hyperglycaemia and hyperinsulinemia after coronary stenting in patients with newly-diagnosed AGT.

DIABETES MELLITUS AND ACUTE HYPERGLYCEMIA IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Aims: To evaluate the prevalence of diabetes mellitus and other disturbances of glucose metabolism in patients with acute coronary syndrome (ACS).

Methods: Prospective study of 411 consecutive patients admitted to the Cardiology Department with a diagnosis of ACS. In patients without a previous diagnosis of diabetes and fasting glucose < 126 mg/dl a standard OGTT was performed on days 4/5 after clinical stabilization. Glucose metabolism was classified as diabetes mellitus(DM), impaired fasting glucose(IFG), impaired glucose tolerance(IGT) or normal glucose tolerance(NGT), according to WHO criteria. Statistical analysis was performed by Student´s t test and results are expressed as mean±SD.

Results: We enrolled 96 females and 315 males, with a mean age of 61,1±11,7 and 64±12,5 years, respectively. One hundred twenty six patients(31,5%) were known diabetics but in the remainder 285(68,5%) this diagnosis was unknown and an OGTT was done. We found 37,9%(108/285) of patients with NGT, 0,7%(2/285) with IFG, 36,1%(103/285) with IGT and 21,4%(61/285) with DM. In patients with previously diagnosed diabetes A1c (7,8±1,8%) and glucose at admission (232,1±104,6) were significantly higher than those without known diabetes. A1c was higher in newly diagnosed DM than in those with NGT (6,1±0,5% vs 5,6±0,4%;p< 0,005) or with IGT (6,1±0,5% vs 5,5±0,3%;p< 0,005).

Conclusions: In this series 166 (40,3%) cases of previously undiagnosed diabetes and intermediate hyperglycemia were identified. This highlights the broad interrelation of patients affected by disturbances of glucose metabolism and CHD. Since glucose disturbances are common and easy to detect they are attractive targets for therapeutic intervention and secondary preventive efforts.

INCREASED CENTRAL AORTIC INDICES ARE ASSOCIATED WITH FUTURE DEVELOPMENT OF DIABETES MELLITUS IN ESSENTIAL HYPERTENSION

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Background: Diabetes mellitus (DM) and hypertension (HT) frequently coexist. Increased central aortic indices are associated with hypertension, however, influences of central aortic indices on future development of DM have never been studied in hypertension.

Methods: We recruited 178 patients with uncomplicated non-diabetic hypertension in this study. Baseline glucose, insulin, lipid profiles, and central aortic indices were measured at the entrance of the study. Two central aortic indices-augmentation (AG) and augmentation index (AIx) were obtained by tonometry with a transformation function (SphygmoCor, Atcor Medical, Sydney, Australia). Patients were followed for the new-onset DM.

Results: After a mean follow-up period of 31 ± 12 months, 22 patients (12%) developed new DM. In comparison between patients with DM and without DM, there were significant differences in age (46 ± 4 vs. 40 ± 7 years, p < 0.001), fasting glucose (105 ± 12 vs. 94 ± 8 mg/dl, p < 0.001), AG (15 ± 10 vs. 7 ± 7 mmHg, p < 0.001), AIx (31 ± 11 vs. 22 ± 11%, p = 0.03), and using beta-blocker (20 vs. 6%, p = 0.004). After multivariate Cox regression analysis, we found that age (Hazard Ratio 1.20, 95% CI 1.04-1.37), glucose concentration (Hazard Ratio 1.12, 95% CI 1.07-1.17), AG (Hazard Ratio 1.08, 95% CI 1.03-1.14), or AIx (Hazard Ratio 1.09, 95% CI 1.03-1.15) were independent predictors for new DM but not using beta-blocker.

Conclusion: AG and AIx were independent factors for future DM in essential HT patients. Increased aortic stiffness was associated with risk of DM.

SELF-MONITORING TECHNOLOGIES FOR TYPE II DIABETES AND THE PREVENTION OF CARDIOVASCULAR COMPLICATIONS: RESULTS FROM FOCUS GROUPS

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Background: The use of devices to monitor blood sugar, blood pressure, and physical activity is important for the prevention and treatment of cardiovascular complications (CVCs) for persons with type 2 diabetes (T2D). Feedback from patients and providers can be a vital link for the development of emerging technologies and the refinement of existing ones.

Methods: Focus groups were conducted with patients with T2D and health care professionals (n=36), as well as primary care physicians (n=2) to explore issues of accessibility, delivery, and the impact of monitoring devices on patient health, specifically for diabetes and risk of developing CVCs.

Results: Participants with T2D (onset ranged from less than one year to more than ten years) typically used a self-monitoring blood glucose device and many routinely monitored their blood pressure. Few people consistently monitored other aspects of their cardiovascular health. Device use or disuse was often determined through a "triage" of personal priorities, in terms of what health- or lifestyle-related changes were required, or what was realistically feasible. Many did not see the usefulness of bringing additional "gadgetry" into their health care routines and wanted to keep their regimens simplified. Barriers to self-management with devices included the lack of knowledge about the connections between diabetes and cardiovascular health; lack of resources available for diabetics; poor communication between patients and their physicians; poor self-management awareness; and the perceived effectiveness of monitoring devices. Perspectives from

health care providers and physicians were in general agreement with the findings from patient focus group interviews.

THE PARAMETERS OF THE OXIDATIVE STRESS AT PATIENTS WITH METABOLIC SYNDROME DURING A HEART ATTACK

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Aims: The present study proposes himself to watch over the parameters of the oxidative stress at patients with metabolic syndrome in the first hours and one month after a heart attack.

Material and method: We included in the study 40 patients who presented one acute heart attak. All patients presented elements of the metabolic syndrome: abdominal obesity, dislipidemy and IGT or IFG. We studied the parameters of the oxidative stress:we evaluated the prooxidative activity by dosage of malondialdehide and carbonilated proteins and the antioxidative activity by dosage of ceruloplasmine. We determined these parameters in the first 24 hours and 72 hours after the heart attack and again one month after.

Results: It was find out that in the first 24 hours and 72 hours, the values of malondialdehide and carbonilated proteins were higher and the value of ceruloplasmine was lower. At one month after the heart attack we saw a decreasing in the concentration of carbonilated proteins and of malondialdehide and an increasing of the values of ceruloplasmine.

Conclusions: The patients with metabolic syndrome and heart attack present an increasing in the intensity of oxidative stress, especially in the first 24 hours after the heart attack.

The antioxidative capacity of plasma is decreased in the first hours after the heart attack.

In patients with a propitious development after the heart attack, with loss of weight and correction of dislipidemy ,at one month we registered the decreasing of prooxidative capacity an the increasing of the antioxidative one.

ESTIMATION OF LEPTIN AND INSULIN CONCENTRATIONS, SERUM LIPIDS AND ANTHROPOMETRIC PARAMETERS IN YOUNG ADULTS WITH ESSENTIAL HYPERTENSION

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Excessive body mass and metabolic abnormalities: hipercholesterolemia, hiperleptinemia and increased insulin resistance, are often detected in population with essential hypertension (EH). The influence of these abnormalities on the development of EH and elevation of blood pressure (BP) still remains under discussion.

Aims: The aim of this study was to estimate concentrations of leptin, insulin, lipids and body mass index (BMI) in young subjects with EH.

Materials and methods: 56 patients with EH, aged 16-31 y., were qualified to the examined group. In the control group there were 10 healthy subjects, matched for age and sex. The anthropometric, BP and heart rate (HR) measurements were taken. The concentrations of leptin, insulin, total cholesterol, LDL, HDL and triglycerides were assessed.

Results: In the analysed group we found significantly higher values of systolic BP (138.8 ± 13.2 v. 113.4 ± 8.4 mmHg), diastolic BP (81.9 ± 8.4 v. 71.4 ± 7.3 mmHg), body mass (87.02 ± 25.10 v. 62.93 ± 12.77 kg), BMI (27.26 ± 6.29 v. 22.19 ± 3.47 kg/m²), triglycerides (1.60 ± 1.28 v. 0.85 ± 0.39 mmol/l) and insulin (37.48 ± 55.77 v. 16.70 ± 14.67 µIU/ml). We noted significantly important difference in positive history of EH (80.3% v. 40.0%). There was no significant difference in leptin, total cholesterol, LDL-, HDL-cholesterol concentrations and HR between hypertensive and healthy subjects.

Conclusions: In young adults with EH the leptin concentration correlates with BMI and insulin concentration but not with arterial hypertension. Subjects with EH and excessive body mass have higher insulinemia.

METABOLIC SYNDROME IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Introduction: The metabolic syndrome is a constellation of abnormalities-central obesity, hypertension, dyslipidemia, glucose intolerance- that together increase risk of diabetes and cardiovascular disease.

Aims: To evaluate and compare the prevalence of metabolic syndrome according to ATP-III and IDF definitions in a group of patients with acute coronary syndrome (ACS).

Methods: Prospective study of patients admitted consecutively to the Cardiology Department with a diagnosis of ACS. Height, weight and waist circumference were measured in all patients by the same observer. Blood lipids were done in the first 24 h after admission and in patients without a previous diagnosis of diabetes mellitus a standardized 75g OGTT was performed on days 4/5 after clinical stabilization. We used the ATP-III (2005) and IDF (2005) criteria for the metabolic syndrome (MS).

Results: We evaluated 411 patients, 315 males (M) and 96 females (F) with a mean age of 61,1±11,7 and 64±12,5 y.o., respectively. The mean BMI of women was 29,3±5,1Kg/m^2 and of men 27,6±3,27Kg/m^2. According to ATP-III criteria the total prevalence of MS was 49,5% being 60% (51/96) in females and 46,2% (129/315) in males. Following the IDF definition we obtained a MS prevalence of 50,1% in the global group, of 67,1% (57/96) in females and of 45% (125/315) in males.

Conclusions: This series illustrates the high prevalence of metabolic syndrome in patients with cardiovascular disease as expected. In our case prevalence in females was much higher than is males, what can be explained by both BMI and waist being more elevated in women.

STROKE IN PATIENTS WITH AND WITHOUT DIABETES MELLITUS: CLINICAL CHARACTERISTICS, GENDER DIFFERENCES AND PREDICTORS OF IN-HOSPITAL MORTALITY

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Objective: The objective of this study was to investigate and compare the clinical characteristics, gender differences and predictors of in-hospital mortality in stroke patients with and without diabetes mellitus (DM).

Methods: All patients admitted to Al-watani governmental hospital from September 2006 until September 2007 and diagnosed with acute stroke

were included in the study. Demographic data, clinical characteristics, and predictors of in-hospital mortality in all patients were compared. Pearson chi-square test and student's t test were used in univariate analysis while multiple logistic regression was used to identify predictors of in-hospital mortality.

Results: 186 stroke patients met the inclusion criteria; their mean age was 69.09±10.9 years; 48.9% of them were males and 45.2% had a positive history of DM. Diabetic stroke patients were significantly younger (*P*= 0.009) and had higher proportion of ischemic heart disease (*P*=0.04) compared to non-diabetic stroke patients. In the total stroke patients, in-hospital mortality was 21%; 27.4% in diabetic and 15.7% in non-diabetic stroke patients. Univariate analysis of diabetic stroke patients based on gender showed that male patients significantly had more hemorrhagic strokes (*P*=0.04), recurrent strokes (*P*=0.003), number of risk factors (*P*=0.001), and in-hospital mortality (*P*=0.034) compared to females. Predictors of in-hospital mortality in diabetic stroke were stroke subtype (*P*=0.049) and number of post-stroke complications (*P*=0.002). However, no predictors of mortality in non-diabetic stroke patients were identified.

Conclusion: Diabetic stroke patients have different clinical characteristics, gender differences, and predictor's of mortality after acute stroke compared to non-diabetic stroke patients.

HIGH PREVALENCE OF ABNORMAL GLUCOSE METABOLISM IN PATIENTS WITH SONOGRAPHICALLY DIAGNOSED PERIPHERAL ARTERIAL DISEASE

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Aims: Epidemiologic studies show an extremely high prevalence of type 2 diabetes mellitus (T2DM) and of impaired glucose tolerance (IGT) in patients with coronary artery disease. However, the prevalence of abnormal glucose metabolism in patients with sonographically proven peripheral arterial disease (PAD) is unknown. We aimed at investigating the prevalence of impaired glucose metabolism in patients with PAD.

Methods: We enrolled 150 consecutive patients (mean age 68 ± 11 years; 108 men and 42 women) who underwent routine duplex sonography for the evaluation of suspected or established PAD and in whom PAD was verified sonographically. Oral glucose tolerance tests were performed in non-diabetic subjects.

Results: From our patients, 68 (45.3%) had a normal glucose tolerance, 24 (16%) IGT, and 58 (38.7%) T2DM (previously known in 44 and newly diagnosed in 14 patients). Impaired fasting glucose was diagnosed in 16 patients with normal glucose tolerance and in 10 patients with IGT.

Conclusions: In conclusion, abnormal glucose metabolism was present in 65.3% of our consecutive patients with sonographically proven PAD. Routine screening for abnormal glucose metabolism (including oral glucose tolerance tests) in PAD patients is warranted.

DIABETES, HYPERGLYCEMIA AND RISK FOR CORONARY HEART DISEASE IN A TAIWANESE METROPOLITAN ADULT POPULATION

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Objective: The objective of this study was to assess the association of coronary heart disease (CHD) risk over a 10-year period with hyperglycemia (impaired fasting glucose [IFG]) and diabetes in a Taiwanese general population.

Methods: We did a cross-sectional survey in a representative random sample of 2,350 Taiwanese adults aged ≥40 years who lived in a metropolitan city, Taiwan in 2004-05. CHD risk over a 10-year period was estimated by Framingham risk score based on the LDL-C level. The high risk group was determined by the upper quartile of its distribution.

Results: The prevalence of high risk group for CHD in individuals with normal glycemia (NG), IFG, and diabetes was 24.42%, 37.74%, and 77.91%, respectively. Framingham risk score was significantly higher in diabetic participants (6.18 points higher compared to NG individuals, p< 0.001) and in those with IFG (1.78 points higher compared to NG individuals, p< 0.001). After adjusting for age, gender, smoking, alcohol drinking, central obesity, BMI, and percent body mass, IFG was associated with an OR of 1.31 (95% confidence interval [CI]: 1.01, 1.71) and diabetes was associated with an OR of 7.15 (95% CI: 4.92, 10.39) for high risk group of CHD. After further adjusting for components of metabolic syndrome, the effect of IFG became insignificant, but diabetes remained statistically significant (OR=5.90, 95%CI: 3.95, 8.79).

Conclusions: Our findings show that dysglycemia is associated with increased CHD risk. This association is consistent in diabetes, but it is explained by components of metabolic syndrome in those with IFG.

COMPARISON OF SOME RISK FACTOR FOR CORONARY ARTERY DISEASE IN PATIENTS WHO REFERRED TO SHAHID MADANI CENTER OF HEART DISEASE IN TABRIZ

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Introduction: Metabolic syndrome is important because of it constitutes a set of coronary artery disease (CAD) and type2 diabetes risk factors. CAD and major non infectious disease are as main health problem worldwide.

Objective: This study was conducted to compare some risk factors between two patients group (with and without CAD).

Methods: This study was a case-control and conducted in Tabriz, Heart Research Center. Two hundred forty one patients (182 males, 59 females) aged 40-77 years(Mean±SD, 54.5±9) that referred for coronary angiography were selected and examined. Exclusion criteria for all subjects were renal, liver, thyroid disease and MI(in previous 3 months) and consumption of blood lipid lowering agents at least in one month prior to study. All parameters were measured by standard methods. Diagnostic coronary angiography was carried out by using the Judkins technique. One hundred sixty eight (69.7%, 34 males, 34 females) had angiographically stenosis at least less than 25% in one coronary artery (with CAD) and 73(30.3%, 48 males, 25 females) had normal arteries (without CAD). Data were analyzed by using t test, Mann WhitneyU, X^2 and fisher tests.

Results: Hypertension, diabetes, obesity (BMI), central obesity (waist and hip circumference) in CAD group were 41%, 11.4%, 47%, 74.1% and in non CAD group were 38.4%,4.1%,41.4%,59.2%respectively.All these risk factors inCAD group were higher than in non CAD group, but significant differeces were not shown other than wias to hip ratio (p=0.023). Mean ± SD for age (year), BMI (kg/m^2), WC (cm), and WHR in CAD group were 55.2± 8.4, 27.8±3.6, 99.6±8.4 and 0.958±0.05 and in non CAD group were 52.8±10, 26.8±4.2, 94.4±11.3 and 0.913±0.069 respectively. Significant differences were shown for WC, WHR between two groups (p=0.001). Mean SD of serum levels of TC, TG, LDL (mg/dl) in CAD group were significantly higher than respective values for non CAD group (216.3 46.4, 230.9 119.4, 134 43.7 versus 189.9 40.8, 193.7 103, 109.7 32 (p=0.001). No significant difference were noticed in serum level of HDL between two groups.

Conclusions: Among with anthropometric and biochemical indices WC, WHR, TC, LDL showed their importantce that need more consider.

BLOOD PRESSURE PROFILE IN DIABETIC AND NONDIABETIC PATIENTS WITH CLINICALLY SIGNIFICANT CORONARY ARTERY DISEASE

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Diabetes is a risk factor of progression of CAD. The aim of our study was assessment of BP profile in diabetic patients with significant coronary artery disease.

Material and methods: The study was performed in 932 patients (640 male and 292 female, mean age 64±9) with at least one significant coronary artery stenosis (≥70%) confirmed by coronary angiography. Study group was divided into 2 subgroups: with diabetes (n=226) and without diabetes (n=671). Glucose plasma level (assessed after 8 hour fasting), weight and height were assessed before coronary angiography.

Results: Analysis of blood pressure profile revealed higher values of mean systolic blood pressure in diabetic group than in non diabetics: 24 h (130±16 mmHg vs. 123±13 mmHg, p< 0,001), day (133±16 mmHg vs. 126±13 mmHg, p< 0,001), night (127±18 mmHg vs. 118±15 mmHg, p< 0,001) and heart rate: 24 h (68±9 bpm vs. 66±9 bpm, p=0,003), day (70±10 bpm vs. 68±10 bpm, p=0,01), night (63±9 bpm vs. 61±9 bpm, p< 0,001). Analysis of relationship between fasting glucose level and mean systolic blood pressure values in diabetics reveled significant correlation in group with one coronary artery stenosis: 24 h (r=0,27, p=0,006), day (r=0,24, p=0,012), night (r=0,27, p=0,005). As distinct from non diabetics, in subgroup of atients with diabetes we did not reveal significant correlation between BMI and mean values of BP.

Patients with significant coronary artery stenosis and diabetes revealed higher mean SBPand HR values than nondiabetics regardless of compensation of diabetes measured by HbA1c level.

THE STUDY ON RELATIONSHIP BETWEEN HBA1C, POSTPRANDIAL HYPERGLYCEMIA , LIPOPROTEIN(A) AND THE ONSET SEVERITY OF CORONARY HEART DISEASE

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Aim: To investigate the relationship between the serum level of postprandial hyperglycemia, HbA1C and Lp(a) and the onset severity of CVD. To study the relationship between HbA1C and MS.

Methods: 120 patients with defined coronary heart disease were divided into acute myocardial infarction (38 cases), unstable angina pectoris (42 cases) and chronic stable coronary heart disease (40 cases). Subjects with no diabetes mellitus were further divided into four groups by quartiles of HbA1C(＜5.4%,5.4%-5.8%,5.9%-6.3%,≥6.4%). The presence of MS was defined according to the definitions of the Adult Treatment Panel III (ATP III) guideline. One-way ANOVA were performed to compare means among different groups. X^2 test was performed to compare proportions among groups. Pearson's correlation analysis and Logistic regression were performed to determine the correlation of HbA1C with cardiovascular risk factors, MS.

Results: There was a significant difference ($P < 0.01$) in the level of postprandial hyperglycemia, HbA1C and Lp(a) in acute myocardial infarction, unstable angina pectoris and chronic stable coronary heart disease. Age, waist circumference, sBP and dBP, serum total cholesterol, triglycerides, LDL cholesterol increased significantly with increasing quartiles of A1C values ($P < 0.01$). HbA1C showed a strong association with most CVD risk factors and the metabolic syndrome.

Conclusions: The serum level of postprandial hyperglycemia, HbA1C and Lp(a) are associated with the onset severity of CVD. HbA1c had a significant correlation with CVD and MS.

RESVERATROL ATTENUATES DIABETES-INDUCED ENDOTHELIAL DYSFUNCTION BY ACTIVATING OF AMPK/AKT/ENOS SIGNALING

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Epidemiological studies have shown that red wine consumption is associated with reduced in cardiovascular mortality in the general population and diabetic patients. The aim of this study was to investigate whether resveratrol (RSV, a red wine antioxidant) can attenuate diabetes progression, improves diabetes-induced endothelial dysfunctions, and delineated its underlying mechanisms. Male C57Bl/6 mice were given high-fat diet for 17 weeks. Animals developed type 2 diabetes characterized by elevated body weight, hyperglycemia, hyperinsulinemia, and hyperlipidemia. Oral gavage fed with RSV (5 or 10 mg/kg/day for 17 weeks) significantly reversed the above symptoms in high-fat diet (HFD) fed mice. RSV also attenuated plasma glucose elevation and improved insulin responses during glucose tolerance test (GTT). Furthermore, diabetic mice exhibited an increasing of leukocytes rolling, adhering, and transmigrating in the post-capillary venules of cremaster muscle. In contrast, treatment of RSV significantly attenuated diabetes-induced leukocyte rolling, adhesion, and transmigration. The phenylephrine (PE)-induced vasoconstriction was dramatically attenuated in HFD mice; whereas, RSV treatment significantly rescued the vessel responsiveness to PE. Our result also shows that the phosphorylated AMPK (5´AMP-activated protein kinase), Akt, and eNOS (endothelial nitric oxide synthase) protein levels were significantly reduced in aorta of HFD mice. Consistence with the observation on increasing of blood vessel responsiveness, RSV also elevated AMPK, Akt, and eNOS protein phosphorylation levels. The SOD and GLUTs protein expressions were not significantly changes.

Overall, these results indicate that RSV attenuated diabetes-induced endothelial dysfunctions, at least in part, by elevation of AMPK, Akt, and eNOS proteins phosphorylation.

IS THE ALTERATION OF GLUCOSE METABOLISM FREQUENT IN SEVERE HEART FAILURE?

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Aim: Investigate the prevalence of new DM and prediabetes in patients with severe HF and to establish differences between different causes of heart failure.

Methods: We have been analyzed 94 consecutive patients included in our Heart Failure Unit. In those without previous diagnosis of diabetes (determined by use of antidiabetic medication or medical previous diagnosis) were determined their glucemic state by fasting plasma glucose test and oral glucose tolerance test (OGTT). The patients were classified according to their levels of fasting plasma glucose and OGTT under three different groups (impaired fasting glycaemia, impaired glucose tolerance or double alteration), following the last recommendations of the ADA.

Results: The middle age of patients was 68 (SD ±11.1) years with a mean left ventricular function of 29% (SD ±7.22). The mean levels fasting plasma glucose was 115 mg/dl (SD ±39.57) and glycosylated haemoglobin of 7mg/dl (SD ±2.33). Of this patients, 40 % were already diagnosticated of

diabetes, 8.5% abnormal metabolism of glucose. Considering the different causes of heart failure, patients with isquemic dilated myocardiothy had a significant increase of the alterations in glucose metabolism (65.2%) compared with idiopatic dilated myocardiopathy (34.8%, $p < 0.05$).

Conclusions: Patients with severe heart falure have a high prevalence of alterations in the carbohydrates metabolism not known before. The systematic indication in this patients of an OGTT can help to the early diagnosis of new diabetes or prediabetes which is important recommend an adapted treatment to improve the prognosis.

INCREASED TROPONIN-T LEVELS SEEN IN IGT & NEW FOUND TYPE 2 DM WITH ACS IN INDIAN CAD PATIENTS

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Aim: Is to identify a better marker of unstable angina between CPK & CK-MB or Troponin-T(TNT). To Compare TNT & CPK, CK-MB in unstable angina patients with impaired glucose tolerance & new found type 2 Diabetes Mellitus(D M) to CAD patients. Unstable angina defined as acute coronary syndrome (ACS) is marked by non-specific ECG changes & associated with problems in its differentiation.

Method: The cardiac (TnT) a predictor in diagnosing patients with ACS is compared . In this study 53 patients of which 21 were without diabetes (group A} were compared with 32 patients having either impaired glucose tolerance or new found Diabetes mellitus type 2 (group B) of Unstable Angina were selected. TnT, CPK, & CKMB values are analysed using electro-chemiluminence & photometric assays, to identify a better indicator of the myocardial damage.

Results: In the non diabetic group A, level of troponin T is 0.03±0.02, and in group B level is 0.20±0.46 thus the p value 0.090 is significant. CPK, CKMB in group A are 129+73.12 & 17.76+ 4.84 and in group B level is 131.75+91.59 & 18.38+6.12, p value is 0.973 & 0.701 respectively. Troponin T is more significant in group B.

Conclusion: Cardiac troponins T is highly sensitive, specific markers for detection of myocardial damage, It compares better to both CPK &CKMB. Troponin-T is excellent marker for diagnosing the unstable angina (ACS) with impaired glucose tolerance or new found type-2DM a silently damaging condition & has high accuracy of test of 98.11%.

PREVALENCE OF NEW DIABETES AND PREDIABETES IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Purpose: Diabetes mellitus type 2 is a known cardiovascular risk factor. The identification during hospitalization of alterations in glucose metabolism in patients with acute coronary syndrome might determine what patients are in a prediabetic state. Once identified, the adoption of changes in lifestyle and a suitable treatment might prevent the develop to new diabetes.

Methods: We include in this study 345 consecutive patients hospitalized with diagnosis of acute coronary syndrome. In those without previous diagnosis of diabetes were determined their glucemic state by fasting plasma glucose test and oral glucose tolerance test (OGTT). Patients were classified according to their levels of fasting plasma glucose and OGTT under three different groups (impaired fasting glycaemia, impaired glucose tolerance or double alteration), following the last recommendations of ADA guidelines.

Results: The included patients had a mean age of 69 years, 68,4% were males, and 42,9% had previous ischemic cardiopathy. The diagnosis at the discharge was unstable angina (37,4%), UNSTEMI (31,5%) or STEMI (31%). We indentified 38,3% patients with previous diagnose of diabetes. During the acute coronary syndrome we determined the presence of alterations in glucose metabolism in those patients without previous diagnosis of diabetes (107 patients, 31%), founding new diabetes in 10,1%, impaired fasting glycaemia 9%, impaired glucose tolerance 9,9% and double alteration in 2%. Only 106 patients (30,7%) had a normal glucose metabolism.

Conclusions: Patients with acute coronary syndrome have a high prevalence of alterations in the carbohydrates metabolism not known before. Only a third of them have a normal metabolism.

INCIDENCE OF NEW DIABETES AND PREDIABETES IN PATIENTS WITH ACUTE CORONARY SYNDROME AND AFTER 6 MONTHS OF THE DISCHARGE

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Introduction: The diagnosis of new diabetes mellitus type 2 and the prediabetic state have been related to an increased risk of cardiovascular events. In this study we want to determine the prevalence of the glucose metabolism alterations in patients hospitalized with diagnosis of acute coronary syndrome and if this diagnosis remains in chronic phase, when the stress process have stopped.

Methods: We include 167 consecutive patients hospitalized with diagnosis of acute coronary syndrome. In those without known diabetes we determined the their glucemic state by fasting plasma glucose test and oral glucose tolerance test. The analysis were realized during the hospitalization and 6 months after hospital discharge. Patients were classified in three groups (impaired fasting glycaemia, impaired glucose tolerance or double alteration), following the last recommendations of ADA guidelines.

Results: All 167 patients were hospitalized with the diagnosis of acute coronary syndrome. Mean age was 68 years, 66,5% were males. 40,7% of this patients had known diabetes. Among the rest of patients we find alterations of the glucose metabolism in 31,2% (new diabetes 11,4%, impaired fasting glycaemia 7,2%, impaired glucose tolerance 10,2% and double alteration 2,4%). After 6 months of discharge, we found an alterated metabolism in 34,7% (19,2% new diabetes, impaired fasting glycaemia 10,2%, impaired glucose tolerance 3% and double alteration 2,4%). Only 24,6% of patients had a normal metabolism in the chronic phase.

Conclusions: Patients with acute coronary syndrome have a high incidence of alterations in the carbohydrates metabolism not known before. These alterations remain without significant changes during the chronic phase.

DECREASING THE RISK OF CADIOVASCULAR EVENTS BY INTERVENTION OF METABOLIC SNDROME - A FOLLOW-UP STUDY IN CHINESE POPULATION

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Aims: To explore decreasing the risk of cadiovascular events in individuals with metabolic sndrome in Chinese population.

Methods: 589 age (55.5+7.0 years) matched cases with MS divided into drug-intervention group and conventional group since 2004, we follow up

4years. we also set up a normal control without MS to observe the natural basal line.

Results: By comprising 3 groups, MS patients with CVD events were 2.45 times higher than that in Normal control (P=0.009, RR=2.45(95%CI:1.23-4.87)). By medicine intervention we saw the survival curve and hazard curve changes.

Conclusions: It was possible to decrease the risk of cadiovascular events by intervention of metabolic sndrome in Chinese population.

THE METABOLIC SYNDROME, ANGIOGRAPHICALLY DETERMINED STABLE CORONARY ARTERY DISEASE, AND SUBCLINICAL INFLAMMATION

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Aims: We aimed at investigating the individual and joint associations of coronary artery disease (CAD) and of the metabolic syndrome (MetS) with subclinical inflammation.

Methods: We enrolled 900 patients undergoing coronary angiography for the evaluation of suspected or established stable CAD. The MetS was defined according to NCEP ATP-III criteria; coronary stenoses with lumen narrowing ≥50% were considered significant.

Results: From our patients 496 (55.1%) had significant coronary stenoses; the prevalence of the MetS was higher in the patients with significant stenoses than in those without such lesions (41.3% vs. 34.4%; p = 0.033). The inflammatory marker hsCRP was significantly higher in MetS patients than in those without the MetS both among patients with significant coronary stenoses (0.49 vs. 0.43 mg/dl; p = 0.004) and in subjects who did not have such lesions (0.46 vs. 0.36 mg/dl; p < 0.001). Whereas hsCRP in univariate analyses was significantly elevated in patients who fulfilled the large waist (p < 0.001), the low HDL (p < 0.001) and the elevated fasting glucose (p = 0.003) criteria of the MetS, onlythe low HDL cholesterol criterion (F = 21.22; p < 0.001) remained significantly associated with hsCRP after multivariate adjustment. In contrast to the results for the MetS, hsCRP irrespective of the presence of the MetS were not significantly elevated in patients with significant stenoses.

Conclusions: Subclinical inflammation is strongly and significantly associated with the MetS but not with angiographically determined stable CAD. Low HDL cholesterol drives the association between the MetS and subclinical inflammation.

MICROALBUMINURIA ELEVATED IN PREDIABETIC& DIABETIC CAD PATIENTS FOLLOWING PCI

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Aim: To evaluate incidence of contrast induced nephropathy (CIN) following Percutaneous intervention (PCI) by changes in serum creatinine and involvement of microalbumin & urine microalbumin per gm creatinine in diabetic and prediabetic patients. In India 30% of population have risk factors of CAD, PCI and coronary angiogram remains the gold standard. Iatrogenic renal function impairment from exposure to contrast media (CM) is unclear. Study to observe effect on serum creatinine levels and microalbumin in urine of CAD patients undergoing PCI having normal renal function, and the association with age, diabetes, for effect of volume of contrast media, to identify CIN & microalbuminuria is taken up with pre-procedure levels as control.

Method: 70 CAD patients having normal renal function selected for PCI, 39 prediabetic & diabetic, 21 normal, Pre- procedure blood & urine samples taken as control, Using Hitachi 912 assays for microalbumin & creatine, an absolute increase of 0.5 mg/dl serum creatinine, at 48 and72 hours following exposure to CM as accepted definition of CIN is taken, urine microalbumin per gm creatinine was calculated & contrast volume measured.

Results: In this study, serum creatinine levels, urine microalbumin and microalbumin per gm creatinine levels.showed risk of CIN 16.7%. In the non diabetic microalbuminuria sample A B, C was 7.05±2.05,10.68±3.29, and13.33±4.25 and in diabetics it was15.14±5.02, 30.01±9.77 and 52.72±8.22 significance 0.034*.

Conclusion: At risk for CIN is 16.7%. The relation between urine microalbumin in diabetic and non diabetic was (p< 0.034) and microalbumin per gm creatinine (p=0.049) Thus elevation post procedure is significant.

COMPLEX TREATMENT INCLUDING ANTIHYPERTENSIVE THERAPY EFFICIENCY IS IMPACT ON THE CARDIOVASCULAR COMPLICATIONS FREQUENCY AT TYPE 2 DIABETES PATIENTS WITH METABOLIC SYNDROME

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Objective: Antihypertensive therapy (AT) efficiency influence on the cardio-vascular complications frequency at type 2 diabetes mellitus (T2DM) patients with metabolic syndrome (MS) was estimated.

Methods: 792 T2DM patients with MS (age 59-69 yrs, disease duration 12-15 yrs) were enrolled. MS has been diagnosed by NCEP ATP III criteria. AT consisted from ACF inhibitors, third generation of calcium antagonists, diuretics, selective ß-adrenoblockators, imidazoline receptors agonists and their combinations. AT duration was three years. T2DM patients were divided on four groups (1 -188; 2nd -189; 3rd - 203 and 4th - 212), which differed from AT composition and efficiency. HbA1c in 1-4 groups was (7.8±0.1; 7.85±0.8; 7.58±0.2 vs 8.15±0.1) %, respectively, triglycerides levels were (3 0±0.2; 3.0±0.273.2±0i vs 3.5±0.3) mmol/l, respectively. Aim arterial pressure level (AAPL) was < 130/80 mm.m.p.

Results: In 4th group (maximum AT efficiency; 43.0±3.4 % T2DM patients arrived AAPL) heart attacks frequency was (10.0±0.63) % as compared with 1sl - 3rd groups (AT efficiency 10.0±2.:'.; 12.0±2.4; 16.0+2.6 %) heart attacks frequencies were (23.0±1.0; 14.0±2.5; 11.0±2.2) %, respectively, p< 0.001. Stroke frequencies in 4lh group in comparison with 1st - 3rd groups,were (7.0+0.02) vs (41.0±1.5; 36.0+-3.5; 39.0±3.4) %, respectively (p< 0.01). Retinopathy frequencies were: (8.0±1.9) vs (13.0+0.9; 10.0±2.2; 11.0±2.2) %. Nephropathy frequencies were, respectively (8.0±1.9) vs (13.0+0.9; 10.0±2.2; 11.0±2.2) %, p< 0.05.

Conclusions: Effective AT considerably decrease heart attacks, stroke, retinopathy, nephropathy frequencies at T2DM patients with MS.

Keywords: 1. Diabetes, 2. Metabolic Syndrome and Cardiometabolic Risk, 3. Peripheral Vascular Disease, 4. Stroke.

CORONARY ARTERY DISEASE PATIENT'S FIRST DEGREE RELATIVES AND ATHEROSCLEROSIS IN INDIA

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Aim of the study was to investigate the relationship between the serologic status concerning Chlamydia pneumoniae (Cp), Helicobacter pylori (Hp),

Cytomegalovirus (CMV), Chlamydia trachomatis (Ct) and high sensitive C-reactive protein (hsCRP) in coronary artery disease (CAD) patient's first degree relatives, which remain an unrevealed issue in literature. We studied 192 CAD patients (pts), 140 CAD-patient first degree relatives (CAD-R) and 192 controls with no evidence of obstructive CAD. Seropositivity for Cp IgG (71 Vs 50, p=0.090), Hp IgA (98 Vs 59, p=0.06), Hp IgG (77 Vs 55, p=0.09), CMV IgG (62 Vs 44, p=1.00), Ct IgG (7 Vs 6, p=0.78) was not significantly higher in CAD- pts compared to CAD-R. However, seropositivity to Cp IgA (154 Vs 96, p=0.020) and hsCRP (114 Vs 65, p=0.014) were significantly higher in CAD-pts compared to CAD-R. Further differences between CAD-R and controls were significant for all seropositive groups and hsCRP. Therefore, this study adds to the strong evidence of association of Cp specific IgA and hsCRP with CAD and CAD-R is at higher risk for disease progression. Our investigation adds to the strong evidence in association of Cp specific IgA and hsCRP with CAD. Furthermore CAD-R is also at higher risk level for CAD progression compared to controls.

THE METABOLIC SYNDROME PARAMETERS AND HEART FAILURE SEVERITY IN PATIENTS WITH PRIOR MYOCARDIAL INFARCTION

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Purpose: The aim study was to analyze the prevalence of metabolic syndrome and the correlation between the metabolic syndrome clustering components and heart failure severity in patients with prior myocardial infarction.

Methods: We performed a cross-sectional study including 65 patients with heart failure post-myocardial infarction with a mean age at 64.1 (9.1). We evaluated the prevalence of metabolic syndrome parameters (individual and additive) and analyzed their impact on heart failure severity by comparing NYHA I+II and NYHA III+IV group regarding. The elements of metabolic syndrome independently correlated with heart failure severity were identified by means of logistic regression method.

Results: The prevalence of metabolic syndrome in our study was high (49.23%). High blood pressure, high fasting glucose, central obesity and low HDL-Cholesterol levels were significantly associated with severe heart failure (NYHA III and IV classification) in univariate logistic regression analyses. The only two independent variables: hyperglycaemia and reduced HDL-Cholesterol returned high enough levels of OR and 95%CI (1.79; 1.45-2.89 and 0.83; 0.67-0.91 respectively) to reach statistical significance beyond adjustment risk factors. In our study was significant correlation between presence of complete metabolic syndrome criteria and heart failure severity, either measured in NYHA IV categories (p=0.002).

Conclusions: Our study has identified the high prevalence of metabolic syndrome among patients with heart failure. Among the criteria for metabolic syndrome, hyperglycaemia and reduced HDL-Cholesterol levels had a strong association with heart failure severity. Our findings are relevant for clinical practice and intervention, and the aggressive treatment for conventional risk factors has also been effective in the prevention of heart failure.

IMPROVED SYNERGESTIC EFFECT IS SEEN WITH BETAINE IN CAD PATIENTS ON ASPRIN /CLOPIDOGREL

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Aim: Whether Betaine a platelet agonist has effect on CAD patients taking Aspirin and Clopidregel. The risk of recurrent vascular events among patients taking aspirin remain relatively high. Platelet function tests based on variability in platelet responses shows aspirin resistance. Betaine ,i.e., trimethylglycine ,has action similar to aspirin is investigated in CAD patients.

Method: To study the potential anti-platelet activity of Betaine & its effect on platelets in CAD patients taking aspirin/aspirin+clopidogrel by doing whole blood impedence aggregometry on patients sample within one hour of blood collection. Whole blood samples of CAD patients on therapy (n=20; 18male ,2 female) were analysed by platelet function tests & repeated with addition of 20 mL Betaine(50 mLml). The procedure assessed platelet activation in pathways directly and indirectly to cyclooxygenase-1, the enzyme that inhibits ASA, using Arachidonic acid, & collagen, ADP,& thrombin that stimulates thrombin receptor, finally Ristocetin was used to induced aggregation and AUC was recorded in both conditions.

Results: In all 20 samples the aggregation with Aspirin was 54.85±9.72 and enhanced response with addition of Betaine was 48.70±8.55 . In Collagen test, it was48.63±8.44 and to Betaine 39.32±7.50 (P=0.002), In ADP test it was 62.74±8.53and with Betaine 55.63±8.11 (P=0.017). In TRAP test it was94.11±8.80, with Betaine 84.37±9.06 (P=0.043), Improved effect seen with Betaine. Maximum significance observed with ristocetin, value was97.80±10.11 and reduced to 6.40±3.12, a significance of< 0.001.

Conclusion: Study demonstrates aspirin resistance exists in CAD patients, Betaine enhances and improves antiplatelet effect, Betaine has a synergistic action with aspirin/clopidogrel.

FEATURES OF CORONARY ATHEROSCLEROSIS OF PATIENTS WITH METABOLIC SYNDROME

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Aims: To investigate connection of metabolic syndrome´s components and expressed of coronary atherosclerosis.

Methods: 32 patients with coronary atherosclerosis (verificated by angiography) and with metabolic syndrome components (obesity, hypercholesterolemia, pre-diabetes/diabetes, hypertension) were examined before coronary artery bypass grafting (CABG). The patients included in 4 clinical groups depending on a quantity of coronary arteries damage: I gr.: 3 arteries damage, II gr.: 2 arteries damage, III gr. 1 vessel damage. IV gr.: arteries intact. Were determined: body mass index (BMI), blood pressure, monitoring lipids, glucose, insulin fasting levels with definition of an index HOMA. At an HOMA index > 2.77 defined insulin resistance (IR) and angiography was made.

Results: Maximal average insulin fasting level found in the 1 group. Insulin resistance was found in all 4 groups. Data of dependence of the rate coronary atherosclerosis from the insulin level and IR in all groups: in patients with diabetes, pre-diabetes, and patients with normal glucose level was found. Highest levels of cholesterol were found in group 2 with 2 arteries damage. But the difference between results achieved on group 1 was not significant. The cholesterol's level in remaining groups found lower than in groups 2 and 1, but with low difference. Exposed the dependence into coronary arteries damage and HOMA index and insulin level.

Conclusions: high insulin level and HOMA index on group 1 with absence of significant difference of the level of cholesterol allows to expect higher dependence of the rate of coronary atherosclerosis.

METABOLIC SYNDROME IN PATIENTS WITH MYOCARDIAL INFARCTION

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Background and aims: The aim of this study was to estimate the prevalence of metabolic syndrome (MS) in patients with acute myocardial infarction (AMI) using the National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) definition.

Materials and methods: Patients with AMI (STEMI and NSTEMI) confirmed by coronary angiography to PTCA were divided into two groups: with diabetes mellitus (DM) and without previously diagnosed DM. BMI, waist circumference, lipid profile, blood pressure were checked, left ventricular ejection fraction (LVEF) by echocardiography. In the group without DM OGTT was performed on the 5-th day after AMI.

Results: The study comprised 210 patients, in this 25% women aged 55.6 ± 9.5 (age range 28-80 yrs), of which 169 (81%) were treated with PTCA while the remaining ones were treated pharmacologically and 18 (8%) received a by-pass. Fifty patients (24%) had previously diagnosed DM. MS prevalence was 39%, in this 10% women. Significant correlations were observed between MS and LVEF and between the number of involved coronary vessels ($p< 0.05$). Prevalence of shock, arrhythmia, heart failure was correlated with MS too ($p< 0.05$).

Conclusions:

1) MS was diagnosed in 39% of patients with AMI, mainly in men.

2) OGTT should become a routine procedure in patients with AMI for final evaluation in the diagnosis of MS.

THREE-YEAR INCIDENCE OF CARDIOVASCULAR DISEASE AND ITS PREDICTORS IN HEALTH CENTER OF GASTOUNI

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Background: The aims of the present work were to investigate whether dietary habits are associated with socio-economic status (SES), and if they modify the relationship between SES and CVD risk factors.

Methods: During 2006-2007, information from 377 men (21-95 years old) and 381 women (18-93 years old) was collected (75 % participation rate). Among several sociodemographic, clinical and biological factors, adherence to the Mediterranean diet was assessed by a special diet score (Mediterranean Diet Score, MDS) that incorporated the inherent characteristics of this traditional diet. CVD risk factors were examined across the participants´ educational level and annual income that defined their SES.

Results: Low SES groups exhibited higher prevalence of CVD risk factors, such as obesity, hypertension, diabetes mellitus and hypercholesterolaemia (all $P < 0.01$). Low SES groups also showed less adherence to the Mediterranean diet than high SES groups (MDS: 23.2 (sd 8.1) v. 25.4 (sd 5.6), $P < 0.001$). Higher SES index was associated with lower likelihood of having hypercholesterolaemia (OR = 0.91; 95 % CI 0.83, 1.00) and diabetes (OR = 0.83; 95 % CI 0.69, 0.95), after adjusting for various potential confounders. However, the previously mentioned inverse relationship observed between SES and prevalence of CVD risk factors was mainly explained by the dietary habits of the participants.

Conclusions: Low SES groups showed less adherence to the Mediterranean diet compared with high SES groups. This finding may, in part, explain the higher CVD risk factors profile observed among low SES participants.

MECHANISMS OF HYPOGLYCEMIC ACTION OF DES-ASPARTATE-ANGIOTENSIN I IN DIET-INDUCED DIABETIC MICE

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Type 2 diabetes mellitus is often associated with obesity and hypertension. Angiotensin II exerts negative modulation on insulin signal transduction and contributes to insulin resistance, which is a major cause of type 2 diabetes. Hence, ACE inhibitors and angiotensin receptor blockers have been reported to improve insulin resistance. Des-aspartate-angiotensin I (DAA-1), a metabolite of angiotensin I that also counteracts the actions of Ang II, has been shown to exert hypoglycemic action in type 2 diabetic animals (1). The hypoglycemic action of DAA-1 was further investigated in unhealthy diet-induced diabetes. Male C57BL/6J mice were fed either a high-fat-high-sucrose (HFD) or normal diet for 52 weeks. The HFD mice were concurrently administered either DAA-1 (600nmole/kg/day) or vehicle (water) by gavage. The weight, blood glucose and blood insulin were measured bi-monthly. HFD animals developed hyperglycemia after 22 weeks and DAA-1 exerted significant hypoglycemic action, but had no effect on the obesity and plasma insulin level. Animals were sacrificed and skeletal muscles excised for cellular studies at 52 weeks. In skeletal muscle of HFD animals, DAA-1 significantly (i) attenuated the overexpression of pJNK and pIRS-1^{307} (ii) restored the depressed insulin-stimulated tyrosine phosphorylation of IRS-1, PI3K activation, pAkt phosphorylation and GLUT4 translocation. The data show that DAA-I is an effective prophylactic oral hypoglycemic agent in unhealthy diet-induced diabetes. It acts by attenuating insulin resistance.

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MECHANISMS OF INSULIN RESISTANCE IN MICE OVEREXPRESSING PREF-1, A NEW MODEL OF PARTIAL LIPODYSTROPHY

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Pref-1 is a preadipocyte-secreted protein that inhibits adipogenesis *in vitro* and *in vivo*. Pref-1 is synthesized as a transmembrane protein whose extracellular domain is cleaved to release a 50 KDa soluble form that acts in a paracrine/endocrine way to inhibit adipocyte differentiation. Mice overexpressing the soluble form of Pref-1 in adipose tissue exhibit impaired adipogenesis, glucose intolerance and insulin resistance. To gain insights into the mechanisms involved in the insulin resistance of Pref-1 transgenic mice, we conducted a hyperinsulinemic-euglycemic clamp assay in Wt and Pref-1 transgenic mice that were chronically fed a high fat diet. Overexpression of Pref-1 prevented diet-induced obesity. However, despite a decrease in fat mass, Pref-1 transgenic mice exhibited higher degree of whole-body insulin resistance after 17 weeks on a high fat diet. Decreased whole-body insulin sensitivity in Pref-1 transgenic mice was associated to a selective decrease in insulin-stimulated Akt activity, IRS phosphorylation and glucose transport in adipose tissue and muscle. Conversely, glucose production and activation of the insulin signaling pathway in liver remained similar in both groups, suggesting comparable hepatic insulin sensitivity. Insulin resistance in Pref-1 transgenic mice was associated to higher circulating levels of FFA and triglycerides, as well as increased accumulation of diacylglyerol in muscle. These findings suggest that decreased adipogenesis in Pref-1 transgenic mice results in a decreased

capacity for triglyceride storage in adipocytes, leading to hyperlipidemia, ectopic lipid accumulation in muscle and the development of insulin resistance. Our study identifies Pref-1 transgenic mice as a new rodent model of partial lipodystrophy.

THE INSULIN SENSITIZER N-(5-ADAMANTANE-1-YL-METHOXY-PENTYL)-DEOXYNOJIRIMYCIN (AMP-DNM) ACUTELY INCREASES WHOLE BODY FAT OXIDATION

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Objective of the study: Treatment of genetically obese *obob* mice with the glycosphingolipid synthesis inhibitor AMP-DNM results in a strong improvement of insulin signaling and glucose homeostasis. To unravel the possible mechanism behind these improvements we investigated the effects of this drug on whole body substrate oxidation and energy expenditure.

Results: In the first hours after initiation of dietary treatment, fat oxidation increased sharply (nocturnal; control 0.071 vs AMP-DNM 0.160 kcal/hr, $p< 0.05$) whereas energy expenditure (nocturnal; control 0.503 vs AMP-DNM 0.437 kcal/hr, $p< 0.05$) as well as food intake decreased significantly. During the third week of treatment diurnal and nocturnal fat oxidation were 75% and 92% higher in the treated animals. During the fifth week of treatment however, no differences were observed in fat oxidation, energy expenditure and food intake between treated and control animals, suggesting induction of a compensatory mechanism. Yet at this point treatment had resulted in highly significant positive effects on plasma glucose (control 10.6 vs AMP-DNM 6.9 mmol/L, $p< 0.05$), HbA1C (6.1 vs 4.3 %, $p< 0.05$), liver weight (3.1 vs 2.2 g, $p< 0.05$) and liver triglyceride content (560 vs 210 nmol/mg protein, $p< 0.05$).

Conclusion: Treatment of *obob* mice with the iminosugar AMP-DNM acutely enhances fat oxidation and lowers energy expenditure. This effect may be mediated by an increase in PDK4 expression, which we observed in liver of AMP-DNM treated animals. The metabolic switch induced by AMP-DNM may contribute to the positive effect of AMP-DNM on manifestations of the metabolic syndrome.

REDUCTION OF GLYCOSPHINGOLIPID BIOSYNTHESIS ENHANCES REVERSE CHOLESTEROL TRANSPORT IN MICE

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Objectives: Recent reports indicate that glycosphingolipids play an important role in regulation of carbohydrate metabolism. We have shown that the iminosugar AMP-DNM (N-(5'-adamantane-1'-yl-methoxy)-pentyl-1-deoxynojirimycin), an inhibitor of the enzyme glucosylceramide synthase, is a potent enhancer of insulin signaling in rodent models for insulin resistance and type 2 diabetes. In the present study we determined whether AMP-DNM also affects lipid homeostasis and in particular the reverse cholesterol transport pathway.

Results: Treatment of C57BL/6J mice with AMP-DNM for 5 weeks decreased plasma levels of triglycerides and cholesterol by 35%, whereas neutral sterol excretion increased twofold. Secretion of biliary lipid also increased twofold, which resulted in a similar rise in bile flow. This effect was not due to altered expression levels or kinetics of the various export pumps involved in bile formation. However, the bile salt pool size increased and the expression of Cyp7a1 was upregulated. In vitro experiments using HepG2 hepatoma cell line revealed this to be due to inhibition of fibroblast growth factor (FGF)19 mediated suppression of Cyp7a1 via the FGF receptor.

Conclusion: Pharmacological modulation of glycosphingolipid metabolism showed surprising effects on lipid homeostasis in C57BL/6J mice. Plasma cholesterol and triglyceride levels decreased, biliary lipid secretion doubled and also the endpoint of reverse cholesterol transport, neutral sterol excretion doubled at 100 mg/kg/day AMP-DNM.

HYPOGLYCEMIC EFFECT OF *ASTRAGALUS POLYSACCHARIDES* IN DIET INDUCED INSULIN RESISTANT C57BL/6J MICEAND ITS POTENTIAL MECHANISM

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To further confirm the hypoglycemic effect of astragalus polysaccharide (APS) and to investigate its possible mechanism underlying the improvement of insulin resistance. Diet-induced insulin resistant C57BL/6J mice treated with or without APS (orally, 700 mg/kg/d) for 8 weeks were analyzed and compared. Simultaneously, an insulin resistant C_2C_{12} cell model and an ER stressed HepG2 cell model were established and incubated with or without APS (200 μg/ml) for 24 hours respectively. Systematic insulin sensitivity was measured with an insulin-tolerance test（ITT）and an homeostasis model assessment (HOMA IR) index. Metabolic stress variation was analyzed for biochemical parameters and pathological variations. The expression and activity of protein tyrosine phosphatase 1B (PTP1B) was measured by immunoprecipitation and Western blot. The ER stress response was analyzed through XBP1 transcription and splicing by real-time PCR.APS could alleviate insulin resistance and ER stress induced by high glucose in vivo and in vitro respectively. The hyperglycemia, hypolipemic and hyperinsulinemia status were controlled with APS therapy. Insulin action in the liver of insulin resistant mice was restored significantly with APS administration. APS enhanced adaptive capacity of the ER and promoted insulin signaling by the inhibition of the expression and activity of PTP1B. Furthermore, the anti-obesity effect and hypolipidemia effects of APS were probably due partly to decreasing the leptin resistance of mice, which would positively couple with the normalization of plasma insulin levels. We have shown that APS has beneficial effects on insulin resistance and hyperglycemia. The mechanism is related to the alleviation of ER stress and insulin resistance under hyperglycemia conditions.

ANTI-METABOLIC SYNDROME ACTIVITY OF ADENOSINE IN STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS

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Despite the well-documented that adenosine has health-related physiological activities in animal and human studies, but the detail mechanisms remain unknown. Thus, the purpose of the present study was to identify whether oral administration of adenosine affects on metabolic syndrome-related parameters in stroke-prone spontaneously hypertensive rats (SHRSP) after high fat diet intake. The rats aged 6-weeks-old were divided into control and adenosine groups, were administered water or water with adenosine, respectively, for 8 week. The rats had free access to high fat diet. The present results showed that oral administration of adenosine has blood pressure lowering effect compared with control group. Oral administration of adenosine also showed increased plasma nitric oxide level; this result corresponded well with its blood pressure lowering effect. We found out that adenosine is effective to improve plasma lipid, glucose, and kidney functions' parameters. Adenosine also increases plasma adiponectin level and accompanied by the alleviation of hyperinsulinemia in SHRSP. In conclusion, oral administration of adenosine is effective to

improve metabolic syndrome-related parameters in SHRSP and could prevent the progression of metabolic syndrome.

LIPOPOLYSACCHARIDE ENHANCED ER STRESS-INDUCED CELL DEATH IN H9C2 RAT CARDIOMYOCYTE

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Aims: ER stress is elevated in obesity and diabetes which initially activates the unfolded protein response (UPR) to promote cell survival by reducing misfolded protein. UPR signaling also promotes apoptotic cell death if ER stress is sustained. The present study aimed to examine whether Toll-ike receptor activation would unbalance the survival and death of cardiomyocyte in face of the elevated ER stress and to investigate the underlying mechanisms.

Methods: ER stress of H9c2 cardiomyocyte was induced by serum- and glucose- deprivation plus deoxyglucose to simulate ischemia (sI). LPS (3 μg) was co-administrated with or without pharmacological tools, such as SB203580 (p38 MAPK inhibitor) and SP600125 (JNK inhibitor). Cells in medium and on the plate were collected after 20h treatment. After staining with Annexin V-FITC and propidium iodide for 10 min, cell survival and death was analyzed by flow cytometry.

Results: LPS did not alter the survival and death of H9c2 cardiomyocytes cultured in DMEM medium containing 2% FBS. However, LPS pronouncedly decreased the cell survival and increased the apoptosis, late apoptosis and necrosis under sI condition. LPS-enhanced cell death under sI condition could not be reversed by SB203580 and SP600125. SB203580 delayed the time to necrosis by increasing the proportion of cells in the end stage of apoptosis within 24h treatment.

Conclusion: LPS could enhance ER stress-induced death of cardiomyocyte in sI condition, and the effect of LPS was not mediated via p38 and JNK signaling pathway. The detailed mechanism remains for further investigation.

INSULIN RESISTANCE IN MICE, BORN TO DIABETIC PREGNANCY, IS ASSOCIATED WITH ALTERED PANCREATIC AND ADIPOSE TISSUE FUNCTIONS

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In the recent years, we have developed a model of insulin resistance in the mice born to dams which were rendered diabetic by the administration of streptozotocin. The present study is conducted on these insulin-resistant (IR) offspring which are hyperinsulinemic, hyperglycemic and hyperlipidemic at adulthood. 12 adult IR offspring and 12 control offspring were selected and we have mainly determined the expression of mRNA of agents known to modulate pancreatic and adipose tissue functions. We observed that serum insulin concentrations, and the mRNA transcripts of insulin gene transcription factors, Nkx6.1 and Maf-A, were upregulated in the pancreas of these IR offspring. Besides, their pancreatic functional capacity seemed to be exhausted as evidenced by low expression of pancreatic Glut2 and glucokinase mRNA. Though IR offspring exhibited low adipose tissues, their adipocytes seemed to be differentiated into macrophage-like cells, as they expressed upregulated mRNA transcripts of CD14 and CD68 antigens, generally expressed by macrophages. However, there was no peripheral macrophages infiltration into adipose tissues, as the mRNA expression of F4/80, a true macrophage marker, was not detectable. Furthermore, the mRNA expression of IL-6, TNF-α and TLR-2, the key players of insulin resistance, was upregulated in the adipocytes of these IR offspring. Insulin resistant state in animals, born to diabetic pregnancy, alters pancreatic and adipose tissue functions and these offspring are prone to develop metabolic syndrome.

EXACERBATED PRODUCTION OF INTESTINAL LYMPH CHYLOMICRONS IS ASSOCIATED WITH INCREASED TRANSPORT OF CHOLESTEROL AND INTESTINAL HYPERTROPHY IN THE PRE-DIABETIC JCR:LA-CP RAT

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Over-production of intestinal chylomicron (CM) is thought to contribute to dyslipidemia during cardiovascular disease (CVD). The impact of insulin resistance (IR) and/or obesity during pre-diabetes on CM production has not been elucidated. The aim of this study was to determine the intestinal lymph apolipoprotien-B48 (apo-B48), (ii) the bi-directional transport of intestinal cholesterol and (iii) intestinal morphology in the obese/pre-diabetic JCR:LA-cp rat.

Lymph CM were collected from IR (n=8) and lean animals (n=8) following a gastric saline or lipid infusion (20% Intralipid, 4.0% glucose in saline for 3 hr). Bi-direction transport of cholesterol was measured by adapted Ussing chamber techniques. Intestinal villi height, width and area, as well as enterocytic and immuno-histochemical (IHC) distribution of apo-B48 was determined.

IR rats had 2.5-fold greater apo-B48 in lymph during the fasted state relative to lean, non-IR controls, but net cholesterol and TG was not different. IR rats had a further increase (x1.8-fold; $p< 0.05$) in apo-B48 following a lipid infusion relative to lean rats. In IR rats, absorptive flux of cholesterol was increased (mucosal to serosal 32.5±2.0 vs 25.5±3.2 %/cm^2), and luminal efflux was increased 2-fold (serosal to mucosal 26.2±5.0 vs 64.5±5.2 %/cm^2) compared to lean rats, respectively. Mucosa villi width and height was increased in IR rats corresponding with increased IHC distribution of apoB48 in the crypt axis.

Hypertrophy of the intestinal mucosa observed during pre-diabetes may contribute to CM over-production. Results suggest that IR alters intestinal lipid transport and CM production, which may contribute significantly to dyslipidemia and CVD risk.

RESVERATROL PROTECTS AGAINST CARDIAC ABNORMALITIES THROUGH AKT/GLUT4 PATHWAY IN RATS WITH INSULIN RESISTANCE SYNDROME

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It has been reported that resveratrol (RSV) protects against insulin resistance by

activating SIRT1 and PGC-1α. Currently, our result also indicates that ER is a key regulator in RSV-stimulating insulin-dependent and independent glucose uptake which might account for the protective effects of RSV on diet-induced insulin resistance syndrome. However, it remains unknown whether RSV can protect against insulin resistance-induced myocardial dysfunctions.

Male Sprague-Dawley rats were given high cholesterol-fructose (HCF) diet for 15 weeks; the rats developed insulin resistance syndrome characterized by elevated blood pressure, hyperlipidemia, hyperinsulinemia, impaired glucose tolerance, and insulin resistance. Oral gavage fed with RSV (1 mg/kg/day for 15 weeks) significantly reversed the above symptoms in HCF rats. Under euglycemic-hyperinsulinemic condition, RSV treatment dramatically increased insulin-stimulated whole-body glucose uptake and steady-state glucose uptake of the heart in HCF-fed rats as well as enhanced membrane trafficking activity of GLUT4 and increased phosphorylation of Akt (thr308) in insulin-resistant cardiac muscles. Our result also shows that the myocardial contractile functions were significantly

impaired in insulin resistant individuals. RSV treatment significantly improved cardiac functions including elevated cardiac output, ejection fraction, stroke volume, and left ventricular end systolic elastance and reduced effective arterial elastance (Ea) in RSV-treated HCF rats compared with vehicle-treated controls. Our results indicate that the beneficial effects of RSV, at least in part, by activating of Akt/GLUT4 in insulin resistant heart. In addition, our findings also demonstrate that RSV is possible therapeutic agents to prevent and treat metabolic syndrome and cardiovascular disease.

HEPATIC TRANSCRIPTIONAL RESISTANCE IN TWO COMPLEMENTARY MURINE MODELS OF OBESITY

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Background: The search for specific genes causing metabolic impairment induced by obesity has been redundant so far; looking for genetic factors that ensue obesity, we probed the hepatic transcriptome in the switch from fast to feeding in complementary murine models of obesity.

Materials and methods: We investigated obesity of both dietary (10 weeks high-fat diet, HF) and genetic (leptin-deficient ob/ob mice) origin. Before sacrifice, a set of mice for each group was fasted (16 hours), while the remaining had free access to food. Histology and serum determinations were performed. Hepatic gene expression (RT-quantitativePCR) examined 40 key regulatory genes, including transcription factors (PGC1alpha, SREBP1c, SREBP2, ChREBP, FXR, LXRs, PPARs), metabolic enzymes (FAS, MCAD, PEPCK, Gys2, G6Pase), receptors (LDL-R, GLUT2, IRS2).

Results: WAT and BAT weight increased after HF, without change of liver weight. Metabolic and hepatic serum profile was normal after HF, but impaired in ob/ob mice (increased transaminases, glucose, cholesterol, triglycerides). At histology, the physiologic replenishment (fasting) and emptying (fed) of lipids in the liver was preserved after HF but lost in ob/ob mice, which displayed hepatic steatosis. During the switch between fasting-feeding, wild type mice fed chow diet displayed strong variation in gene transcription: mean difference of 6.2 ± 2.8 times (mean ± sem). On the opposite, obesity resulted in decreased activation of gene transcription: 2.4 ± 0.4 and 1.9 ± 0.2 in HF and ob/ob mice, respectively.

Conclusions: Our work provides new hints on what obesity is, revealing unanticipated transcriptional resistance during the switch from fast to feeding.

DYSLIPIDEMIA IN A RODENT MODEL OF THE METABOLIC AND POLYCYSTIC OVARY SYNDROME

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Background: Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disorder affecting up to 10% of women during their reproductive years. The diagnosis of PCOS is highly associated with the metabolic syndrome risk factors including obesity, insulin resistance and dyslipidemia. The aim of this study was to investigate the JCR:LA-cp rodent as an animal model of PCOS in the metabolic syndrome.

Methods: Animals were age-tracked from 6 to 12 wks of age (adolescent to adult) to assess plasma endocrine hormones, fasting and postprandial lipid, and insulin/glucose metabolism. Estrus cycling was monitored by the cytology of vaginal smears, and follicular development was assessed in replicates of H&E stained ovarian sections.

Results: At 6 wks and 12 wks of age the cp/cp genotype had both elevated plasma testosterone and insulin concentrations, compared to control animals. The cp/cp genotype were observed to have irregular estrus cycling coupled with altered follicular development, with a decreased incidence of corpus lutea and increased incidence of cystic follicles. Compared to control animals the cp/cp genptype with PCOS had marked elevations in fasting plasma concentrations of triglyceride, total cholesterol, apolipoprotein-B48, and also presented with postprandial dyslipidemia.

Conclusion: The JCR:LA-cp rodent is a unique model of spontaneous PCOS in the metabolic syndrome and may be a potential model to investigate the etiological mechanisms associated with the development of cardiometabolic risk factors, in particular dyslipidemia in PCOS.

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ROSUVASTATIN TREATMENT INDUCES HEPATIC INSULIN SENSITIZATION AND AMELIORATES DYSLIPIDEMIA IN AN ANIMAL MODEL OF METABOLIC SYNDROME

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Statin-treatment of fructose-fed/insulin resistant hamsters was recently shown to ameliorate metabolic dyslipidemia and hepatic VLDL overproduction. Here, we provide evidence that rosuvastatin treatment of insulin resistant hamsters can induce improvements in hepatic and whole body insulin sensitivity. Treatment with 10 mg/kg/day rosuvastatin for 10 days significantly reduced fasting insulin and triglyceride levels in fructose-fed hamsters. Following an intraperitoneal (IP) glucose challenge, rosuvastatin-treated hamsters exhibited enhanced glucose clearance compared to untreated hamsters maintained on the high-fructose diet with a significant reduction in 2 h post-challenge glucose. Rosuvastatin-treatment also significantly improved sensitivity to an IP insulin challenge. At the molecular level, significant increases in tyrosine-phosphorylation of the hepatic insulin receptor and IRS-1 were observed for rosuvastatin-treated hamsters compared to fructose-fed controls following an intravenous (IV) bolus of insulin. Increases in insulin receptor and IRS-1 phosphorylation were also observed in muscle and adipose tissue. Analysis of hepatic Akt phosphorylation and mass revealed a small increase in serine phosphorylation of Akt with no significant change in Akt mass, although serine-phosphorylation and mass of Akt2 were significantly increased. Interestingly, expression of PTP-1B, a key negative regulator of insulin signaling, showed a non-significant trend toward reduction in liver and was significantly reduced in adipose tissue. Taken together, these data suggest that statin treatment increases whole body and peripheral tissue insulin sensitivity via improved cellular insulin signal transduction.

LPS INDUCED CARDIOVASCULAR DIFFERENT IN WILD TYPE AND DPP4 MUTATION RAT

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Aims: Dipeptidyl peptidase-4 (dpp4) inhibitors prolong the half life of GLP-1, which enhance insulin release and contribute to glucose lowering action. In addition to the degradation of GLP-1, DPP4 participate in many physiological effects, including neuropeptide Y degradation and T cell mediated immune responses. This study aimed to examine the hemodynamic changes and vascular NO production in wildtype (wt) and dpp4 mutant (dpp4m) fisher 344 rats.

Methods: The blood pressure was monitored in pentobarbital-anethesized rats. After 3.5 h LPS (10 mg/kg, i.v.) treatment, the aorta was excised to examine the response of acetylcholine (Ach)-induced vasorelaxation.

Results: In dpp4m rats, the blood pressure was dramatically decreased by LPS to 62.4 ± 5.4% in 1.5 h, and recovered to 79.5 ± 3.7% at 3.5 h. There was no significant alteration in the heart rate during LPS treatment. In wt

rats, the blood pressure was gradually decreased to 82.5 ± 5.2% at 3.5 h after LPS administration. LPS elicited the hyperglycemic effect more in wt rats than in dpp4m rats. Ach-induced vasorelaxation was more pronounced in aorta isolated from LPS-treated dpp4m rats than that from wt rats. However, LPS induced NO production in cultured aortic smooth muscle cell of dpp4m rat was less than that in cultured wt rat.

Conclusions: Dpp4 may play a role in the change of blood pressure during the early phase of endotoxemia. The underlying mechanisms for the difference between wt rat and dppm rat in LPS-induced NO production and vascular response remain to be investigated.

EFFECT OF INCREASING INTRAVENOUS GLUCOSE LOAD IN THE PRESENCE OF NORMOGLYCEMIA ON OUTCOME AND METABOLISM IN CRITICALLY ILL RABBITS

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Aims: Endocrine disturbances during critical illness lead to a feeding-resistant wasting-syndrome, characterised by profound protein breakdown, promoting delayed recovery and poor outcome. Parenteral nutrition failed to counteract the hypercatabolic state, possibly due to aggravation of the detrimental hyperglycemic response to critical illness. In our rabbit model of prolonged critical illness we investigated the impact of varying intravenous glucose load, while maintaining normoglycemia, on mortality, organ damage, and catabolism/anabolism.

Methods: Critically ill rabbits were randomised into a fasting group, a standard parenteral nutrition group, and two groups receiving either an intermediate or high additional amount of intravenous glucose within the physiological range, all maintained normoglycemic with insulin. These normoglycemic groups were compared with a hyperglycemic group (similar high glucose load as the last normoglycemic group) and with healthy rabbits. Protein and lipid load was equal for all fed groups.

Results: Varying intravenous glucose load did not affect mortality or organ damage, provided normoglycemia was maintained. Fasted critically ill rabbits lost weight, which was attenuated by increasing intravenous glucose load. As compared to healthy rabbits, mRNA expression of several components of the ubiquitin-proteasome-pathway was elevated in skeletal muscle of fasted critically ill rabbits, which was counteracted by intravenous feeding. Except in the normoglycemic group with intermediate glucose load, circulating IGF-1 and thyroid hormone levels decreased in all groups, most pronounced in hyperglycemic rabbits.

Conclusion: Provided normoglycemia is maintained, increasing intravenous glucose within the physiological range is safe for organ function and survival of critically ill rabbits and reduces catabolism compared to fasting.

AN ORIENTAL HERBAL MEDICINE (*BOFUTSUSHOSAN*) IMPROVES ABDOMINAL OBESITY IN HIGH-FAT DIET FED KK/TA MICE

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Bofutsushosan (BOF), an oriental herbal medicine, has been used as an anti-obesity drug in overweight patients. In the present study, to evaluate the anti-obesity and anti-diabetic effects of BOF, we investigated the effects of BOF on the white adipose tissue (WAT) weight, the size of adipocytes, adiponectin expression, and oral glucose tolerance test results in high-fat diet-fed male KK/Ta mice. In addition, the mRNA expression measured levels of uncoupling protein 1 (UCP1) in WAT. 6-week-old KK/Ta mice were divided into four groups and fed a control diet (C group), a high-fat (HF) diet (HF group), a HF diet plus 1.0% BOF treatment (BOF group), or a HF diet plus 1.0% daisaikoto (DAI) treatment (DAI group) for 4 weeks. The weight of WAT and the size of adipocytes were increased in HF group compared with those in C group, and these increases in the HF group were significantly inhibited in BOF group, but not affected in DAI group. There were no statistically significant differences in plasma levels and tissue mRNA levels of adiponectin among the four groups. The expression of UCP1 mRNA in WAT was found in BOF group, but little expression was seen in the WAT of C, HF, or DAI groups. The elevated plasma glucose levels and responses after the glucose loading in the HF group tended to decrease in BOF group. These results suggest that BOF decreases the weight and size gains of WAT along with up-regulating UCP1 mRNA in WAT in HF diet-fed mice.

INFLUENCE OF COQ10 SUPPLEMENTATION ON OXIDATIVE, INFLAMMATORY AND METABOLIC STRESSES ASSOCIATED WITH DIET-INDUCED OBESITY IN MICE

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Diabetes and obesity are metabolic disorders induced by an excessive dietary intake of fat, usually related to inflammation and oxidative stress.

Aims: The aim of the study is to analyse the effect of the antioxidant CoQ_{10} in a model of diet-induced obesity and glucose intolerance, with a main focus on its association with oxidative stress and inflammation.

Methods: C57bl6/j mice were fed for 8 weeks, either a control diet (CT) or a high fat diet (72% energy as lipids) plus 21% fructose in the drinking water (HFF). CoQ 10 supplementation was performed in this later condition (HFFQ).

Results: HFF mice exhibit increased energy consumption, fat mass development, fasting glycemia and insulinemia and impaired glucose tolerance upon an oral glucose tolerance test. HFF diets paradoxically decreased TBARS (reflecting lipid peroxides) levels in liver, muscle and adipose tissue versus CT group, an effect related to vitamin E content of the diet. However, HFF treatment promoted the expression of genes involved in reactive oxygen species production (NADPH oxidase), inflammation (CRP, STAMP-2) and metabolism (CPT1a) in the liver. CoQ_{10} supplementation had no effect on obesity and tissue lipid peroxides but decreased the global hepatic mRNA expression of the genes mentioned above, involved in inflammatory and metabolic stresses.

Conclusion: In conclusion, HFF model promotes glucose intolerance and obesity by a mechanism independent on the level of tissue peroxides. CoQ10 tends to decrease hepatic stress gene expression, independently of any modulation of lipid peroxidation, which is, however, classically considered as one of its most relevant effect.

ROSIGLITAZONE/METFORMIN INCREASES MITOCHONDRIAL BIOGENESIS IN GOTO-KAKIZAKI RATS: BIOENERGETIC CONSEQUENCES FOR DIABETES

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Given the worldwide increase in diabetes mellitus, it is critical to understand the upstream genetic and transcriptional mechanisms mediating mitochondrial dysfunction. In this work, we evaluated the effects of the in vivo administration (for 6 weeks) of Rosiglitazone/Metformin on rat liver mitochondria bioenergetics, as well as on mitochondrial gene expression in a rat model of type 2 diabetes (Goto-Kakizaki rat). GK treated animals showed a normalization of the glycemia levels, while GK rat liver mitochondria from treated animals showed improvement of mitochondrial respiration and membrane potential capacities. Induction of mitochondrial permeability transition (MPT), involved in several vital cellular signalling pathways, was prevented in GK treated animals. Gene transcripts associated with mitochondrial energy production clearly shown an increase in adenine nucleotide translocator (ANT) and cytochrome oxidase (COX) in GK treated animals, as well as PGC-1alpha (transcription factor involved in mitochondrial biogenesis regulation). The increase in mRNA content was confirmed by western blot. All these data was further confirmed by the observed increase in mitochondrial biogenesis, after 6 weeks in vivo administration of Rosiglitazone/Metformin in GK rats. The efficiency of this formulation as antidiabetic is certainly related with the observed improvement of mitochondrial bioenergetic capacity in GK treated animals, being this improvement related with increased mitochondrial biogenesis.

EFFECTS OF KS-C370G ON ISCHEMIA-REPERFUSION INJURY IN STZ-INDUCED TYPE 1 DIABETIC RAT MODEL

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Cardiovascular disease is the most complication in diabetic patients. Our preliminary study found that KS-C370G, a catechol derivative, have hypoglycemic activity in streptozotosin (STZ)-induced and nicotinamide-STZ-induced diabetic rats, and exerted cardioprotective activity against ischemia-reperfusion injury in normal SD rats. In the present study, we compared the ischemia-reperfusion injury between normal and diabetic rat model induced by STZ for 4 weeks, and evaluated whether administration with KS-C370G (1 mg/kg, PO, QD, 4 weeks) could protect diabetic hearts from ischemia-reperfusion injury. The type 1 diabetic rats were induced by STZ injection via tail vein at the age of 8 weeks old, and after 4 weeks of induction, the animals were divided into 4 groups: Control-group: age, sex - matched normal SD rats, STZ-group: STZ induced type 1 diabetic rats, STZ-insulin group: insulin injection (1 IU/kg, IP, QD, 4 weeks), and STZ-KS-C370G group: (1 mg/kg, PO, QD, 4 weeks). After treatment for 4 weeks, the left main coronary artery of anaesthetized rats was occluded for 45 min and followed by reperfusion for 2 hours. Chronic therapy with KS-C370G was found to reduce the infarct size and increase the heart rate in the period of ischemia and reperfusion. The detailed mechanisms of KS-C370G produced cardioprotection against ischemia-reperfusion injury remain to be clarified.

ALL-*TRANS*-RETINOIC ACID REPRESSES OBESITY AND INSULIN RESISTANCE BY ACTIVATING BOTH PPARB/D AND RAR

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Many biological activities of all-*trans*-retinoic acid (RA) are mediated by the ligand-activated transcription factors termed retinoic acid receptors (RAR), but this hormone can also activate the nuclear receptor PPARb/d. We show here that adipocyte differentiation is accompanied by a shift in RA signalling which, in mature adipocytes, allows RA to activate both RAR to PPARb/d, thereby enhancing lipolysis and depleting lipid stores. *In vivo* studies using a dietary-induced mouse model of obesity indicated that onset of obesity is accompanied by down-regulation of adipose PPARb/d expression and activity. RA treatment of obese mice upregulated expression of PPARb/d and RAR target genes involved in regulation of lipid homeostasis in adipose tissue, muscle and liver, leading to weight loss and improved insulin responsiveness. RA treatment also restored adipose PPARb/d expression. The data indicate that suppression of obesity and insulin resistance by RA is largely mediated by PPARb/d and is further enhanced by activation of RAR. By targeting two nuclear receptors, RA may be a uniquely efficacious agent in therapy and prevention of the metabolic syndrome.

REGULATORY EFFECTS OF RESVERATROL ON FATTY ACID METABOLISM IN APO E-DEFICIENT MICE

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Aims: This study investigated the additional effects of the trans-resveratrol (RV) on fatty acid metabolism.

Methods: Effects of RV were examined in normal diet fed apo E-deficient (apo $E^{-/-}$) mice by supplementing 0.02% and 0.06% (w/w) each in diet for 20 weeks. Clofibrate (CF, 0.02% (w/w)) was used as a positive control on lipid-lowering action.

Results: In hepatic enzyme activities, β-oxidation activity was significantly increased in the 0.02% CF and 0.06% RV groups than in the control group. Carnitine palmitoyl transferase (CPT) activity was significantly increased in the CF group than in the control group. Also, fatty acid synthase (FAS) activity was significantly decreased in the RV groups, and β-oxidation activity was significantly increased in the 0.02% CF and 0.02% RV groups in the adipose tissue.

Conclusions: The current results suggest that the resveratrol may be effective to regulate fatty acid metabolism by increasing hepatic β-oxidation and decreasing FAS activity in the adipose tissue.

DIAVITE• HAS INSULIN SECRETING, ANTI-HYPERTENSIVE AND CARDIOPROTECTIVE EFFECTS IN RAT MODELS OF PRE-DIABETES AND TYPE 1 DIABETES

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While obesity and its complications,the metabolic syndrome, hypertension, diabetes and CVD are escalating world wide, untested remedies against these, are flooding the market. We utilized four animal models to scientifically validate the claims of one such product, Diavite™.

(i) Type 1 diabetes.Adult rats injected 40mg/kg Streptozotocin (Stz), animals treated with 25mg/kg/day (w/w human dose) Diavite™ for 4 weeks; pancreases analyzed histologically. **(ii)** Hyperphagia-induced obesity/pre-diabetes (DIO = diet supplemented with sucrose and condensed milk); isolated, perfused hearts subjected to 35min regional ischaemia/120min reperfusion and infarct size determined. Cardiomyocytes prepared (collagenase perfusion digestion) and insulin sensitivity measured via [^{3}H]-2-deoxyglucose accumulation. **(iii)** DIO + 40% animal fat causing hypertension. BP monitored weekly by tail cuff. In DIO and DIO + BP, pathology was induced for 8 weeks followed by 8 weeks treatment. Trunk blood collected for glucose, insulin, and oxidative stress products determinations, body weight and ip fat mass recorded. **(iv)** Non-human primates: toxicity screening (Diavite™ given orally at 1X, 5X and 25X doses @ 3months).

Results: In Stz; significantly enhanced insulin secretion and beta-cell neogenesis. No hypoglycaemic incidents. In DIO; improved basal and

insulin stimulated glucose uptake plus smaller infarct size in both control and DIO hearts (P< 0.05, 2way ANOVA). In DIO + BP animals, Diavite™ both (a) prevented a rise in BP and (b) corrected elevated BP. No toxic effects detected. No anti-oxidant effects in plasma or liver.

Conclusion: Diavite™ is safe, has insulin sensitizing and insulin secretory effects, improves glucose homeostasis, is cardioprotective and anti-hypertensive in relevant animal models.

HIGH FAT DIET FED MICE DEVELOP PERIPHERAL NEUROPATHY SIMILAR TO THE ONE IN HUMAN SUBJECTS WITH METABOLIC SYNDROME

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Subjects with metabolic syndrome have increased risk for developing peripheral diabetes-like neuropathy. Animal model of this type of neuropathy has not been described. This study evaluated neuropathic changes and their amenability to dietary interventions in mice fed high-fat diet. Female C57Bl6/J mice were fed normal or high fat diets for 16 weeks. High fat diet fed mice developed obesity, increased plasma FFA and insulin concentrations, and impaired glucose tolerance. They had motor and sensory nerve conduction deficits, tactile allodynia and thermal hypoalgesia, in the absence of intraepidermal nerve fiber loss or axonal atrophy. Despite the absence of overt hyperglycemia, the mice displayed augmented sorbitol pathway activity in the peripheral nerve, as well as 4-hydroxynonenal adduct, nitrotyrosine and poly(ADP-ribose) accumulation and 12/15-lipoxygenase overexpression in peripheral nerve and dorsal root ganglion neurons. A 6-week feeding with low fat diet after 16 weeks on high fat diet alleviated tactile allodynia and essentially corrected thermal hypoalgesia and sensory nerve conduction deficit without affecting motor nerve conduction slowing. 12/15-lipoxygenase gene deficiency alleviated motor and sensory nerve conduction deficits, but not manifestations of sensory neuropathy. In conclusion, similarly to human subjects with metabolic syndrome, high fat diet fed mice develop peripheral nerve functional but not structural, abnormalities, and, therefore, are a suitable model for evaluating dietary and pharmacological approaches to halt progression and reverse diabetic neuropathy at the earliest stage of the disease.

FENOFIBRATE AMELIORATES DIABETIC AND DYSLIPIDEMIC PROFILES IN KKAY MICE PARTLY VIA DOWN-REGULATION OF *11-B HSD1, PEPCK* AND *DGAT2. COMPARISON OF PPARA, PPARΓ, AND LXR AGONISTS*

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Fenofibrate (feno) and rosiglitazone (rosi) are prescribed to treat hypertriglyceridemia and diabetes, respectively. The aim of the present study was to examine the mechanism of antidiabetic effects of feno in KKAy mouse, an animal model of diabetes and dyslipidemia. KKAy mice were treated with feno, rosi, LXR (liver x receptor) agonist (T0901317), and a combination of feno and T317 for 2 weeks. Feno lowered serum TG by 90% and free FFA by 50% via inhibition of hepatic fatty acid synthesis. Feno also prevented T317-induced increases of TG by dampening T317-mediated SREBP1c upregulation. Glucose lowering was comparable (~40%) in feno and rosi treated mice. T317 also showed mild reduction in serum glucose, in part, via down-regulation of phosphoenol pyruvate carboxykinase (PEPCK). Combining feno with T317 caused greater reduction in serum glucose, suggesting an additive effect. The mechanism of lipid and glucose lowering in KKAy mice was examined. Liver PEPCK showed down-regulation in all treatment groups with feno showing greater effects. Combination of feno with T317 showed additive effects on PEPCK down-regulation. Feno decreased hepatic diacyl glycerol acyl transferase 2 (DGAT2) mRNA leading to reduced TG synthesis. Most importantly, feno down regulated expression of hepatic and adipose 11beta hydroxysteroid dehydrogenase (*11β-HSD1*) gene, which contributed in attenuating diabetic state. Thus, amelioration of antidiabetic and hyperlipidemic state by fenofibrate in KKAy mice occurred via down-regulation of *DGAT2*, *PEPCK* and *11β-HSD1*. It is also shown that the undesirable lipogenic effects of T317 could be reduced by combining with fenofibrate.

THE MTOR COMPLEX 1 SUPPRESSES LIPOLYSIS AND PROMOTES ACCUMULATION OF TRIGLYCERIDES IN MAMMALIAN CELLS BY INHIBITING EXPRESSION OF ATGL

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In 3T3-L1 adipocytes, the mTORC1 inhibitor rapamycin alleviates the inhibitory effect of insulin on basal and isoproterenol-stimulated lipolysis. Activation of mTORC1 signaling in 3T3-L1 adipocytes and C2C12 myoblasts by ectopic expression of Rheb inhibits lipolysis and markedly stimulates accumulation of triglycerides. On the contrary, knock down of raptor with siRNA stimulates basal and isoproterenol-stimulated lipolysis. Similar results have been obtained in mouse embryonic fibroblasts with genetic ablation of TSC2. In every cell model, hyper-activation of mTORC1 inhibits expression of adipocyte triglyceride lipase (ATGL) mRNA and protein, while rapamycin increases levels of ATGL mRNA and protein in cells. Expression of several key enzymes of the triglyceride synthesis pathway, such as DGAT1, DGAT2 and FAS, is not significantly affected by activation of mTORC1. The luciferase reporter construct containing ~3kb ATGL promoter is expressed much more efficiently in wild type than in TSC2-/- MEFs showing that mTORC1 signaling is implemented in the transcriptional control of ATGL expression. Importantly, ectopic expression of ATGL blocks accumulation of triglycerides in TSC-/- MEFs suggesting that regulation of ATGL plays the principal role in the control of lipolysis and lipid storage exerted by mTORC1.

As the rate of lipolysis in adipocytes and other cells depends on the levels of ATGL expression, we suggest that down-regulation of ATGL via the insulin-and nutrient-regulated mTORC1 pathway represents an important physiological factor in the overall control of lipid homeostasis in the mammalian organism.

THE ANTI-TNF-A DRUG IMPROVES SYSTEMIC AND HEPATIC ALTERATIONS INDUCED BY HIGH-FAT DIET IN MICE

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Pro-inflammatory cytokines, such as TNF-α, have been identified as being involved in the establishment of insulin resistance and in the development of type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). This led to the hypothesis that TNF-α blockade may have an effect on experimental obesity. The effects of thalidomide, an anti-TNF-α drug, upon systemic and hepatic alterations induced by high-fat diet in mice were studied.

Swiss mice were feed with high-fat diet for 12 weeks (HFD) and received thalidomide (100 $mg.kg^{-1}.day$) in the last 10 days (HFD+T). Control animals received standard diet (C).

The basal glucose blood levels were 134.6±16.4, 340.7±45.9 and 195.2±13.5 mg/dl for C, HFD and HFD+T, respectively (p< 0.01) and after

the insulin administration, the slope of glucose curves were 3.0±0.7, 0.5±0.5 and 1.2±0.5 for C, HFD and HFD+T, respectively ($p< 0.05$). The molecular analysis of insulin signaling revealed a restoration of insulin substrate receptor (IRS)-1 and AKT phosphorylation in response to insulin after the thalidomide treatment. The serum levels of TNF-α were 58.8±17.3, 388.3±96.4 and 80.0±13.9 pg/ml for C, HFD and HFD+T, respectively, ($p< 0.01$). The hepatic expression of *TNF-α* was inhibited in HFD+T with a significant reduction in steatosis area (4.9 fold compared HFD with HFD+T). Other inflammatory markers, such as *iNOS*, SOCS-3 and macrophage infiltration, were also reduced in the liver by the thalidomide treatment. We suggest that drugs that inhibit TNF-α production and reduce the inflammatory markers associated to the obesity could be a therapeutic option in NAFLD and type 2 diabetes.

THE EFFECTS OF AN ANTI-TNF-A AND ANTI-ANGIONGENIC DRUG ON ADIPOSE TISSUE DURING EXPERIMENTAL OBESITY

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Development of obesity is associated with extensive modifications in adipose tissue involving adipogenesis, angiogenesis and establishment of a pro-inflammatory status including TNF-a production.

The effects of thalidomide, an anti-TNF-α and anti-angiogenic drug, upon adipose tissue alterations in obese mice were investigated.

Swiss mice were feed with high-fat diet for 12 weeks (HFD) and received thalidomide (100 $mg.kg^{-1}.day$) in the last 10 days (HFD+T). Control animals were maintained with standard diet (C).

The final body weights were 47±3, 60±2 and 53±1 g for C, HFD and HFD+T, respectively ($p< 0.01$) and the epididymal adipose tissue depot were 3.5±0.3, 5.5±0.4 and 3.9±0.3 % of body weight for C, HFD and HFD+T, respectively ($p< 0.05$). The VEGF expression was increased in HFD mice and thalidomide treatment restore the expression to control level. In short-time cultures, the explants of epididymal adipose tissue from HFD mice were able to release higher levels of TNF-α and it was inhibited by thalidomide (49±5, 76±1 and 29±1 ng/ml for C, HFD and HFD+T, respectively, $p< 0.05$). Adiponectin and IL-6 releasing were not altered by thalidomide treatment. Interleukin-10 and IL-1ra protein expression were also analyzed and thalidomide treatment was able to increase their expression.

Thus, drugs that present anti-angiogenic properties and inhibit TNF-a production were able to modify the expansion and production of pro- and anti-inflammatory substances by adipose tissue during experimental obesity.

INCREASING WHOLE-BODY FAT OXIDATION IN RATS VIA ACUTE ACTIVATION OF AMPK DOES NOT ALTER ENERGY EXPENDITURE

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Objective: To investigate the relationship between fat oxidation and energy expenditure we examined whole-body energy metabolism in rats treated with compounds that stimulate fat oxidation via activation of the AMP-activated protein kinase pathway.

Methods: Energy expenditure (VO_2) and substrate oxidation (indicated by the respiratory exchange ratio [RER]) were measured using an Oxymax indirect calorimetry system. Rats were dosed at 10am with vehicle (saline, n=12), metformin (500mg/kg, n=10), AICAR (250mg/kg, n=11) or the mitochondrial uncoupler, dinitrophenol (DNP; 30mg/kg, n=10).

Results: In the 8-hours after dosing, rats treated with metformin, AICAR and DNP all displayed increased fat oxidation (RER 0.87-0.89 $P< 0.001$) compared with vehicle-treated animals (RER 0.92). Only DNP however, increased VO_2 (1957±22 ml/kg/hr, $P< 0.001$) compared with vehicle-treated animals (1633±17 ml/kg/hr), with no difference observed for metformin (1619±23 ml/kg/hr) or AICAR (1627±16 ml/kg/hr). To test if increased fat oxidation was associated with a decrease in oxidation of other substrates, palmitate and glucose oxidation was examined in isolated EDL muscle treated *ex vivo* with AICAR (2mM) or DNP (0.5mM). AICAR increased palmitate oxidation (+45%, $P< 0.001$), but decreased glucose oxidation by 28% ($P< 0.01$). In contrast DNP treatment caused a significant increase in the oxidation of both palmitate (+41%, $P< 0.01$) and glucose (+77%, $P< 0.01$).

Conclusion: These results suggest that acute increases in fat oxidation caused by activation of AMPK are accompanied by a concomitant decrease in the oxidation of other substrates rather than any change in whole-body energy expenditure.

CHRONIC APELIN TREATMENT STIMULATES FATTY ACIDS OXIDATION IN SOLEUS MUSCLE BOTH IN WILD TYPE AND INSULIN-RESISTANT MICE

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Introduction: We have recently shown that apelin stimulates glucose utilization in skeletal muscle through an AMP-activated protein kinase (AMPK) dependent pathway. AMPK is also involved in lipid metabolism, activating fatty acid oxidation. So, we studied apelin chronic treatment effects on lipid metabolism in normal and insulin resistant mice.

Methods: Chow fed or high fat fed C57bl6/J mice were ip injected with apelin (0,1µmol/kg/day) during 8 or 28 days. Total [1-14C] palmitate oxidation was determined in soleus muscle as the sum of 14CO2 release and acid soluble metabolites (corresponding to the incomplete oxidation. Intramuscular triglycerides (IMTG) content was measured after extraction of muscle lipids.

Results: Eight days of treatment with apelin decreased perigonadic adipose tissue weight but didn't change neither body weight nor plasma levels of triglycerides and free fatty acids in chow-fed mice. Palmitate oxidation was increased by 68% and IMTG content was decreased by 20% in apelin-treated mice. Similar results were obtained after 28 days of treatment. In obese and insulin-resistant mice, eight days treatment with apelin decreased both perigonadic adipose tissue weight and plasma levels of triglycerides and free fatty acids. Moreover, palmitate oxidation was increased and IMTG content was decreased by 39% in soleus of apelin-treated mice.

Conclusion: By decreasing deleterious lipid accumulation and by stimulating fatty acid oxidation in muscle, apelin chronic treatment seems to to improve insulin resistance. Apelin can thus be considered as a promising therapeutic target.

RADIOGRAPHIC ANALYSIS OF GASTROINTESTINAL MOTOR FUNCTION IN A MODEL OF TYPE 2 DIABETES, THE ZUCKER DIABETIC FATTY (ZDF) RAT

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Introduction: Diabetic patients commonly complain of gastrointestinal symptoms. A delay in gastric emptying and in small bowel and colonic transit is generally reported. The Zucker Diabetic Fatty (ZDF) rat is a genetic model of type 2 diabetes, which reproduces many aspects of the human disease. However, gastrointestinal motor function in this model is not well known.

Aim: To analyse, using non-invasive radiographic techniques, gastrointestinal motor function in the ZDF rat, a genetic model of type 2 diabetes.

Methods: Gastrointestinal motility was evaluated in conscious animals. Both ZDF rats and their genetic controls (LEAN), at 18 and 30 weeks of age, were used. Rats received an intragastric dose of medium contrast and serial X-rays were taken 0-24 h afterwards. Alterations in gastrointestinal motility were quantitatively evaluated in each radiograph by assigning a compounded value (0-12) to each region of the gastrointestinal tract (Cabezos et al, 2008).

Results: Transit of the medium contrast in the ZDF rats was delayed in all gastrointestinal regions as compared to LEAN animals. At 18 weeks of age, differences were statistically significant only for the colorectal region, whilst at 30 weeks of age, differences were significant for all gastrointestinal regions.

Conclusions: In ZDF rats, gastrointestinal transit is decreased in an age-dependent manner. The use of non-invasive radiographic methods to study gastrointestinal motor function in this model may speed up the search for new pharmacological tools in the gastrointestinal complications of diabetes.

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EFFECTS OF ACYLATION STIMULATING PROTEIN (ASP) INTRACEREBROVENTRICULAR INJECTION ON FOOD INTAKE AND ENERGY EXPENDITURE IN RATS

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Introduction: Understanding the mechanism behind food intake and energy expenditure is important for obesity treatment. Acylation stimulating protein (ASP, C3adesArg) is an adipokine stimulating triglyceride synthesis and glucose transport via interaction with its receptor C5L2. This receptor is expressed peripherally (adipose tissue, muscle) and centrally. Previous studies have shown that ASP-deficient mice (C3KO) and C5L2-deficient mice (C5L2) are hyperphagic (59% to 229% increase, $P < 0.0001$) counter-balanced by increased oxygen consumption (V_{O2}) and a lower RQ.

Objectives: Elucidate the ASP-C5L2 pathway in the brain by assessing the central effect of ASP on food intake, energy expenditure and neuropeptide expression.

Methods: Male Rats were surgically implanted with intracerebroventricular (i.c.v.) cannulas directed towards the third ventricle. After a 5 hr fast, rats were injected. Food intake was assessed at intervals of 0.5, 1, 2, 4, 16 and 24 hr. Body weight was measured pre-injection and after 24 hours. There was a 5-7 day washout period between each injection. For energy expenditure assay rats were housed in a calorimetric chamber for 48 hours before injection.

Results: We observed that acute i.c.v. injections of ASP have a dose dependent effect on food intake. ASP injection interestingly diminishes food consumption by 20% to 50% ($P< 0.05$) at according to time and concentration over a 24 hour span. Furthermore, acute ASP injection affected energy substrate usage demonstrated by a lower RQ, and affected movement with a 49% decrease in total activity but there was no change in oxygen consumption (V_{O2}).

VARIATIONS OF MATERNAL CARE ARE ASSOCIATED WITH THE DEVELOPMENT OF METABOLIC SYNDROME IN FEMALE RATS

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An increased quality of maternal care in rats is associated with less stress reactivity in the adult offspring. Several hypothalamic areas involved in the control of stress are also involved in the control of energy balance. Moreover, there is strong association between glucocorticoids and metabolic syndrome(MS). Our Hypothesis is that the offspring that received low quality of maternal care will develop MS with aging. Rat maternal care was assessed by scoring the amount of licking/grooming received by the offspring during the first 6 days of life. Low maternal care(Low_MC) was defined as a score lower than 1SD below mean and high maternal care(High_MC) as 1 SD above mean. Female offspring were used because of their importance in phenotype transmission. Rats were evaluated at the age of 45 days, 7 months and 12 months for glucose and lipid metabolism, body weight(BW) and adiposity index(AI). At all ages Low_MC offspring showed higher BW and AI. At 7months Low_MC showed a higher fasting glucose to insulin ratio and Triacilglycerol. At 12 months they showed an altered intraperitoneal glucose tolerance test and lipid profile. We concluded that the Low_MC offspring developed MS as a function of age, and this seems to be related to the programming of obesity in earlier ages. This might be an interesting model of natural occurring MS.

ASPECTS OF THE METABOLIC SYNDROME IN DOMESTIC PIGS FED A HIGH SATURATED-FAT, FRUCTOSE, CHOLESTEROL DIET

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Pigs and man share many anatomical and physiological similarities.

Aim: Starting at 30 kg body weight, control (C) Landrace pigs (n=7) on a low-fat diet were compared with "metabolic syndrome" (MS) pigs (n=7) on a high-saturated fat, fructose, cholesterol diet.

Results: After 4 months on ad libitum diets, body weight of MS tended ($p< 0.08$) to be higher (133±5 kg) than C (122±3 kg). Both fasting and postprandial plasma glucose (but not insulin and triglycerides) concentrations were higher by ~10% ($p< 0.02$) and ~18% ($p< 0.008$), respectively, in MS compared to C. Plasma total cholesterol, LDL, VLDL, ratio HDL/LDL and ratio HDL/total-cholesterol were adversely affected (>4-fold, $p< 0.001$) in MS compared to C. Fasting hepatic glucose production was higher by 26% in MS compared to C (2.84±0.28 vs 2.26±0.08 mg/kg.min, $p< 0.03$) but insulin-mediated whole body glucose uptake and hepatic glucose production were not statistically different between MS and C. At necropsy, relative liver and omental fat weights were higher by 37% and 53% in MS compared to C (19.2±0.6 vs 14.0±0.5, $p< 0.001$ and 2.9±0.4 vs 1.9±0.2 g/kg pig, $p< 0.04$, respectively). Aorta fatty streaks tended ($p< 0.06$) to be increased in MS compared to C (3.2±1.6 vs 0.1±0.1%).

In conclusion: High saturated-fat, fructose, cholesterol feeding of young, growing Landrace pigs induced a limited number of abnormalities, related to the metabolic syndrome. It may be necessary to use adult, non-growing pigs of an obese breed to observe most of the abnormalities related to the metabolic syndrome.

RESISTANT STARCH PROMOTES PREFERENTIAL FAT OXIDATION IN RATS FOLLOWING WEIGHT LOSS

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We have shown that weight gain during the relapse to obesity following weight loss is associated with increased energy intake, decreased total energy expenditure (TEE), and preferential carbohydrate utilization. Resistant starch (RS) is any starch which is not digested/absorbed in the small intestine and passes to the large bowel. RS consumption has been shown to increase fat oxidation in humans and rats, and attenuate weight regain during relapse to obesity in rats. This study examined the effects of RS on fat oxidation during the early stages of weight regain during relapse to obesity. Obesity-prone rats were fed an obesogenic diet for 16 weeks then weight-reduced for 8 weeks on a digestible starch (DS) or RS diet. Rats were then allowed ad libatum access to RD or DS diet during the relapse period. Dietary tracer studies were performed in a whole-room calorimeter on days 0, 1, and 3 of relapse. RS significantly increased whole body and dietary fat oxidation and reduced carbohydrate and protein oxidation in the weight-reduced state. RS blunted the relapse-induced suppression of dietary fat oxidation on day 1 without any change in TEE. These data suggest that the drive to regain weight is not significantly affected by RS during the first three days of relapse, and its effects on attenuating weight regain occur later in the relapse process. The preferential oxidation of whole body and dietary fat indicates that there will be less fat storage in response to RS feeding which has positive implications for long-term metabolic health.

CTP:PHOSPHOETHANOLAMINE CYTIDYLYLTRANSFERASE (*PCYT2*) DEFICIENT MICE IS A NEW MODEL FOR THE METABOLIC SYNDROME

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Phosphatidylethanolamine (PE) is the main inner-membrane phospholipid and is synthesized *de novo* by the CDP-ethanolamine (Kennedy) pathway. CTP: phosphoethanolamine cytidylyltransferase (*Pcyt2*) catalyses the formation of CDP-ethanolamine, which is often the rate-regulatory step in the pathway. In the current investigation, we show that a reduced rate of formation of CDP-ethanolamine in $Pcyt2^{+/-}$ mice limits the rate of PE synthesis. This increases the availability of diacylglycerol and results in an increased hepatic fatty acid uptake and *de novo* synthesis, increased formation of triglycerides and reduced fatty acid utilization as an energy substrate. During development, $Pcyt2^{+/-}$ mice experience weight gain, elevated diacylglycerol and triglyceride and develops insulin resistance. Accordingly, liver and muscle gene expression analyses demonstrated the up-regulation of the main lipogenic genes, down-regulation of the mitochondrial and β-oxidation genes and perturbations in insulin and Ras/MAPK signalling pathways and key gluconeogenic and glycolytic genes. These data demonstrate that partial *Pcyt2* deficiency preserves membrane phospholipids but generates compensatory changes in triglyceride, fatty acid and glucose metabolism resulting in a progressive development of liver steatosis, hypertriglyceridemia, obesity and insulin resistance, the main features of the metabolic syndrome.

PPAR'S AND UCP-2 EXPRESSION ALTERED BY GLYCINE IN MONOSODIUM GLUTAMATE-OBESE MICE

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The obesity is the cause of metabolic and cardiovascular diseases, associated with a chronic inflammatory process. Thus, an impairment of inflammatory profile in obese people leads to the development of micro and macro-vascular complications. Fat tissue is responsible, for at least part of the control of energetic balance (through the PPARs) and the inflammation (through the adipokines) state. Glycine, an essential amino acid has been proposed as an anti-inflammatory molecule in several studies. Previously, we demonstrated that glycine reduced the expression of TNF-alpha and IL-6, and increased adiponectin expression in 3T3-L1 adipocytes cells, and in lean and obese mice (Ob/MSG). In the present study we analyzed the effect of glycine in obese mice, through gene expression of the molecules involved in the storage and combustion of energy such as the PPAR-gamma, PPAR-alpha, PPAR-delta, and UCP-2 in the obese animal model Ob/MSG. The results showed that in the presence of glycine adiponectin and the PPAR-gamma from fat tissue were increased only in lean, but not in Ob/MSG mice. In liver, PPAR-gamma and PPAR-alpha expressions were repressed by glycine, in both lean and obese animals, and decreased PPAR-delta only in lean mice. Interestingly, the treatment with glycine decreased the expression of UCP-2 in lean mice, and correlated with the increased level of insulin in plasma. These findings showed novel effects of glycine on PPARs and UCP-2 expressions that might prevent the development of vascular complications associated to inflammation, as well as liver diseases.

EFFECTS OF ROSIGLITAZONE ON METABOLIC PROFILE, ADIPONECTIN LEVEL AND ADIPOSE TISSUE DISTRIBUTION IN FRUCTOSE FED-RATS

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Aims: To investigate the effect of the peroxisome proliferator-activator receptor gamma agonist, rosiglitazone, on metabolic parameters and adipose tissue distribution in an animal model of the metabolic syndrome.

Methods: Metabolic syndrome was induced in 32 male Wistar rats by adding a fructose in drinking water (10% solution) for 12 weeks. During the last 4 weeks, 16 rats were treated with rosiglitazone (5 mg/kg/day), while the remaining 16 did not receive any medication (fructose group). Another control group consumed standard rat chow and water for 12 weeks.

Results: Chronic fructose administration for 12 weeks induced a significant increase in systolic blood pressure (SBP), body weight, serum triglycerides (TG), free fatty acids (FFA), insulin, glucose AUC0-120 (during oral glucose tolerance test-OGTT) and decreased serum adiponectin concentrations compared with the control group. Treatment with rosiglitazone over the final 4 weeks reversed these effects and significantly reduced SBP (130±6 vs 146±4 mmHg), TG (1.31±0.17 vs 2.09±0.21 mmol/l), FFA (0.45±0.14 vs 0.62±0.12 mM), insulin concentration (152±18 vs 260±22 pmol/l) and glucose AUC0-120 (623±40 vs 810±48 mmol/L*min) compared with the fructose group. In addition, rosiglitazone increased serum levels of adiponectin twofold from 3.44±0.46 to 7.03±1.30 μg/ml. Rosiglitazone promoted weight gain and significantly decreased the weight of the visceral (epididymal+perirenal) fat pads, but increased the weight of the subcutaneous (inguinal) fat pads.

Conclusion: This study indicates that rosiglitazone improves the components of the metabolic syndrome, which is accompanied with an increase in adiponectin concentrations and a body fat redistribution from visceral towards subcutaneous depots.

Keywords: Rosiglitazone, adiponectin, metabolic syndrome, fructose.

ROLE OF HEPATIC NITRIC OXIDE AND HEPATIC GLUTATHIONE ON A HIGH FAT DIET INDUCED OBESE INSULIN RESISTANCE ANIMAL

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We have previously described the relevance of nitric oxide (NO) and glutathione (GSH) in the liver for normal post-prandial insulin sensitivity. High Fat Diet (HFD) obese animals had a significant decrease in total post-prandial insulin sensitivity. Our aim was to characterize the regulation of hepatic NO and GSH synthesis in this obesity model. We hypothesize that hepatic nitric oxide synthase (NOS) and glutamylcysteine synthase (GCS) activity/expression are decreased in HFD rats, relating these markers not only to the observed insulin resistance but also as predictors of it. Hepatic GCS activity was measured by a fluorescence technique. Hepatic NOS activity was determined by radioactivity. NOS and GCS expression was measured using real time RT-PCR. Even though the GCS isoforms, catalytic and modified subunits, in this HFD group had no change when compared to the control animals, GCS activity was altered: standard animals had higher GCS activity (3576±177.3 μM/min/g liver) than HFD animals (2390±200 μM/min/g liver, $p< 0.001$). NOS activity in the liver was also decreased in the HFD animals (2.9±0.3 pmol/mg protein/g liver) when compared to the control animals (3.7±0.2 pmol/mg protein/g liver, $p< 0.05$). The NOS isoforms had significant alterations: constitutive isoforms, eNOS and nNOS were 49.2±5.5% and 34.6±7.0% less expressed, respectively, when compared to the control animals. iNOS isoform had an increase of 186.7±19.2% when compared to the normal diet.

According to our data, synthesis of NO and GSH is compromised in the HFD-obese animal, being these parameters related with the insulin resistance observed.

CHANGES IN HEPATIC COPPER, SELENIUM AND CALCIUM LEVELS IN STREPTOZOTOCIN-DIABETIC RATS: INFLUENCE OF VANADIUM MALTOLATE

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The aim was to study the influence of diabetes on copper, selenium and calcium metabolism in rats after the administration of streptozotocin as a diabetogenic agent and also to determine whether treatment with vanadium maltolate as a hypoglycemic drug affects the metabolism of these elements.

Three groups of male Wistar rats were used:Control rats, untreated STZ-diabetic rats, and STZ-diabetic rats treated with vanadium maltolate(7mgV/kg body weight). Homogenized liver samples were acid-digested in a microwave digestion system. Total metal content was analyzed by ICP-MS, evaluating the accuracy of the method by the analysis of a bovine muscle certified reference material, and studies of recovery in samples of liver enriched with multielementary standards.

The results showed that diabetes induces significant increases in the hepatic levels of Cu and Se, as well as a significant decrease in the hepatic level of Ca ($P< 0.01$,$P< 0.001$ and $P< 0.05$ respectively). Concentrations of Cu and Se in the liver showed a linear correlation ($r =0.69$,$P< 0.01$). Treatment with vanadium maltolate, significantly reduced the hepatic Cu and Se levels to normal ($P< 0.02$ and $P< 0.01$ respectively), not showing any effect on the hepatic level of Ca.

In conclusion, diabetes causes imbalances on the metabolism of certain elements such as Cu, Ca and Se. This study has evidenced the efficacy of the pharmacological treatment with vanadium maltolate (as a hypoglycemic drug), at restoring the hepatic levels of Cu and Se, what could have positive repercussions on the normalization of the oxidative stress occurring in diabetes.

ADMINISTRATION OF PIGMENT EPITHELIUM-DERIVED FACTOR (PEDF) IMPROVES INSULIN RESISTANCE IN OLETF RATS

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There is accumulating evidence that oxidative stress and inflammation are involved in the pathogenesis of insulin resistance. We have recently found that pigment epithelium-derived factor (PEDF), a glycoprotein with neuronal differentiating ability, inhibits cytokine- or growth factor-induced vascular inflammation through its anti-oxidative properties. However, effects of PEDF on insulin resistance in vivo remain to be elucidated. In this study, we investigated whether administration of PEDF could improve insulin resistance in OLETF rats, an obese type 2 diabetic animal. OLETF rats and control LETO rats, aged 8 weeks, were used in this study. OLETF rats were given tail vein injections with vehicle or 2.5 mg PEDF/100g body weight 3 times a week. Each rat was followed to 30 weeks of age. Administration of PEDF significantly inhibited the increase in body weight, fasting blood glucose, fasting insulin, and triglyceride levels in OLETF rats at 30 weeks of age. PEDF injection also decreased urinary 8-isoprostan excretion levels and tumor necrosis factor-a expression in adipose tissues in OLETF rats. Further, adiponectin levels in adipose tissues and serum were decreased in OLETF rats, both of which were ameliorated by the treatment with PEDF. The present study suggests that PEDF may improve insulin resistance in OLETF rats through its anti-oxidative and anti-inflammatory properties. PEDF may be a novel therapeutic target for insulin resistance.

THE EFFECT OF FORMULA DIET (MICRODIET®) ON GLUCOSE AND LIPID METABOLISM IN ZUCKER FATTY RAT, AND THE ELUCIDATION OF ITS MECHANISMS

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Aims: To investigate the effects of formula diet on glucose and lipid metabolism, especially on visceral fat weight and the expression of adiponectin, lipoprotein lipase (LPL) and PPARγ in subcutaneous adipose tissue of Zucker fatty rats.

Methods: Sixteen week-old male Zucker fatty rats were divided into 4 groups: Control group (n=10, 72kcal/kg, P:F:C=25:15:60), High Carbohydrate Diet group (n=10, 54kcal/kg, P:F:C=25:15:60), Low Carbohydrate Diet group (n=10, 54kcal/kg, P:F:C=25:40:35), Formula diet (FD) group (n=10, 54kcal, P:F:C=49:13:38), and treated for 4 weeks by each dietary therapy. MicroDiet^{R} (Sunny Health Co, Ltd, Tokyo, Japan) was used as a formula diet. The expressions of adiponectin, LPL and PPARγ were evaluated by real time PCR.

Results: The decreases of fasting blood sugar and serum triglyceride levels and the increases of serum HDL-cholesterol levels were greatest in FD

group among the four groups. The decrease of visceral fat weight was greatest in FD group among the four groups, while the decrease of body weight was almost the same in the four groups. The mRNA expression of LPL and PPARγ in subcutaneous adipose tissue was enhanced in all groups, with similar enhancement in four groups. The mRNA expression of adiponectin was most enhanced in FD group among four groups.

Conclusions: These results indicate that formula diet is much more effective than normal diet in the improvement of glucose and lipid metabolism. As its mechanism, formula diet might be superior over normal diet in the reducing effect of visceral fat and enhancing effect of adiponectin in adipose tissues.

ORAL ADMINISTRATION OF L-TRYPTOPHAN IS EFFECTIVE TO IMPROVE GLUCOSE METABOLISM AND HYPERTENSION IN STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS

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Multiple factors related to the metabolic state, such as changes in glucose metabolism and insulin resistance involved in the management of hypertension. We studied the effects of single oral and chronic administration of L-tryptophan (Trp) on the regulation of glucose metabolism and hypertension in stroke-prone spontaneously hypertensive rats (SHRSP). Male 9-week-old of SHRSP was administered Trp or saline (Control) via a gastric tube. The systolic blood pressure through blood tail vein were measured before and 1, 2, 4, and 6 h after the administration. Hypotensive effect was observed after 1 and 2, and back to the basal condition after 4 and 6 h. Plasma glucose and insulin levels were lower after 4 and 6 h the administration. Subsequently, the effects of chronic Trp administration in SHRSP were studied. SHRSP aged 9-week-old were divided into Control and Trp groups that were administered water or Trp solution, respectively for 3 weeks. Hypertension was significantly improved in the Trp group. We found out that chronic administration of Trp showed increased plasma nitric oxide levels in plasma corresponded well with the hypotensive effect observed in SHRSP. Plasma glucose and insulin levels were also significantly decreased in the Trp group after 2 and 3 week of the administration. In conclusion, single oral and chronic administration of Trp has beneficial to improve glucose metabolism and hypertension in SHRSP.

ORALLY GIVEN BENZYLAMINE IMPROVES GLUCOSE TOLERANCE IN MICE RENDERED DIABETIC BY HIGH-FAT DIET

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Benzylamine (BzA) is found in the plant Moringa Oleifera endowed with antidiabetic properties in folk medecine. Once ingested, BzA is mainly metabolized by the semicarbazide-sensitive amine oxidase into benzaldehyde, ammoniac and hydrogen peroxide. Hydrogen peroxide has been demonstrated to be responsible for the insulin mimicking actions of BzA on human adipocytes. Our aim was to examine the effect of oral chronic benzylamine treatment on glucose tolerance, insulin responsiveness, plasma lipids, liver gene expression and nitrogen monoxide bioavailability in vessels. First, BzA was shown to diffuse across everted gut sacs, with one half of the amine being not oxidized during its passage of intestinal barrier. Then, C57Bl6 male mice were fed a high-fat diet (HFD) before and during BzA chronic administration (3600 µmol/kg/day in drinking water for 17 weeks). Oral BzA reduced body weight gain, and lowered fasting blood glucose. Oral BzA also reduced cholesterol and uric acid plasma levels, and improved glucose tolerance (AUC BzA: 573 ± 66 vs ctrl: 808 ± 82 arbitrary units n=12, $p< 0.05$). In isolated adipocytes, insulin-induced glucose transport and antilipolysis remained unchanged. In the aorta, benzylamine treatment partially restored the nitrite levels that were reduced by HFD. In the liver, expression of genes involved in insulin signalling, and of the antioxidant enzymes catalase and superoxide dismutase was unaltered. The improvement of glucose metabolism and nitrogen monoxide bioavailability reported here in HFD fed mice allow to consider benzylamine as a potential oral agent to delay the onset of diabetes which deserves to be further studied.

PREGNANCY RESTORES GLUCOSE-STIMULATED INSULIN SECRETION (GSIS) IN ISLETS FROM CAFETERIA DIET-INDUCED OBESE RATS

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Insulin resistance during pregnancy associated with obesity increases the risk of gestational diabetes. Here, we investigated pancreatic islets functionality in control nonpregnant (Con) and pregnant (ConP), and cafeteria diet-induced obese nonpregnant (Caf) and pregnant (CafP) Wistar rats. Impaired glucose tolerance was established in Caf and CafP rats at 14th week of diet. After, the rats were sacrificed and isolated islets were used for measurement of: insulin secretion; metabolic activity and; cytosolic Ca^{2+} levels in response to glucose. The dose-response curve of insulin secretion (2.8-27.7 mmol/L glucose) was shifted to the right in Caf compared with Con but was normal in ConP and CafP islets (12.3±0.6, 10.6±0.2, 9.3 ±0.1 and 9.6±0.5 mmol/L, respectively; $P< 0.05$). The production of reducing equivalents and $^{14}CO_2$ were increased in ConP and CafP, but not in Caf, compared with Con islets. Glucose-induced Ca^{2+} increase was significantly lower in Caf islets compared with the other groups. Also, the frequency and amplitude of the Ca^{2+} oscillations was lower in Caf compared with CafP islets. In conclusion, cafeteria diet-induced obesity impairs GSIS in islets from nonpregnant rats, and these alterations seem to be due to impairment of Ca^{2+} handling in Caf islets, independently of alterations in metabolic parameters. At the contrary, pregnancy increases metabolic activity improves Ca^{2+} handling and restores GSIS in the islets. These alterations were not sufficient to overcome the impaired glucose tolerance, observed during an ipGTT, but enough to maintain normoglycemia at fast and fed states.

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BENFOTIAMINE AMELIORATES CARDIAC AUTONOMIC NEUROPATHY IN STREPTOZOTOCIN-INDUCED DIABETES IN RATS

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Benfotiamine is a transketolase activator that shows a beneficial effect on patients with diabetic polyneuropathy. Herein, we determined the effects of benfotiamine on cardiac autonomic nerve function in streptozotocin (STZ)-induced diabetes in Wistar rats, using modern spectral estimation technique. Diabetes was induced by a single tail vein injection of 65 mg×kg^{-1} STZ. After induction of diabetes, animals received daily treatment for 2 weeks with benfotiamine (100 mg×kg^{-1}) by oral gavage and compared with the untreated age-matched diabetic controls. An autoregressive process was performed to each detrended signal of heart rate (HR) and systolic blood

pressure (SBP) measured in animals with anesthesia. The power of low-frequency (LF) and high-frequency (HF) oscillations was automatically quantified with each spectral peak by computing the residuals. The closed-loop baroreflex gain was estimated using the square root of the ratio between HR and SBP powers in the LF band (a_{LF}). Compared with the age-matched controls, the STZ-diabetic rats showed a significant decline in baroreflex gain, from 1.191±0.158 to 0.641±0.059 ms×mmHg^{-1} (P<0.005) and a fall in the LF-to-HF power ratio of the heart period (LF/HF), from 1.524±0.194 to 0.323±0.050 (P<0.001). After exposure to benfotiamine, the diabetic animals exhibited a beneficial effect on the baroreceptor-HR reflex sensitivity, as evidenced by the increase of 62.2% in a_{LF} (P<0.05). Meanwhile, benfotiamine prevented the diabetes-induced disturbance in sympatho-vagal balance of the heart control, as reflected in the rise of 108.9% in LF/HF (P<0.05). We conclude that benfotiamine ameliorates the diabetes-related deterioration in cardiac autonomic nervous system in the STZ-treated rats.

INVOLVEMENT OF MATRIX METALLOPROTEINASE-2 IN DOWN-REGULATION OF PIGMENT EPITHELIUM-DERIVED FACTOR IN EXPERIMENTAL DIABETIC NEPHROPATHY

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Background and aims: Pigment epithelium-derived factor (PEDF) has anti-oxidative and anti-inflammatory properties in diabetic nephropathy. Indeed, overexpression of PEDF was reported to alleviate microalbuminuria and reduce the production of an extracellular matrix protein in the diabetic kidney. Since PEDF is known to be a substrate for matrix metalloproteinnase-2 (MMP-2), we investigated the role of PEDF and MMP-2 system in diabetic nephropathy.

Materials and methods: Nine wk-old Sprague-Dawley rats received intravenous injection of streptozotocin. After 16 weeks, MMP-2 expressions in the glomeruli and urine were evaluated by zymography. PEDF expression in the kidney was evaluated by western blot analysis and immnohistochemistry.

Results: Plasma level of glucose, HbA1c were increased by about 2-3-folds in diabetic rats, compared with non-diabetic control rats (plasma glucose; 589+/-38 mg/dl, HbA1c; 8.8+/-0.3 % in diabetic rats). Zymography revealed that active MMP-2 expression in the glomeruli and urine were increased to about 4-5-folds in diabetic rats, which were associated with the elevation in urinary albumin excretion. PEDF expression in the glomeruli was down-regulated in experimental diabetes. Further, when proteins extracted from glomeruli of control rats were exposed to MMP-2, PEDF levels were found to be decreased in an MMP-2-dose-dependent manner.

Conclusions: The present study demonstrated for the first time that MMP-2 overexpression at early phase of diabetic nephropathy was involved in PEDF down-regulation in the diabetic kidney. Our observations suggest that restoration of PEDF via MMP-2 suppression may offer a promising strategy for halting the development and progression of diabetic nephropathy.

THE PLASMA GLUCOSE LOWERING ACTION OF NTU-SLR-C IN NORMAL AND DIABETIC MICE

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Aims: In this study, the antihyperglycemic principle of NTU-SLR-C isolated from a herbal plant was examined and compared with other antidiabetic agents in mice.

Methods: 8 to 10-week-old male ICR, streptozotocin (STZ)-induced diabetic (IDDM) and diet-induced obese (NIDDM) mice were enrolled in the study. Mice were treated with single intraperitoneal (i.p.) injection of NTU-SLR-C (5mg/kg) or other active agents. Biochemical parameters such as blood glucose and plasma insulin were measured using the glucose oxidase method and insulin ELISA. The protein level of hepatic phosphoenolpyruvate carboxykinase (PEPCK) was determined using Western blotting analysis.

Results: After 60-min injection, NTU-SLR-C decreased the plasma glucose concentrations in a dose-dependent manner from 0.1 to 5 mg/kg. The hypoglycemic actions of NTU-SLR-C in normal and NIDDM mice were associated with an increase of plasma insulin level; however, the insulin levels remained unchanged in IDDM mice. NTU-SLR-C attenuated the elevation of plasma glucose induced by an intraperitoneal glucose tolerance test (IPGTT) and increased glycogen synthesis. Moreover, elevated protein levels of PEPCK in liver from STZ-diabetic mice were reversed after treatment with NTU-SLR-C two times daily for seven days.

Conclusion: Our study proved that the mechanisms contributing to the hypoglycemic effect of NTU-SLR-C include insulin-dependent and insulin-independent pathway. Both the increase in the glucose utilization in peripheral tissue and the reduction in hepatic gluconeogenesis contribute to the lowering of plasma glucose. Thus, this compound may become a useful agent for the treatment of diabetic disorders.

INTERACTION BETWEEN LEPTIN AND INSULIN IN SKELETAL MUSCLE DURING AGEING IN WISTAR RAT

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Wistar rats develop adiposity, hiperleptinemia and whole body insulin resistance during ageing. Here we study how hiperleptinemia influences directly insulin action in skeletal muscle (SM) during ageing and the effect of moderate caloric restriction (CR). We determined the insulin effect (100 nM, 20 min) on 2-deoxyglucose uptake in type I (soleus) and type IIa (EDL) isolated muscles pre-incubated with leptin (5 nM, 20 min). Studies were carried out on 3-, 8- and 24-month old rats fed ad libitum, and in 8- and 24-months old animals after three months of CR.

Our results show that insulin-induced activation of 2-DOG uptake decreases with ageing in SM, mainly in soleus. The CR increases the insulin effect in 8-month, but not in 24-month old rats. Leptin also stimulates the 2-DOG uptake but to a lesser extent than insulin. This effect decreases with ageing in soleus and is restored by CR in both 8- and 24-month old rats.

Pre-treatment with leptin decreases the insulin stimulation of 2-DOG uptake only in leptin sensitive soleus from 3-month old animals and 8-month old rats after CR, but not in soleus from leptin resistant aged animals.

These data indicate that leptin exerts direct effects on SM and these effects might impair insulin action in contrast to its insulin-sensitizing effects on SM elicited through the CNS. Development of hyperleptinemia during ageing leads to central leptin resistance. Thus, it is tempted to propose that leptin, acting directly on SM, could contribute to the insulin resistance of this tissue in old animals.

PIGMENT EPITHELIUM-DERIVED FACTOR (PEDF) PREVENTS PLATELET ACTIVATION AND AGGREGATION IN DIABETIC RATS BY BLOCKING DELETERIOUS EFFECTS OF ADVANCED GLYCATION END PRODUCTS (AGES)

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Alteration of platelet function contributes to microthrombus formation and may play an important role in the pathogenesis of diabetic vascular complications. In addition, there is a growing body of evidence that oxidative stress generation is involved in platelet activation and aggregation in vivo. Since we have recently found that pigment epithelium-derived factor (PEDF) inhibits thrombus formation in rats through its anti-oxidative properties, we investigated here whether PEDF prevented platelet activation and aggregation in diabetic or advanced glycation end products (AGEs)-injected rats. Experimental diabetes was induced by injecting streptozotocin to Sprague-Dawley (SD) rats. Diabetic or non-diabetic SD rats were injected intravenously with or without 1 mg AGEs-bovine serum albumin (BSA) or non-glycated BSA in the presence or absence of 10 μg PEDF every day. Administration of PEDF or pyridoxal phosphate, an inhibitor of AGEs formation, inhibited platelet P-selectin expression and aggregation by suppressing NADPH oxidase-driven superoxide generation, and subsequently ameliorated a shortened tail vein bleeding time in diabetic rats. Further, intravenous administration of AGEs to normal rats mimicked the effects of diabetes on platelet activation and bleeding time, which were also blocked by simultaneous administration of PEDF. These results demonstrated for the first time that PEDF inhibited platelet activation and aggregation in diabetic rats through its anti-oxidative properties. Our present study suggests that PEDF may play a protective role against diabetic vascular complications by attenuating the deleterious effects of AGEs on platelets.

OVEREXPRESSION OF HUMAN NLRP3 IN MURINE MACROPHARGES/GRANULOCYTES ENHANCED THE DIET-INDUCED OBESITY

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NLRP3 (NLR family, pyrin domain containing 3) interacts with the apoptosis-associated speck-like protein PYCARD/ASC, which contains a caspase recruitment domain. The NLRP3-ASC-caspase1 complex is called as NALP3 inflammasome and functions as an upstream activator of NF-kappaB signaling, and caspase1, which leads to processing and release of IL1B and IL18. Previously, we found the variable expression level of NLRP3 individually in peripheral leukocytes. The individuals carrying genotype associated with higher expression level of NLRP3 showed significantly higher blood pressure and a trend with higher HbA1c. Then we studied the influences of the higher expression of NLRP3 on the metabolic parameters in mice. The major isoform of Human NLRP3 cDNA was inserted under CD11b promoter. This transgenic construct was injected into oocytes of C57BL6, and a mouse line expressing NLRP3 in macropharges/granulocytes was established. The Tg-mice grew up without obvious difference from wild type littermates under regular chow. After 8 weeks high-fat diet, however, the Tg-mice showed significantly higher body weight than wild littermates. The food intake was same under regular chow but it became significantly higher in Tg-mice than wild mice under high-fat diet. The Tg-mice showed significantly higher plasma glucose level at 120 min in glucose tolerance test, before the high-fat diet. The plasma leptin levels increased after high-fat diet in both animals but those were significantly higher in Tg-mice. These data indicated that constitutive expression of NLRP3 in leukocytes induced insulin and leptin resistance in the Tg-mice, which was enhanced by high-fat diet.

NORMAL 0 21 GENETIC PREDISPOSITION FOR JUVENILE OBESITY IN THE BERLIN FAT MOUSE INBRED LINE

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The high fatness selected Berlin Fat Mouse Inbred line BFMI860 as a novel model for polygenic obesity. BFMI860 males have 5.1fold higher fat percentage in comparison to the unselected mouse line C57BL/6 (B6) under standard diet at 10 weeks. BFMI860 mice between 6 and 10 weeks show the highest body weight gain. Hyperphagia, higher respiratory quotients, and abnormally high blood triglyceride levels accompanied the high body fat accumulation in BFMI860 mice. The endocrine profile of BFMI860 mice is typical for the obesity status in humans with highly increased serum leptin and insulin and reduced adiponectin levels compared to B6. Despite the increased insulin levels, a glucose tolerance test showed a better blood glucose clearance in BFMI860 mice compared to B6 on standard diet. High fat diet-feeding resulted in an additional increase of body weight and body fat mass as well as in a marked hyperleptinemia and hyperinsulinemia with high variability in glucose levels. The adiponectin levels continued to decline under high fat diet. The blood glucose clearance, however, was delayed compared to high fat diet-fed B6 mice. From our observations, we conclude, that our BFMI860 mouse line is a model for juvenile obesity with features of dyslipidemia and metabolic syndrome. Genetic studies showed that 60% of the BFMI860 phenotype result from a gene defect on chromosome 3.

The project is supported by the BMBF (NGFNplus) and the DFG (GRK1208).

MILDRONATE IMPROVES GLUCOSE AND LIPID METABOLISM IN STREPTOZOTOCIN DIABETIC RATS

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Mildronate, a γ-butyrobetaine analogue is used as an antiischemic drug. There is data that it might increase utilization of glucose.

Methods: Diabetes mellitus in Wistar rats was induced by injection of streptozotocin (50 mg/kg). After confirmation of diabetes, treatment with Mildronate (100 mg/kg daily, *per os*), was started and lasted for 6 weeks. Weight, blood glucose concentration, blood triglyceride concentration, blood ketone body concentration, glycated hemoglobin percent (HbA1c%), glucose tolerance were monitored throughout the experiment.

Results: In diabetic rats, Mildronate treatment caused a significant decrease in mean blood glucose concentration after 4 weeks of treatment (streptozotocin group - 40.27±3.34 mmol/l, streptozotocin + Mildronate group - 29.82±2.12 mmol/l). Mildronate produced positive effect on triglyceride level in diabetic rats: after 4, 5 and 6 weeks of treatment streptozotocin+Mildronate group showed lower triglyceride levels, than streptozotocin group (after 4 weeks - 1.29±0.10 mmol/l versus 1.91±0.26 mmol/l; after 5 weeks - 1.04±0.03 mmol/l versus 1.23±0.08 mmol/l; after 6 weeks - 1.12±0.09 mmol/l versus 1.77±0.30 mmol/l). Mildronate was able to slow down significantly the rise of HbA1c% in treated diabetic group (after 6 weeks of treatment HbA1c% in streptozotocin group - 9.66±0.21%, in streptozotocin+Mildronate group - 8.75±0.33%). Oral glucose tolerance test after 4 treatment weeks revealed significantly better glucose tolerance in streptozotocin+Mildronate group at 120 minutes after glucose ingestion.

Conclusion: Mildronate exhibits positive effect on parameters of carbohydrate and lipid metabolism in experimental diabetes mellitus model.

KIOM-201 REVERSES DIABESITY INDUCED IN RATS WITH HIGH-FAT DIET

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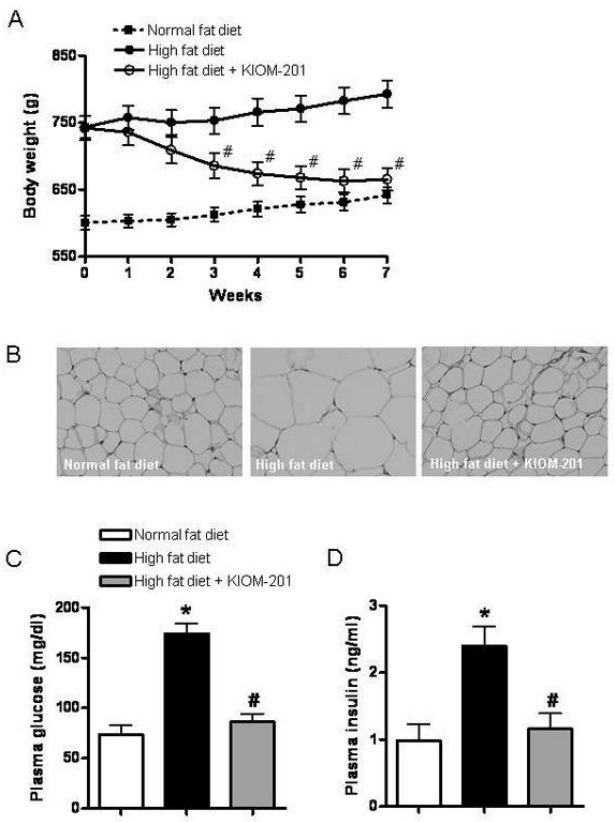
Diabesity, obesity-dependent diabetes, has emerged as a major public health problem that is increasing in frequency. This study investigated the effects of KIOM-201, an herbal medicine, in rats previously fed a high-fat diet for 120 days to induce obesity and related diabetes. High-fat fed rats became obese and developed hyperglycemia and hyperinsulinemia, indicating that they were insulin resistant. KIOM-201 were then administrated orally for 7 weeks. The treatment of KIOM-201 significantly decreased body weight compared with non-treated rats without change of high-fat diet intake. Plasma glucose, glycated hemoglobin, and insulin were restored to levels of normal fat-fed rats, and circulating triglyceride and cholesterol were significantly decreased. KIOM-201 also reverses the altered circulating adiponectin level. Adipose tissue mass, adipocyte hypertrophy, and deposition of triglyceride in liver were significantly decreased. These changes were accompanied by significant improvement of insulin sensitivity in KIOM-201 treated rats. These data indicate that KIOM-201 provides an effective means of countering obesity and related diabetes induced by consumption of a high-fat diet.



[Figure1]

Figure1. Effects of KIOM-201 (A) body weight, (B) adpocyte hypertrophy, (C) plasma glucose, and (D) insulin in rats with diabesity. All values are means±SE. $^{*}P< 0.01$ vs. normal fat diet, $^{\#}P< 0.01$ vs. high fat diet.

PROTECTIVE EFFECT OF A POLY-PHYTOCOMPOUND ON EARLY STAGE NEPHROPATHY SECONDARY TO EXPERIMENTALLY-INDUCED DIABETES

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Diabetic nephropathy (DN) is a severe and life-threatening complication of long-standing diabetes. Male Wistar rats were randomly assigned to two groups. One group of rats (SZT-diabetic group) was fed a normal pellet diet (groupA) while group B was fed the diet added with DTS (panax pseudoginseng, eucommia ulmoides, ginseng radix, in the weight percentage of 50%/25%/25%, Kyotsu Jigyo, Tokyo, Japan) at the dose of 50mg/kg/day throughout the experimental period. At the end of 8th week, 24-hour urine was collected for the measurement of the albumin concentration, blood samples were collected for serum biochemistry and rats sacrificed for kidney measurement of oxidative stress parameters, histo-morphological features while nephrin and Macrophage Chemoattractant Protein-1 (MCP-1) gene expression were assessed by fluorescence real-time quantitative PCR. STZ-treated animals showed significantly increased lipid peroxidation in kidney tissue and proteinuria ($p< 0.001$ vs control). DTS supplementation did not affect plasma glucose but it significantly decreased MDA plasma level and the overall redox parameters ($p< 0.05$ vs untreated diabetic rats) together with a partially mitigation of proteinuria DTS ($p< 0.05$). Histological analysis showed that DTS significantly reduced the glomerular volume together with glomerulosclerosis and interstitial fibrosis score ($p< 0.05$), the latter two being correlated to proteinuria ($p< 0.05$). Nutraceutical supplementation enables also a reduction of diabetes-induced decrease of nephrin mRNA expression and a 67% reduction of MCP-1 mRNA expression up-regulation ($p< 0.01$). Taken altogether, these data show that, besides the mandatory control of glycemia, a nutraceutical intervention may offer promising therapeutic options to be integrated within mainstream medicine.

EFFECT OF VITAMINS A,E,C AND OMEGA-3 FATTY ACIDS SUPPLEMENTATION DISTINCTLY ON THE LEVEL OF PARAOXONASE AND ARYLESTERASE ACTIVITY IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Aims: The aim of this study is to investigate the effect of supplementation with vitamins A, E and C and ω-3 fatty acids on paraoxonase and arylesterase activity in streptozotocin (STZ) induced diabetic rats.

Methods: 64 male wistar rats weighing 250g were divided into four groups as normal control, diabetic control, diabetic with vitamin A, E and C supplementation and diabetic with ω-3 fatty acids supplementation. After four weeks the rats were anesthetized and paraoxonase and arylesterase activity was investigated in blood samples, liver and heart homogenate.

Results: In diabetic rats heart and liver arylesterase ($P< 0.01$) activity was significantly less than normal control rats. Vitamin A, E and C supplementation and ω-3 fatty acids supplementation significantly increased liver arylesterase ($P< 0.05$). No significant change was observed in other samples.

Conclusion: Supplementation of Vitamin A, E and C and ω-3 fatty acids was found to increase liver arylesterase activity in diabetic rats and they can be valuable candidates in the treatment of the complications of diabetes.

THE SPECIFIC O-GLCNAC GLYCOSYLATION OF HSP70 AND P65-NFKB NUCLEOPROTEINS IN THE LIVER OF DIABETIC RATS

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The diabetes-related chronic increase of blood glucose levels generates a rise in the glucose flux through the hexosamine biosynthesis pathway, thereby increasing the substrates for protein O-GlcNAcylation. Intracellular signaling transduction pathways which operate through an increased glucose flux rely on changes in O-GlcNac levels globally and on specific proteins to modulate cellular behavior. There are many O-GlcNAc susceptible proteins that are involved in cell stress response. In this study, we investigated O-GlcNAcylation of nucleoproteins in the livers of streptozotocin (STZ)-treated Wistar rats four weeks after an i.p.injection of 65 mg STZ/kg. We identified the specific O-GlcNAcylation of stress-induced proteins Hsp70 (heat-shock protein 70) and p65-NF-kB by WGA affinity chromatography and subsequent Western immunoblot analysis. Although we observed a non-significant increase in the overall nucleoprotein expression level of Hsp70 in diabetic rats, a 3.8-fold ($p<0.01$) increase in its O-GlcNac level was measured. O-GlcNAcylation of p65-NF-kB was not detected in control, nondiabetic rats while the diabetes-associated increase in expression level (1.2-fold, $p<0.05$) was followed by a pronounced O-glycosylation of activated p65-NF-kB. Since Hsp70 and NF-kB are beneficial in the defence against oxidative injury that characterizes the chronic hyperglycemic state, we concluded that insulin-signaling and the stress-response pathways in the liver are interlinked and that O-GlcNAcylation of Hsp70 and p65-NFkB are important determinants of hyperglycemic injury.

CHANGES IN TISSUE LIPID COMPOSITION IN INSULIN RESISTANT RATS AFTER SHORT TERM TREATMENT WITH METFORMIN

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Insulin resistance (IR) is a pre-diabetic state caused by high fat diet (HFD) and sedentary lifestyle. IR is typically associated with dyslipidemia. We have determined the lipid profile of liver, muscle and adipose tissue from HFD-induced IR-rats, in comparison to rats treated with Metformin. Rats were fed HFD (40 kcal% fat) for 12 weeks to induce IR, while the control rats were fed a normal diet (< 10 kcal% fat). After confirming the onset of IR, a parallel group of rats started a treatment regime with Metformin (13mg/kg BW/d). The rats were sacrificed after 28 days and blood and tissues were analysed. HFD rats were insulin resistant, displayed decreased glucose uptake in liver, muscle and adipose tissue as well as increased plasma free fatty acid (FFA) and triglyceride (TG) levels. Pathological changes in the tissue lipid composition were observed in the HFD rats. Treatment with Metformin increased the glucose uptake into muscle and liver, and decreased glucose uptake into adipose tissue. FFAs were considerably decreased in the plasma, liver and adipose tissue of the Metformin treated rat group. However, there was no change in FFA content in the muscle tissue. Total cholesterol was significantly decreased in muscle and adipose tissue, although there was no change in the plasma and liver cholesterol levels. TG levels were unaltered in plasma, muscle and adipose tissue but significantly decreased in the liver. This presentation will discuss the possible causes and implications of the action of short term Metformin treatment on glucose and lipid metabolism.

ROBUST INDUCTION OF APOA-IV EXPRESSION AND INCREASE IN HDL CHOLESTEROL LEVELS BY FEEDING SESAME IN MICE

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ApoA-IV is a 46 kDa plasma protein and circulates freely or is associated with chylomicrons and HDLs. Its physiological role has not been fully understood but several studies suggested that plasma apoA-IV is a key determinant of HDL levels and that the increased apoA-IV is protective against the development of atherosclerosis. In this study, we found that feeding sesame largely induced apoA-IV expression and increased the HDL cholesterol levels in mice. We first performed proteomic analysis of serum proteins from mice fed sesame for a few days and identified apoA-IV as a most induced protein by feeding sesame. Quantitative RT-PCR analysis of the intestine and liver RNA revealed that quick and robust induction of apoA-IV mRNA occurred in the liver. The induction of other lipoprotein mRNAs were not observed and the elevated levels of apoA-IV mRNA quickly dropped but twice higher levels than the control were maintained for more than a week. A concomitant increase in the levels of HDL cholesterol was also evident. These effects were observed only with sesame but not other oily plant seeds or nuts. Major sesame lignans alone could not reproduce the effects at all. The mechanism of the robust induction of apoA-IV mRNA in the liver by feeding sesame, so far examined, seems to be similar to that by fasting although sesame feeding did not induce the expression of PGC1a and HNF4a mRNAs that have been reported to be essential for the induction by fasting.

METABOLIC EFFECTS OF A DIETARY SUPPLEMENT OF ROSE HIP IN THE HIGH-FAT FED C57BL/6J MOUSE

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The aim of this study was to investigate the long term metabolic effects of a dietary supplement of rose hip (Rosa canina) using the high-fat fed C57BL/6J mouse as an experimental model. This study comprised both male and female mice and the effects of three different concentrations of rose hip were evaluated, 6, 12 and 30% by weight. In pilot-studies, 30% rose hip has been shown to improve insulin resistance and reduce body weight and body fat mass compared to control.

We show that 30% rose hip, as expected, suppress body weight gain and reduce body fat mass in both male and female mice compared to control, whereas the two lower concentrations do not have the same effect. No differences in energy intake between the groups were detected. A small but significant increase in oxygen consumption in brown adipose tissue was observed in the group fed 30% rose hip compared to control. Rose hip tended to improve glucose tolerance and to reduce plasma insulin in male mice in a dose dependent manner, however, only the 30% group showed statistically significant differences compared to control. Also, an insulin tolerance test showed a strong tendency toward improved insulin sensitivity in the 30% group compared to control. These effects were not as pronounced in the female mice and did not reach statistical significance. Taken together these data suggests that a dietary supplement of rose hip ameliorate the diabetic state imposed by high-fat feeding in the C57BL/6J mouse.

HEPATIC PROTEOME ANALYSIS OF INSULIN RESISTANT RATS TREATED WITH METFORMIN

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Insulin resistance, a prediabetic condition, is becoming a growing problem worldwide.

The **objective** of this study was to identify and quantify liver proteins associated with insulin resistance (IR) and IR treated with metformin.

Methods: Insulin resistance in rats was induced via a high fat diet. Liver proteins of three groups of rats were determined: lean controls, insulin resistant rats and insulin resistant rats treated with metformin

(11.3mg/kg/day for 7 weeks). Proteome analysis was done via 2D gel electrophoresis and mass spectrometry.

Results: The high fat diet promoted the activation of certain enzymes associated with gluconeogenesis and β-oxidation, while suppressing glycolytic enzymes. Significant changes were also found with the citrin/oxyglutarate shuttles, which may be linked to increased amino acid deamination, a process necessary to produce the substrates needed for gluconeogenesis. Metformin reversed both gluconeogenesis and β-oxdation while promoting glycolysis, which indicates an increase in insulin sensitivity. Metformin also significantly decreased enzymes associated with cholesterol and fatty acid oxidation. The results provide a physiological comparison of the liver metabolism of insulin resistance and metformin treatment.

Conclusion: This study allows us to gain insight into the hepatic intracellular biochemical changes during the development of insulin resistance and provides potential avenues for future research.

CANNABINOID AGONIST WIN 55,212-2 IMPROVES THE ISCHAEMIA-REPERFUSION INJURY IN ISOLATED HEARTS FROM ZUCKER DIABETIC FATTY RATS

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Introduction: Diabetes leads to a markedly increased risk for cardiovascular disease including heart failure. Cannabinoids exert cardiovascular effects and they have been proposed as cardioprotective drugs in ischaemia-reperfusion (IR) injury in rats.

Aim: To investigate the effect of the cannabinoid agonist Win55,212-2 (Win) on cardiac IR injury in isolated hearts from Zucker Diabetic Fatty rats (ZDF).

Methods: 20-week-old male ZDF and their corresponding controls (LEAN) received an intraperitoneal injection of Win (1mg/kg) or vehicle. After 40 minutes, hearts were isolated and mounted in a Langendorff system. An IR process was then performed. The cardiac parameters analyzed were: Left Ventricular Developed Pressure (LVDP), End Diastolic Pressure (EDP), Coronary Perfusion Pressure (CPP) and Heart Rate (HR). Responses are expressed as mean ± s.e.m (n=5-7). Two way ANOVA followed by Bonferroni/Dunn *post hoc* test was used for statistical comparisons. $P < 0.05$ was considered significant.

Results: After the IR period, a cardiac damage in LEAN and ZDF rats was observed. In ZDF, Win provoked a significant improvement in CPP and HR after IR (ZDF Win: CPP = 117.9±12.6 (7) $P< 0.05$ *vs* ZDF vehicle: CPP = 197.6±34.8 (5); ZDF Win: HR = 117.9±12.6 (7) $P< 0.05$ *vs* ZDF vehicle: HR = 0.0±0.0 (5)). No improvement was observed in LEAN rats.

Conclusions: Win partially improves the cardiac function after an IR process in ZDF, affecting mainly CPP and HR. More research is needed to investigate the underlying mechanisms.

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LONG-TERM RESVERATROL ADMINISTRATION IMPROVES METABOLIC ALTERATIONS IN OBESE ZUCKER RATS

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Aims: This study addresses the effects of long-term administration of the polyphenolic stilbene resveratrol on functional alterations arising from the metabolic syndrome experimental model of obese Zucker rats, and the possible mechanisms involved.

Methods: 14 male obese Zucker rats and 14 lean littermates were randomly distributed in two groups (n=7): one of them received resveratrol (10 mg/kg/day) and the other one received the vehicle (water) for ten weeks.

Results: The high plasma concentrations of triglycerides, total cholesterol, free fatty acids, insulin and leptin found in obese Zucker rats were reduced in obese rats that received resveratrol. Furthermore, the elevated hepatic lipid content was significantly lower in obese rats treated with resveratrol, an effect which was related to the increased phosphorylation of 5'-AMP-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC) in the liver of these animals. Resveratrol treatment also improved the inflammatory status peculiar to this model, as it increased adiponectin secretion and lowered tumor necrosis factor-α production by the visceral adipose tissue (VAT) of obese Zucker rats. Moreover, chronic intake of resveratrol enhanced VAT eNOS expression among obese Zucker rats. These effects parallel the activation of AMPK and inhibition by phosphorylation of ACC in this tissue. The raised systolic blood pressure and reduced aortic eNOS expression found in obese Zucker rats were significantly improved in the resveratrol-treated obese rats.

Conclusion: Resveratrol improved dyslipidemia, hyperinsulinemia, hyperleptinemia and hypertension in obese Zucker rats, and produced anti-inflammatory effects in VAT, effects that seem to be mediated by AMPK activation.

EFFECT OF EZETIMIBE AND SIMVASTATIN ON INTESTINAL LYMPHATIC CHYLOMICRON OVER-PRODUCTION IN THE INSULIN-RESISTANT AND PRE-DIABETIC JCR:LA-CP RAT

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Ezetimibe (EZ) and its analogue SCH4861 selectively inhibit intestinal cholesterol absorption via the NPC1L1 transporter. EZ, either alone or in combination with Simvastatin (SV) can decrease plasma LDL-C. However, it is unknown if EZ+SV has synergistic effects on intestinal lipoprotein production. We have recently established the insulin-resistant (IR) JCR:LA-cp rat as a useful model to study over-production of lymph chylomicrons (CM). The aim of this study was to determine the effect of both EZ and SV monotherapy, as well as combination therapy, on CM production in the pre-diabetic JCR:LA-cp rat.

IR rats 6 wks of age were randomized to either EZ (0.01%), SV (0.01%) or both for 8 weeks. CM were collected from animals by cannulation of the superior mesenteric lymph duct. Plasma and lymph lipid as well as apolipoprotein B48 (apoB48) were measured by commercially available kits and by western-immunobloting techniques.

EZ, alone (43%$P< 0.01$) or EZ+SV (46%$P< 0.05$) lowered plasma LDL-C in IR rats compared to non-treated IR rats. Plasma TG was reduced in IR rats treated with both SV or SV+EZ relative to non-treated IR rats. Interestingly, SV elevated CM-TG (49%$P< 0.05$) and CM-cholesterol (108%$P< 0.01$) in IR rats relative to non-treated IR rats. Whereas EZ+SV increased apoB48 in lymph (54%$P< 0.01$) compared to non-treated IR rats.

EZ lowers plasma LDL-C independent of effects on CM production in IR rats. EZ also appears to ameliorate SV-induced cholesterol content of CM in IR rats. These findings support the efficacious properties of EZ in modulating dyslipidemia.

APPLE JUICE SHOWS ANTISTEATOTIC ACTIVITY IN OBESE ZUCKER RATS

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Obesity epidemic is associated with increased prevalence of nonalcoholic fatty liver disease characterized by an excessive hepatic lipid accumulation and functional impairment of hepatocytes. In context with preventive strategies, interest has been on dietary flavonoids, which might cure or delay the progression of hepatic steatosis through modulation of lipid metabolism. The objective of the present study was to examine an antisteatotic potential of high-flavonoid containing apple juice *versus* an isocaloric softdrink in the Zucker obese rat. Three groups (lean, obese pair fed (pf) to lean, obese *ad libitum* (al)) were objected to 11-week intervention with apple juice (n=6/group) or an isocaloric control drink (n=6/group). Besides general parameters in plasma (e.g. total triglycerides (TG), cholesterol, adiponectin, insulin, glucose) and liver (total lipids, TG, cholesterol) gene expression profiles of transcripts relevant for hepatic lipogenesis and lipolysis/β-oxidation have been quantified by RT-PCR. Results show that apple juice significantly reduced the hepatic total lipid and TG content in obese pf and obese al compared to respective softdrink groups. This decreased lipid content was associated by normalization of hepatic PPARγ- without affecting PPARα- gene expression in the obese pf. Fasting plasma insulin was decreased significantly by apple juice paralleled by a significant elevation of plasma adiponectin in the obese pf. In summary, these data show a strong reduction of hepatic steatosis and improved insulin sensitivity by apple juice. We suggest that yet unidentified apple ingredients may account for the antisteatotic effect by decreased hepatic lipogenesis rather than induction of lipolytic pathways in the steatotic liver.

EFFECT OF GLIBENCLAMIDE IN HYPERGLYCEMIA INDUCED CONTRACTILE DYSFUNCTION AND STRESS SIGNALING CHANGES IN DIABETIC HEART: ROLE OF OXIDATIVE AND NITROSATIVE STRESS

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Diabetes causes myocardial dysfunction through accumulation of reactive oxygen species and/or reactive nitrogen species which leads to loss of mitochondrial membrane potential resulting in apoptotic cell death. This is accompanied by dyslipidemia, proinflammatory cytokine shift, cardiac fibrosis all of which ultimately affects cardiac structure and function.

Glibenclamide reduces plasma glucose levels and improves glucose tolerance without elevating plasma insulin levels. It restores elevated lipid levels, reduces intracellular and mitochondrial ROS levels.

Availability of a compound that simultaneously decreases hyperglycemia, restores insulin secretion, lowers cholesterol and triglycerides levels and inhibits oxidative stress produced by hyperglycemia seems to be an interesting therapeutic prospect for prevention of cardiac complications.

We investigated role of glibenclamide on cardiac function, dyslipidemia, inflammation, apoptosis, oxidative and nitrosative stress in an *in vivo* model of experimental diabetes.

Diabetes was induced in 18 Wistar rats by injecting streptozotocin (55 mg/kg) followed by treatment with glibenclamide (n = 12) for 12 weeks. Non-diabetic rats served as controls (n = 6). Left ventricular function was assessed after 12 weeks. Blood serum was analyzed for cardiac markers, lipid profile and cytokine levels. Cardiac tissue was analyzed for the expression of antioxidant enzymes, oxidative and nitrosative stress and apoptosis.

Left ventricular performance was depressed in untreated diabetic animals. Serum biochemistry showed low insulin levels, elevated glucose, cholesterol, triglycerides levels in untreated diabetic rats compared to controls. Increased ROS and RNS levels were observed in untreated diabetic animals. These changes were significantly attenuated in the group treated with glibenclamide.

EFFECTS OF ANORECTIC DRUGS ON FOOD INTAKE BEHAVIOUR OF SWINE

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We have investigated whether oral administration of clinically effective anorectic drugs reduces food intake of pigs.Six male domestic pigs of 60 kg bodyweight were fed two meals per day. Rimonabant®, a serotonin reuptake inhibitor, or Sibutramine®, a cannaboid receptor-1 antagonist, were mixed with mashed food and offered to the pigs one hour before the morning meal. Doses were 0.3, 1.0 or 3.0 mg/kg. One hour after drug administration the standard diet was available unrestrictedly for 60 minutes. Food intake was measured every 90 seconds. Meal size and speed of consumption on (drug) test days were compared to meal size of control days (no drug in the pre meal).

Average control meal size was 1.0 - 1.2 kg. Half-maximum and maximum food intake per 90 seconds were measured at 10-12 minutes and 30-40 minutes after the onset of eating, respectively. The final phase of the meals was characterized by a lower speed of eating. Administration of Rimonabant® and Sibutramine® reduced total food consumption. Maximum reduction of food intake was 250 - 300 g ($p< 0.05$). Drug treatment resulted in an earlier onset of the final meal phase. The initial meal phase characterized by a high level of food intake per 90-second interval was not affected.

It is concluded that pigs are responsive to treatment with clinically effective anorectic drugs. The applied doses support the notion of a high level of pharmacological homology between pigs and humans, and the translational relevance of pigs for pharmacological studies.

THE OBESE GÖTTINGEN MINIPIG AS A MODEL OF THE METABOLIC SYNDROME: BLOOD PRESSURE AND THE ELECTROCARDIOGRAM

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Obese Göttingen minipigs share metabolic impairments seen in obese humans, such as decreased insulin sensitivity, glucose intolerance and hypertriglyceridemia. Hypertension, however, has only been observed for Ossabaw minipigs and not for Yucatan minipigs. For obese Göttingen minipigs blood pressure and electrocardiogram need to be determined.

For five months, one group of 3-4 years old female Göttingen minipigs (retired breeders) was fed restrictedly a low-fat/low-energy diet and the other group ad libitum a high-fat/high-energy diet provided twice a day for a period of one hour. The pigs were fitted with a jugular vein and a carotid artery catheter. Five weeks after surgery arterial blood pressure measurement and electrocardiographic monitoring were done on three separate days three hours after feeding in unrestrained lean (n=3; 47 kg) and obese (n=3; 85 kg) pigs. The day before the measurements all pigs got a restricted amount of food, to assure similar food intake at the day of monitoring. Systolic and diastolic arterial blood pressure were significantly higher in the obese than in the lean pigs (169 versus 121 and 117 versus 85 mm Hg, respectively). Also heart rate was significantly higher in obese (93 bpm) than in lean pigs (78 bpm). The RR-interval in the electrocardiogram

was significantly shorter for the obese (683 msec) than for the lean pigs (810 msec) but there were no significant differences in QRS interval.

The increased arterial blood pressure and the higher heart rate indicate that obese female Göttingen minipigs may also share cardiovascular impairments with obese humans.

REGULATION OF HAPTOGLOBIN GENE EXPRESSION BY THE GLUCOCORTICOID RECEPTOR DURING STREPTOZOTOCIN-INDUCED DIABETES

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The glucocorticoid receptor (GR) is responsible for mediating the numerous and widespread effects of glucocorticoids including transcriptional regulation of the haptoglobin (Hp) gene. Hp is an acute-phase protein. Previous studies have demonstrated a strong correlation between the diabetes-related oxidative status and expression of Hp suggesting that its antioxidative property is an important part of antioxidative defense mechanisms. Since an attractive therapeutic approach is to target key transcriptional regulators for pharmacological intervention, this study was aimed to investigate streptozotocin (STZ)-induced diabetic effects on the level of the glucocorticoid receptor (GR) in rat liver nuclei and its involvement in the regulation of Hp gene expression at different times after treatment. Diabetes was induced in male Wistar rats by a single STZ injection (65 mg/kg body weight). A 3.4-fold elevation of GR level was obtained (Western-immunoblot) two weeks after treatment where the maximal serum level of Hp and transcriptional activation of its gene in the liver was detected. Four end seven weeks after treatment, the nuclear level of GR was reduced while Hp expression was still elevated but lower than after two weeks. DNA-affinity chromatography with the Hp gene hormone-responsive element revealed that GR mediated Hp gene regulation only during the early stage of diabetes that was characterized by strong anti-inflammatory and antioxidant activities. Since glucocorticoids are used extensively for the treatment of a wide range of diseases, these results point to the significance of glucocorticoid treatments during the early phase of diabetes.

EFFECTIVENESS OF MICROBIAL TOXIC SUBSTANCES AT THE EXPERIMENTAL PANCREATIC DIABETES

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The purpose of research is to study influence of microbial toxic substances (MTS) representing an analogue to Coley's vaccine and characterized by immunostimulating effect on the course of experimental pancreatic diabetes (EPD). EPD was reproduced on white rats of Vistar breed of weight 150-200 g by administration of alloxan by a standard procedure. Animals were divided into 3 groups of 10 pcs: 1st group was control which was made of intact rats; 2nd group were animals with diabetes (without treatment), 3rd group were rats with diabetes, treated by MTS (intramuscular administration within 6 days). Researches were carried out at two stages: in 6 and 14 days after modeling. In blood of animals we determined the concentration of glucose and α-amylase activity. It is determined, that in 6 days after EPD modeling the average level of glucose increased by 1,6 times ($P< 0,05$) at uncured animals, and α-amylase activity: by 2,6 times ($P< 0,05$) in relation to a testing level. In the group of treated rats statistically reliable changes in relation to uncured ones were not registered during this period. In 14 days after modeling the glucose content in blood of treated animals was 63,6% lower ($P< 0,05$), than of untreated animals, decreasing to a level of the control group (100,8%). α-amylase activity at treated rats was also 25% lower, but continued to remain a slightly heightened making 153,5% ($P< 0,05$) of the testing level. Thus, MTS improve the course of EPD and promote normalization of the basic biochemical parameters.

TWO PLANT EXTRACTS FROM THE CANADIAN BOREAL FOREST PREVENT OBESITY AND DIABETES IN A DIET-INDUCED OBESITY MOUSE MODEL

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The prevalence of type 2 diabetes (T2D) and obesity is increasing among the Cree of Eeyou Istchee (CEI - Northern Quebec), consistent with observed increases in the metabolic syndrome. Cultural inadequacy of modern T2D therapies, along with non-traditional diet and sedentary lifestyle are involved. Exploring treatments from CEI traditional pharmacopeia may be an interesting alternative. We thus evaluated the effectiveness of two plant extracts (AD03 and W7) in preventing obesity and the metabolic syndrome in C57/Bl6 mice. The mice were subjected to high fat (HF) diet with or without plant extracts for eight weeks resulting in obesity, hyperinsulinemia and mild hyperglycemia. Plant extracts significantly decreased body weight by 13 to 17.6%, and retroperitoneal fat pad by 16 to 18% compared to controls. Mild reduced food intake was seen with W7, but could not totally explain weight loss. Glycemia was significantly decreased by 17 to 19% in treated animals compared to controls, as was the ratio of insulinemia to glycemia. This could be related to the reduction in triglyceride content in liver and skeletal muscle, as confirmed by histological analysis of lipid content revealing a reduced proportion of steatotic livers in W7 animals as compared to HF controls. Plant extracts significantly increased adiponectin by 25 to 62% and skin temperature by 1.5 to 2°C in animals treated with AD03 or W7 respectively. These plant extracts thus exhibit promising anti-obesity and consequently anti-diabetic effects. Mechanisms remain to be elucidated but results point towards a stimulation of metabolic rate. Funded by CIHR.

HIGHT GLUCOSE AND HIGH INSULINE SUPPRESSED CELL VIABILITY ON HEPG2 AND H9C2 CELLS

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Insulin resistance is an independent risk factor for the development of cardiovascular atherosclerosis and diabetes. The object of this study would like to investigate how the HepG2 cell and H9c2 cell respond to high glucose and high insulin in the culture medium. Both HepG2 and H9c2 cells were cultured in the medium containing DMEM with different insulin concentrations (0ug/ml, 5 ug/ml, and 50ug/ ml) and DMEM plus extra 4.5g/L glucose with different insulin concentration (0 ug/ml, 5 ug/ml, and 50ug/ ml) respectively. The MTT and glucose uptake assay were used in this study. The results found that both HepG2 and H9c2 decrease cell viability with the increase in insulin and glucose concentrations in the medium, but the glucose utilization rate decreased following the culture time increase in the medium of DMEM plus extra glucose added with different insulin concentrations (5ug/ml, and 50ug/ ml). On the other hand, glucose utilization didn't show the same parameter as cell viability. The glucose utilization rate was decreasing slowly followed as the culture time increased. From these results, it could be concluded that constant culture cells in a high insulin and high glucose concentration may change the metabolic pathway of H9c2 and HepG2 cell and induce the reduction of H9c2 and HepG2 cell lifespan.

EFFECTS OF SARDINE PROTEIN ON GLYCEMIA, GLUCOSE INTOLERANCE AND GLUCOSE METABOLISM IN RATS FED A HIGH-FRUCTOSE DIET

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Dietary fructose has been suspected to contribute to development of metabolic syndrome.

The effect of sardine protein (SP) as compared to casein (CAS) on plasma glucose, glucose intolerance, and lipid levels and glycogen and lipid contents in rats fed a high-fructose diet (64%) has been investigated. Twelve male Wistar rats were divided into two groups and were fed diets containing 20% purified sardine protein or casein and 64% of fructose for 8 weeks.

As compared to casein, sardine protein rats lowered serum glucose and glucose intolerance after glucose injection in rats. Serum triglycerides and phospholipids levels were decreased by 47% and 11%, respectively in SP-fed rats as compared with casein-fed rats. Consumption of SP led to decreased liver total cholesterol (27%) and phospholipid levels (26%). The concentrations of albumin, fibrinogen, apo A-I and B100 were similar in the both groups. Glycogen in liver was 1.45-fold higher in SP than in CAS group, while in muscle and kidney the values remained unchanged. Liver glucose 6 phosphatase activity was not significantly affected. In rats fed SP diet, the glucose concentration in brain was elevated by 18% as compared to CAS diet.

These observations show that SP has beneficial effects and contributes to a reversal of lipid and glucose abnormalities induced by high fructose diet.

THE EFFECTS OF DEFATTED EGG YOLKS HYDROLYSATES IN INSULINE SECRETION ON OVERIECTOMIZED RATS

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Bioactive peptides are specific protein fragments that positively impact the body's function or condition and ultimately may influence health. In this study, defatted egg yolks were hydrolyzed with papain enzyme for 4 hours, then used freeze-drying to dry the sample. 8 weeks old 24 female SD rats were divided into three groups after ovariectomized. Group A fed normal diet only; Group B fed normal diet mix with dwfatted egg yolks (0.0245% of total energy); Group C fed normal diet mix with defatted egg yolks hydrolysates (0.0245% of total energy). After 12 weeks experiment period, the animal was sacrificed and blood was collected. The body weight, fasting blood glucose, insulin secretion were examined. The body weight did not show significantly different between the groups. Serum level of insulin was higher in group B and C, fasting blood glucose concentration showed the same parameter as insulin level. These finding suggest that mix defatted Egg Yolks hydrolysates in the diet may change the insulin secretion level and insulin effective in the ovarietomized rats, and which might cause impairment of energy metabolic pathway.

ALTERED MEMBRANE FUNCTIONS IN ALLOXAN DIABETIC RAT BRAIN. EFFECT OF *TRIGONELLA FOENUM GRAECUM* AND INSULIN

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Objective: To study changes in monoamine oxidase (MAO) activity, lipid peroxidation levels, membrane fluidity and lipofuscin accumulation occurring in diabetic rat brain and to see whether these changes are restored to normal levels after administration of insulin and Trigonella foenum graecum (TSP).

Methods: Animals were made diabetes by injecting 15mg/100g body weight alloxan to each rat. Diabetes animals were given Trigonella seed powder (5% w/w) mixed with their standard food for 21 days. MAO activity was assayed in synaptosomal and supernatant fraction of brain. Lipid peroxidation was measured in different brain regions by measuring formation of 4-Hydroxynonenal (4HNE) levels. The presence of lipofuscin was observed by fluorescence microscopy in different brain regions.

Results: Present work revealed that alloxan diabetes was associated in significant increases in MAO activity, lipid peroxidation and lipofuscin accumulation in brain of rats. Activity of catecholamine degrading enzyme, MAO showed a significant increase in the synaptosomes membrane fractions of whole brain in diabetic animals. Present study also showed that insulin administration and TSP to diabetic animals significantly decreased MAO activity, lipid peroxidation, membrane fluidity and lipofuscin accumulation in brain of rats.

Conclusions: It can therefore be suggested that Trigonella foenum graecum (TSP)'s beneficial effects seemed to arise from their antioxidative, antiobesity, antilipofuscin and antilipidperoxidative actions. The results of such studies will be useful for pharmacological modification of the diabetes process and development of new drugs.

STUDIES ON THE HYPOGLYCEMIC AND HYPOLIPIDEMIC EFFECT OF TERMINALIA SUPERBA IN DIABETES RATS

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Diabetes is often accompanied by lipid abnormalities, which contribute significantly to cardiovascular morbidity and mortality in diabetic patients. Terminalia superba, used in traditional medicine in Cameroon for the treatment of diabetes, is widely accepted as one of the medicinal herb with the highest antidiabetic activity. Previously, we have demonstrated potent hypoglycemic activity of aqueous extract of Terminalia superba roots in normal and alloxan induced diabetic rats for short duration of 5 h. In this study, we examined the effect of 2 weeks oral administration of Terminalia superba aqueous roots extract in alloxan induced diabetic rats, at the dose of 300 mg/kg bw, on various biochemical parameters, like fasting blood glucose (FBG), total cholesterol (TC), HDL-cholesterol (HDL), triglyceride (TG), LDL-cholesterol (LDL), serum glutamate oxaloacetate and pyruvate transaminases (ASAT) and (ALAT). The results obtained showed that (FBG) levels of treated diabetes rats reduced by 50.58.2% after 14 days treatment with the aqueous leaves extract. A fall of 32.60%; 60.94%, 40.91%; 34.45% and 35.03% respectively in TC, TG, LDL, ASAT and ALAT levels were also observed, as compared with their initial values. Meanwhile we notice in increase of 46.36% in the level of HDL in diabetes treated rats. This indicates that the aqueous extract of Terminalia superba has favorable hypoglycemic and hypolipidemic as well as cardio- protective potentials in Wistar rats.

Keywords: Terminalia superba; hypoglycemic; Hypolipidemic; ASAT; ALAT.

THE EFFECT OF LICORICE ROOT EXTRACT ON BLOOD SUGAR LEVEL IN STREPTOZOTOCIN INDUCED DIABETIC IN RATS

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Objective: Present study was performed to determine weather if licorice could reduce blood sugar.

Materials: This experimental study was done on eight groups of matured male rats . Diabetes were established in five groups by injection of 55 mg/kg of streptozotocin. The rats with a blood sugar of higher than 250 mg/kg were entered in the study. Three groups of diabetic animals were fed (100, 200, 300 mg/kg) by licorice extract, respectively per day through mouth and throut tubes for 35 days. One group of the diabetic rats were injected by insulin NPH at a dose of 4 units and One group of the diabetics was considered without any special treatment. The Plasma level of the blood sugar of the rats were measured on zero, 7 , 14, 21 and 35 th of days, receptively.

Results: This research showed that the dosage of 100 mg/kg had not affected blood sugar but dosage of 200 mg/kg during various days of the test (7, 14, 21, 35) had significantly decreased blood sugar. The dose of 300 mg/kg only could significantly decrease blood sugar on 7 th and 35 th days of treatment.

Conclusion: Results show that extract of licorice roots had no change in healthy rats blood sugar but in diabetic rats the blood sugar was reduced

Keywords: Blood Sugar, Licorice Root, Stereptozotocin, Diabetes Mellitus.

HYPOGLYCAEMIC ACTIVITY OF AQUEOUS EXTRACT OF *MEDICAGO SATIVA* SEEDS IN DIABETIC RATS

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Although new antidiabetic agents with unique properties have been introduced into the therapy of type 2 diabetic patients in last few years, the search for new antidiabetic agents represents a challenge to the medical profession. *Medicago sativa* (lucerne) has been used the treatment of diabetes but only as a traditional plant. This study has been undertaken to evaluate the effects of *Medicago sativa* seeds extract on glucose homeostasis in normal and streptozotocin (STZ) diabetic rats. Neonatally streptozotocin-induced diabetic (n5-STZ) rats treated with aqueous extract of *Medicago sativa* seeds were compared to diabetic rats receiving glibenclamide/vehiculum treatment and to control (non-diabetic) animals. An aqueous extract (1g/kg) of seeds of *Medicago sativa* or water or glibenclamide (5mg/kg) were given orally once daily for 28 consecutive days. Blood glucose levels (fasting, 2 and 4 hours after tested compounds administration) were monitored on 1st, 7th and 28th day of experiment. After termination the blood was collected to estimate 1,5-anhydroglucitol (1,5-AG) level in plasma - a retrospective indicator of acute hyperglycaemia. On the basis of fasting and postprandial glycaemia the mean blood glucose (MBG) was calculated.Postprandial plasma glucose levels (2 h and in 4 h after extract administration), MBG were significantly reduced in *Medicago sativa*-treated diabetic group with reference to diabetic non-treated control. 1,5-AG levels in plasma in *Medicago sativa*-treated group were similar to those observed in non-diabetic rats and were higher in comparison to diabetic controls.We conclude that chronic treatment with extract of Medicago sativa seeds decreases plasma glucose levels in n5-STZ-diabetic rats.

EFFECT OF WATER EXTRACT FROM PUPAE OF SILKWORM *ANTHERAEA PERNYI* ON INSULIN RESISTANCE IN RATS

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Aims: We used a rat experimental model of the metabolic syndrome to study the effects of water extract from pupae of silkworm (EPS) *Antheraea pernyi* on insulin resistance.

Methods: Male Wistar rats (230-250 g) were fed *ad libitum* on the high-fat Lieber-DeCarli diet (HFD) during 12 weeks. One HFD-fed group was treated i.g. with EPS in doses of 7 μg free amino acids/100 g b. w. during the last 4 weeks.

Results: The feeding of HFD during 12 w caused a significant blood glucose elevation starting from the 3rd w of the trial. The serum insulin content was increased nearly 1.8-fold in HFD-fed rats. As a result of this, the HOMA-IR index was more than 2-fold elevated in these rats. The final body weight was significantly higher compared to the control group. Serum marker enzymes (ALT and AST) in HFD-fed animals were activated and the liver triglyceride content was 3-fold increased. The serum TNFα content was dramatically raised (51.2±0.8 vs 7.2±0.9 in control rats). The treatment with EPS normalized blood glucose concentration and decreased serum insulin, HOMA-IR and final rat body weight with statistical significance in HFD-fed rats. However, the EPS administration did not affect serum marker enzyme activities, liver triglyceride and serum TNFα contents.

Conclusions: The treatment of the metabolic syndrome with EPS led to a decrease of obesity and correction of insulin resistance, but did not affect concomitant steatohepatitis in experimental rats.

IMPROVEMENT OF INSULIN RESISTANCE, HYPERTENSION AND DYSLIPIDEMIA BY *COCHLOSPERMUM VITIFOLIUM* AND NARINGENIN ON ANIMAL MODELS

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Objective: To verify anti-metabolic syndrome effect of methanolic extract (MECv) and naringenin obtained from *Cochlospermum vitifolium* bark on animal models with hypertension, dyslipidemia and insulin resistance.

Methods: Three experimental animal models were implemented using male Wistar rats. Insulin resistance (WRI) model was carried out by oral administration of high caloric emulsion during 10 days and, subsequently, including test samples (MECv 160 mg/Kg or naringenin 50 mg/Kg) until 21st day. Additionally, CCl_4-induced dyslipidemia (TID) model was implemented by daily (3 days) administration of sample, after that, CCl_4 (8 mL/Kg o.p.) was administered. Finally, bile duct-ligated rats (BDL) were developed to probe whether samples modify bile acid-mediated metabolic regulation after 10 days. In three models lipid profile and pharmacological assays were carried out.

Results: MECv increased insulin sensivity (about 300%) and decreased systolic (140 *vs*. 120 mmHg) and diastolic (130 *vs*. 90 mmHg) blood pressure in WRI. Additionally, thoracic aorta from WRI treated group showed improved reactivity to carbachol (E_{max}= 80 *vs*. 130). On the other hand, naringenin decreased serum triglyceride levels (110 *vs*. 40 mg/dL) in TID. Finally, naringenin decreased serum triglycerides (115 *vs*. 80 mg/dL), LDL (70 *vs*. 30 mg/dL) and VLDL (23 *vs*. 16 mg/dL) levels in BDL as well as increased serum HDL (18 *vs*. 27 mg/dL) levels. MECv only showed improvement in LDL (70 *vs*. 50 mg/dL) and HDL (18 *vs*. 35 mg/dL) levels.

Conclusions: MECv is promising source of bioactive compounds for treat metabolic syndrome, naringenin is one of them.

LOW DOSE ISOSORBIDE MONONITRATE-INDUCED INSULIN SENSITIZATION IN CONSCIOUS RABBITS

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Aims: We have found that transdermal nitroglycerin induces an insulin sensitizing effect in healthy volunteers at a dose used for angina prophylaxis. Our aim was to study the effect of single oral isosorbide mononitrate (ISMN) doses of 1, 2, 4 and 8 mg/kg on insulin sensitivity and global myocardial ischaemia (MI) induced by rapid ventricular pacing (RP, 500 b.p.m. over 10 minutes) in chronically instrumented conscious rabbits made insulin resistant (IR) by a preceding 4-week exposure to 1.5% cholesterol-enriched diet.

Methods: Insulin sensitivity was measured by hyperinsulinaemic euglycaemic glucose clamping. Average glucose infusion rate (GIR, mg/kg/min) to mainain euglycaemia (5.5 mmol/l) at clamped hyperinsulinaemia (100 uU/ml) was used to assess insulin sensitivity. Post-pacing intracavitary ST-segment elevation (mV) and an increase in left ventricular end-diastolic pressure (LVEDPI, mmHg) were used to estimate the severity of pacing-induced MI.

Results: Table shows that ISMN attenuated RP-induced changes at an oral dose of 8 mg/kg, however, a significant insulin sensitizing effect appeared in a dose range of 2-8 mg/kg.

Effect of ISMN on RP-induced MI and insulin sensitivity

ISMN Control 1 2 4 8 mg/kg

ST 2.3±0.3 2.2±0.4 2.2±0.2 1.9±0.3 1.4±0.2 mV

LVEDP 18±2.9 19±3.0 16±2.7 14±3.2 9±1.4*

GIR 8.6±1.7 11.6±2.2 14.4±2.6* 15.2±1.3* 15.5±1.8*

The data are means±S.D. obtained with 6 rabbits/group. *: significant difference from control at $p< 0.05$

Conclusion: ISMN applied orally, produces an insulin sensitizing effect at doses much lower than those required to produce an anti-ischaemic effect against RP-induced MI in IR conscious rabbits.

ENDURANCE TRAINING *PER SE* INCREASES METABOLIC HEALTH OF OVERWEIGHT MEN

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Aim: To investigate the effect of endurance training *per se* on metabolic health of overweight men.

Methods: 48 healthy overweight men (age: 31±1 [mean±SEM] years, BMI: 28.1±0.2 kg/m^2) were randomized to 12 weeks of Training (T), Diet (D), Training inversed diet (T-iD) or Control (C). An energy deficit of 600 kCal/day was induced by either endurance training or diet in T and D. T-iD followed the same training regimen, but increased dietary intake by 600 kCal/day. C maintained their habitual lifestyle. Before and after the intervention body composition, maximal oxygen consumption (Vo_2max), fat oxidation (FATmax), insulin sensitivity (hyperinsulinemic euglycemic clamp, 40mU/m^2/min) and plasma lipids were determined.

Results: The interventions reduced ($P< 0.001$) body mass in T and D by 5.9±0.6 and 5.3±0.7 kg, respectively, whereas T-iD and C remained weight stable. Fat mass was reduced ($P< 0.01$) in T, T-iD and D by 7.7±0.8, 1.9±0.3 and 4.4±0.7 kg, respectively. Vo_2max increased ($P< 0.001$) in T and T-iD and did not change in D and C. FATmax increased ($P< 0.05$) in T, T-iD and D. Glucose clearance increased ($P< 0.01$) in T and T-iD and remained unchanged in D ($P=0.09$) and C ($P=0.9$). Plasma total cholesterol, LDL and ApoB decreased ($P< 0.05$) in T and D, and plasma HDL and ApoA1 increased ($P< 0.01$) and VLDL decreased ($P< 0.01$) in T-iD.

Conclusion: Endurance training *per se* induces beneficial changes in fat mass, Vo_2max, FATmax, insulin sensitivity, HDL and ApoA1 in overweight men and is thus metabolically healthy.

RELATIONSHIP BETWEEN PHYSICAL ACTIVITY, OBESITY STATUS, AND GLYCEMIC CONTROL

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Aims: We aimed to evaluate the relationship of physical activity and obesity with glycemic control and insulin resistance.

Methods: Subjects included 505 men and 509 women without evidence of cardiovascular or other chronic disease. Participants were classified as inactive, minimally active, or health-enhancing physical activity (HEPA) active based on the International Physical Activity Questionnaire. Insulin sensitivity was assessed by the homeostatic model (HOMA), and overweight or obesity was assessed according to BMI (BMI >or= 25).

Results: (34.3%) men and (29.3%) women were classified as physically active. From the (34.8%) subjects who were classified as active,(9.1%) met the criteria for HEPA active, and the rest were minimally active. HEPA active and minimally active subjects smoked less and had lower BMI, waist, and waist-to-hip ratio. Lean and overweight or obese subjects with sedentary lifestyle had greater levels of glucose, insulin, and insulin resistance [corrected] However, overweight or obese volunteers with physical activity levels classified as HEPA had similar levels of glucose and insulin sensitivity, with lower insulin than lean inactive individuals. Linear regression analysis between HOMA and physical activity, taking into consideration several social and biological factors, showed that physical activity (MET x min x wk(-1)), age, BMI, and total energy intake are important predictors of HOMA, whereas other factors such as waist circumference did not reach statistical significance.

Conclusion: Our data show that physical activity is a significant factor on insulin sensitivity, whereas increased physical activity may ameliorate the well-known effects of obesity on insulin sensitivity.

IMPACT OF PHYSICAL EDUCATION ON THE BODY COMPOSITION AND METABOLIC HEALTH OF PRIMARY SCHOOL CHILDREN

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Aims: To assess the impact of differences in timetabled physical education (PE) on physical activity (PA), body fat and metabolic health in primary school children.

Methods: Subjects: 206 children (115 boys, age 7-11y) from three primary schools (S1, S2, S3) offering widely different amounts of timetabled PE (9.2, 2.4 and 1.7 hours/week respectively). The children varied in socio-economic status (SES) from high (mostly S1) and intermediate to very low (mostly S3).

Outcome measures (repeated on four consecutive occasions over 12 months

and adjusted for age, gender and weather): 1. Accelerometer-recorded PA and its moderate-and-vigorous component (MVPA) (in-school, out-of-school and total weekly). 2. Body fat (sum of five skinfolds, SSF). 3. Metabolic risk (composite metabolic z-score combining insulin resistance [HOMA-IR], triglycerides and cholesterol/HDL ratio).

Results: S1 children recorded substantially more PA in-school than S2 and S3 (+42% and +40%, $p< 0.001$), but there were no significant differences in total weekly PA between the three schools. S1 children also recorded more MVPA than S3 (+51min/week, $p< 0.01$), their body fat was less (SSF -16.4mm, $p< 0.001$) and their metabolic risk lower (z-score -0.34, $p< 0.01$). MVPA explained 17% of the difference in metabolic risk between S1 and S3, body fat explained a further 41%.

Conclusions: More PE does not result in more PA, confirmed on four occasions. More MVPA is associated with better metabolic health, but seems to be more closely related to the lower body fat that characterises higher SES children generally than to PE opportunity in school.

PREVALENCE OF DIABETES (TYPE 2) AND PHYSICAL ACTIVITY STATUS IN ELDERLY MEN AND WOMEN, FROM THE MEDIS STUDY

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Background: The aim of this work was to evaluate the prevalence of diabetes mellitus among elderly people living in Mediterranean islands, and its relation to physical activity status.

Methods: During 2005-2007, 1190 elderly adults (300 men and women from Cyprus, 142 from Mitilini, 100 from Samothraki, 114 from Kefalonia, 131 from Crete, 150 from Corfu and 103 from Zakynthos) were enrolled. Socio-demographic, clinical and lifestyle factors were assessed through standard procedures. Dietary habits were assessed through a semi-quantitative food frequency questionnaire, while physical activity status through the IPAQ tool. Diabetic subjects were defined those with fasting glucose measurements ≥ 125 mg/dl or those who were under medication.

Results: Prevalence of diabetes was 21% in men and 23% in women. Regarding the lifestyle characteristics, 44% of men and 29% of women were reported as being moderately or vigorously active; 14% of the participants reported that they smoked. After various adjustments, people in the upper tertile of the IPAQ score (vigorous activities) were 0.26 times less likely to have diabetes ($p < 0.05$); on the other hand people in the lower tertile of the score were 1.7 times more likely to have diabetes ($p < 0.05$).

Conclusion: Our findings support the notion of a beneficial effect of physical activity on the burden of diabetes in the elderly.

ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND THE METABOLIC SYNDROME IN ANGIOGRAPHIED CORONARY PATIENTS

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Aims: Hardly any data on the association of self-reported physical activity with the Metabolic Syndrome (MetS) are available. We aimed at investigating the association of self-reported physical activity with the MetS in the clinically important population of angiographied coronary patients.

Methods: We performed standardized FEG questionnaires in 197 patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD).

Results: Patients with the MetS (NCEP ATP-III definition; n = 86) had lower scores of physical activity (encompassing both work and leisure time activities) and of being content with their level of activity than subjects without the MetS (1.83 ± 0.38 vs. 1.97 ± 0.44; p = 0.027 and 0.14 ± 1.74 vs. 0.98 ± 1.53; p = 0.002, respectively). Furthermore, MetS patients estimated the health benefits of exercise with lower scores (0.14 ± 1.74 vs. 0.98 ± 1.53; p = 0.002) and had higher scores for problems with changing their physical activity behaviour than subjects without the MetS (3.2 ± 0.92 vs. 2.71 ± 0.91; p = 0.016). Further, scores of general physical discomfort were higher in MetS patients than in subjects without the MetS (3.24 ± 1.10 vs. 2.87 ± 0.88; p = 0.018). In contrast to these results for the MetS, no association of FEG scores with the presence of significant stenoses at angiography was observed.

Conclusion: Among angiographied coronary patients, low levels of self-reported physical activity are significantly associated with the MetS. Exercise counselling in coronary patients with the MetS is mandatory.

ANTI-INFLAMMATORY ACTIONS OF EXERCISE TRAINING IN ZUCKER DIABETIC (TYPE 2) FATTY RATS

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In the present study we evaluated the effect of exercise on the circulating adiponectin and associated mediators of inflammation, including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP) in the Zucker diabetic fatty (ZDF) rats, that are more prone to develop type 2 diabetes mellitus.

Sixteen obese ZDF (Gmi *fa/fa*) rats (8 weeks-old, 228.4±4.0 g) were randomly assigned to one of two groups (n=8 each): an exercise trained group and a sedentary one. In addition, 16 lean ZDF (Gmi +/+) rats (8 weeks-old, 199.0±3.5 g) were also submitted to identical sedentary and exercise conditioning (n=8 each). Initially, rats swam 15 min/day (5 days/week) in a 36ºC bath. The exercise protocol was gradually increased by 15 min/day until a swimming period of 1h/day (1week) was attained. Thereafter, rats swam 1h/day, 3 days/week, for an additional period of 11 weeks. Rats were sacrificed 48h after the last training period and blood and pancreas was collected. Circulating levels of adiponectin, PCR, IL-6 and TNF-α were assessed. The concentrations of pro-inflammatory cytokines in the pancreas were also evaluated by immunohistochemistry.

In the diabetic ZDF (*fa/fa*) rats, exercise increased adiponectinemia (+28.0%) and decreased IL-6, TNF-α and CRP levels (-14.8%, -19,0% and -26.1% respectively). The immunohistochemistry has revealed a marked decrease in the expression of TNF-α and IL-6 in the pancreatic islet cells of the ZDF (*fa/fa*) rats.

In conclusion, exercise training improves insulin sensitivity in type 2 diabetic ZDF rats, which seems to be related with its anti-inflammatory action.

AN ALTERNATE TRAINING PROGRAM OF LOW AND HIGH INTENSITY EXERCICE IMPROVES ANTHROPOMETRIC PARAMETERS AND INSULIN RESISTANCE AMONG YOUNG OBESE WOMEN

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Objective: We aimed to evaluate the effect of a special training program on anthropometric parameters, on insulin resistance and on lipid profile among young obese women.

Methods: The prospective study enrolled 14 young obese women with body mass index (BMI) ≥ 30Kg/ m^2, aged 20 to 37 years without hypertension and diabetes.

No specific diet was recommended, the group was trained by walking exercice on alternate program: low intensity 50% of maximal oxygen uptake (VO_2 max) and high intensity 75% VO_2 max, 12 weeks, 5 days/ week.

The anthropometric measurements were: weight, heigh, BMI, waist circumference, hip circumference. Fat mass and skeletal muscle were measured by bioelectrical impedance.

We also measured glucose, insulin and lipid concentrations. The insulin resistance was appreciated by HOMA index.

We practiced these measurements before and at the end of the training program.

Statistic calculations were performed using SPSS version 15.0.

Results: After 12 weeks, the group had had a very significant decrease ($p< 0,01$) in weight, BMI, waist and hip circumferences, fat mass, insulin level, HOMA index, total cholesterol and LDL cholesterol.

We also noticed a non significant decrease in glucose, triglycerides plasma concentration and in apolipoproteine B.

On the contrary, we noticed a significant decrease ($p< 0,05$) in HDL cholesterol and apolipoproteine A.

Conclusion: This alternate training program improved anthropometric parameters and insulin sensitivity, a key factors in the improvement of profile lipid. These results suggest a reduced metabolic syndrome incidence and a reduced risk of cardiovascular disease among this young population.

POSTPRANDIAL BLOOD GLUCOSE RESPONSES IS ATTENUATED BY LIGHT POST MEAL PHYSICAL ACTIVITY IN FEMALE PAKISTANI IMMIGRANTS LIVING IN OSLO

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Background: Female Pakistani immigrants living in Oslo have elevated risk of diabetes type 2. The magnitude and duration of the postprandial blood glucose elevation is important risk factors for diabetes and coronary heart diseases. It has previously been established that even light physical activity after a meal blunts the rise in blood glucose. In this study we aimed to identify practical prevention strategies for female Pakistani immigrants by evaluating the influence of light physical activity on the postprandial levels of blood glucose after ingestion of carbohydrate rich meals.

Method: After an overnight fast, 11 healthy subjects participated in three experiments in a crossover design. Day 1, the subjects were given cornflakes with milk corresponding to 50 g carbohydrate (control). Blood glucose was determined before the meal and each 15 min. for the next 2 hours. Day 2 and 3 were similar to day 1, but included 20 min. or 40 min. of light physical activity respectively after the meal.

Preliminary results: Post meal very light physical activity of two durations blunted the rise in blood glucose. Levels of blood glucose seemed to stabilise as long as the subjects were physically active. The reduction in IAUC due to exercise correlated with IAUC the control day.

Preliminary conclusion: Light post meal physical activity after ingesting a high glycemic meal blunts the rise in blood glucose in female Pakistani immigrants living in Oslo, and can be prescribed as a lifestyle advice for prevention of type 2 diabetes.

IMPACT OF AN EXERCISE PROGRAM ON ARTERIAL STIFFNESS IN METABOLIC SYNDROME PATIENTS

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Aims: Some research results indicated that arterial stiffness and pulse wave velocity were major risk factors of cardiovascular diseases and they increased among metabolic syndrome patients. This study investigated the effects of continued aerobic exercise on metabolic syndrome and arterial stiffness.

Methods: The subjects were 18 middle-aged female metabolic syndrome patients , 8 control group, 10 exerecise group who underwent medical check-up, met the criteria of NCEP-ATP III and had not taken exercise over the last 3 months. The exercise program was made up of 2 dance sports programs with the level of 50-80% of HRR (Heart Rate Reserve) that lasts 1 hour 2 times a week and walking a time with the level of 13 to 15 (slightly hard- hard) of RPE (Rate of Perceived Exertion) for 10 weeks. The level of arterial stiffness was measured by CAVI (Cardio Ankle Vascular Index) that used autonomic waveform analyzer. CAVI, anthropometry and blood sampling were conducted before and after the exercise program.

Results: CAVI that reflects the level of arterial stiffness significantly declined from 7.5±1.0m/s to 7.2±0.7m/s in exercise group($P=0.037$). Waist circumference significantly decreased from 91.2±6.9 Cm to 87.8±5.4 Cm($P=0.008$), systolic blood pressure from 126.1±12.5mmHg to 121.6±10.4mmHg($P=0.037$), fasting blood sugar from 102±18.9mg/dL to 90.2±16.3mg/dL($P=0.005$),and triglyceride from 184.5±65.7mg/dL to 152.2±67.5mg/dL($P=0.047$).In control group, there were no significant changes in metabolic factors including CAVI.

Conclusions: Aerobic exercise significantly induced improvement of arterial stiffness and clinical indices among metabolic syndrome patients.

EFFECTS OF A WALKING PROGRAM ON BODY COMPOSITION AND CARDIOVASCULAR RISK FACTORS

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Objective: The aim of this study is to assess the impact of a walking based training program on weight, total fat, blood lipid profile and insulin resistance among young obese women.

Methods: 10 obese women (mean age 26 ± 4.5 years) took part in a 12 week physical activity program. They practiced a 60 - minute supervised aerobic exercises five times a week. The activity was at moderate intensity approximately 50% peak oxygen uptake (VO_2max).

We measured weight, body composition and total fat by bioelectrical impedance. Blood sugar, insulin, total cholesterol (TC), low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c) and triglycerides plasma concentrations were also measured. We calculated HOMA-IR index. All these measurements were carried out before and after the training program.

Results: A significant weight and total fat reduction ($p < 0.001$) were noticed. This improvement in body composition was associated to a significant reduction in insulin levels (-3.19 UI/l, $p< 0.05$), LDL-c (-0.59 mmol/l, $p< 0.05$) and insulin resistance (HOMA-IR index $p< 0.05$).

In addition, we noticed a non significant reduction in serum glucose concentration (-8.1%, p=0.09), total cholesterol (-8.9%, p=0.105) and a slight increase of HDL-c (+4.3%, p=0.606).

Conclusion: Walking exercise reaching 50% of VO_2max was effective on reducing weight, total fat as well as insulin resistance, with a slight improvement of lipid profile. These results are suggestive of a positive effect on cardiovascular risk factors.

ANTI INFLAMMATORY EFFECT OF HIGH COMPLEX CARBOHYDRATE DIET AND PHYSICAL ACTIVITY IN SEVERELY OBESE VOLUNTEERS

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The presence of low grade, internal inflammation is one of the main causes for development of insulin resistance, type 2 diabetes mellitus and atherosclerosis. Life style modifications have been found to improve the prognosis of individuals with diabetes and atherothrombosis. The aim of the study is to evaluate the effect of such modifications on the inflammatory profile of obese volunteers.

Methods: Blood samples were taken before and after 8 months of intensive life modification program, including consumption of high-complex carbohydrate diet and intensive physical activity in a group of 20 apparently healthy severely obese volunteers.

Results: Substantial improvement was noted in the biometric, metabolic and inflammatory biomarkers. The study results in significant weight loss and BMI reduction. The concentrations of high sensitivity C-reactive protein (hs-CRP), Erythrocyte Sedimentation Rate, triglycerides, LDL and total cholesterol, as well as insulin concentration and HOMA-R were reduced. A reduction was found in the concentration of the pro-inflammatory cytokines TNFalpha and IL6, and the adhesion molecule ICAM1. Significant increment in fibrinogen concentrations was noted. Despite that, a significant reduction was found in the degree of red cell aggregation as measured by using a slide test and direct visualization of the aggregates. The pro-aggregating properties of fibrinogen following intense physical activity are probable counterbalanced by the anti-aggregatory properties of an improved lipid profile and an attenuated acute phase response.

Conclusion: The study suggests that strenuous physical activity is not advised for untrained obese individuals. However, the study shows the beneficial anti inflammatory properties of this intervention program.

OBESITY IN FORMER SPORTSMEN

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Introduction: Obesity risks are multiples, medicals, economics, socials and esthetics. Medical risks can be: metabolic, cardiovascular, digestive, oncologic and other medical risks

Purpose: Evaluation of obesity epidemiology in former performance sportsmen, after sport (activity) quitting.

Material and methods: It´s a retrospective study in 210 former performance sportsmen (122 males and 88 women). Each patient had a record with personal data, anthropometric data (BMI, abdominal circumference) personal history of diseases, type of practiced sport and competition level, alimentary habits before and after sport quitting, history of tobacco and alcohol use.

Results: 95 of 210 former sportsmen were of normal weight, 115 (59,5%) were of different degrees of overweight, those being more frequent in males, and directly proportional with age (the number of years elapsed from sport quitting). There has been an increased prevalence of overweight in football players (team sports) and decreased in those who played individual sport types. We couldn't correlate obesity and overweight with competition level because all patients in our study were all first league players.

Conclusions:

1. The incidence of obesity in former sportsmen is conditioned by sport quitting and keeping the same nutritional intake, sedentary and increased alcohol use.

2. Prevention of obesity in former sportsmen has to be started early by being aware of the incidence of obesity after sport quitting and its serious complications.

3. For the prevention of obesity in former sportsmen it is recommended to continuing the physical activity constantly, avoiding the use of alcohol, tobacco, sweets and avoiding eating during night.

PHYSICAL ACTIVITY-INACTIVITY RATIO AND ITS ASSOCIATION WITH C-REACTIVE PROTEIN IN MEXICAN ADOLESCENTS

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Objective: To evaluate the association of the activity and physical inactivity ratio (AIR) and the C-Reactive protein levels (CRP).

Methods: The population base of this report are children of participants of the project "Cohort of Workers IMSS-INSP-UAEM". The methods have been described previously. Briefly, the level of physical activity (PA) was evaluated by means of a questionnaire used previously that allows measuring the PA level during the daily life, the free time and the time inverted in activities of low energetic expenditure, which is considered physical inactivity (PI) in this analysis. A greater AIR means that more PA

is realized than PI. CRP levels were determined using the highly sensitive technique. By means of a model of multiple logistic regression the association between the RAI and the levels of CRP was evaluated, adjusting by diverse factors.

Results: The information of 336 clinically healthy adolescents was analyzed. 215 (64%) adolescents with elevated levels (3-10 mg/l) of CRP were detected. The adolescents in the first quintil of AIR have a greater risk to have elevated levels of CRP in comparison with those of the last quintil (OR=4.6 CI95% 1.4-14.7). Additionally, we observed that the adolescents with overweight and/or obesity have a greater risk to have elevated levels of CRP.

Conclusion: Our data suggest it AIR is inversely associated with the CRP levels, independently of other factors; which agrees with some previous reports. However, it is necessary to confirm these findings in other populations.

EFFECT OF ACUTE EXERCISE ON LIPID AND CARBOHYDRATE METABOLISM IN HEALTHY MEN

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Aim: To investigate the influence of acute physical exercise of moderate and high intensity on lipid and carbohydrate metabolism in clinically healthy middle-aged men.

Methods: 53 non-obese, non-smoking clinically healthy men aged 30-45 years (mean age 35.7±0.7) were enrolled in the study. Two separate single bouts of aerobic exercise (moderate intensity: cycling for 20 minutes at heart rate (HR) 60-70% of HR_{max}; and high intensity: cycling for 20 minutes at HR >70% of HR_{max}) were performed with intervals of 3-7 days in each patient. Fasting triglycerides (TG), total cholesterol (TCh), high density lipoproteins (HDLP), plasma glucose and insulin were measured before each bout of exercise and immediately after it. The upper quarter of insulin level was classified as insulin resistance (IR; n=13).

Results: Significant increase of TCh level was found in total group ($p=0.001$ for moderate and $p< 0.0005$ for high-intensity exercise). The main part of such enhancement was for increased HDLP level ($p< 0.0005$ and $p=0.001$, respectively). Sufficient decrease of fasting glucose level was demonstrated after high-intensity exercise only ($p=0.009$). TG and insulin levels were not changed significantly. Parameters of lipid and carbohydrate metabolism were not changed significantly after acute exercise in IR patients.

Conclusions: Results demonstrated improvement of lipid metabolism after acute exercise in healthy middle-aged men. Sufficient decrease of fasting glucose level was revealed after high-intensity exercise only. Acute exercise did not cause any significant changes of lipid and carbohydrate metabolism in IR patients.

COMPARATIVE STUDY UPON EFFECTS OF PHYSICAL EXERCISE IN THE TREATMENT OF METABOLIC SYNDROME

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Introduction: Today is generally accepted that the aerobic exercise has been shown to be a powerful strategy for the prevention and treatment of the metabolic syndrome (MS). The question is witch type of exercise is better. Starting to the additionally expenditure energy after exercise, our study proposes to compare the effects of continuous aerobic exercise (CAE) versus intermittent aerobic exercise (IAE) on subjects with MS. This sample is part of a research project about the effects of physical exercises in prevention and treatment of MS.

Material and method: The study included 30 male patients with MS, with ages between 18-24years, which have been separated into two groups: group A(n=15), who has undertaken 40minutes of CAE, 5days/week, at submaximal intensity (70-75%VO_2max), and group B(n=15) who has undertaken same type of exercise but daily session was divided in two events of 15minutes at minimum 2hours interval. The training program, that consisted in stationary cycling, has been monitored and recorded by a heart rate monitor (Polar RS800). General indications regarding the diet were set for each patient.

Results: After 18weeks of physical exercises we noticed a significant evolution of several anthropometrics parameters at L1group comparative with L2group. Weight(kg): 89.8±12.2/83.5±11 versus 89.8±12.2/83.5±11; waist circumference(cm): 103±7.8/98.86±7.7 versus 110±15.4/100.9±13.9; BMI: 33.3±3/30.85±3.0 versus 33.3±6.8/30±5.4; %BodyFat: 28.83±4.59/24.77±4.21 versus 37.6±6.7/32.7±5.7.

Conclusions: For treatment of MS, the using of IAE has better results comparative with the CAE. Additionally, we recommend the insertion of a minimum 2 hours rest between physical exercises sessions for a greater caloric expenditure after exercise.

PHYSICAL ACTIVITY COULD BE INVOLVED IN THE OVEREXPOSURE OF ASIAN INDIAN GUADELOUPEANS TO TYPE 2 DIABETES

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Aims: Asian Indians and their descents are widely documented to be particularly exposed to diabetes, coronary heart disease, insulin resistance, visceral obesity and metabolic syndrome. The same statement realized in Guadeloupe (French West Indies) led us to wonder about the potential involvement of physical activity.

Methods: We assessed the physical activity energy expenditure (PAEE) of 122 Guadeloupean adults with three 24-h recalls and the leisure time physical activity (LTPA) of 780 Guadeloupean adolescents with the modifiable activity questionnaire on a 7-d period. Two-way analyses of variance were conducted to test the hypothesis of an effect of ethnicity, taking the potential effect of sex into account, on this variable.

Results: Asian Indian adults reported lower PAEE ($p< 0.05$) than their Afro-Carribean counterparts. Asian Indian adolescents reported lower weekly LTPA ($p=0.001$) with a mean difference of 13.6 MET-Hr/week and less intense LTPA ($p< 0.001$) than controls. They spent higher absolute and relative times in light intensities activities ($p< 0.001$ for both) and higher times in vigorous ones ($p< 0.001$ for both).

Conclusions: Given the documented involvement of sedentariness in several features of the metabolic syndrome and in type 2 diabetes Asian Indians have previously been reported to be overexposed to, the lower levels of physical activity reported in Asian Indian Guadeloupeans should be considered as a target in public health policies for disease prevention.

PHYSICAL EXERCISE EFFECTIVELY REDUCES ABDOMINAL AND TOTAL FAT IN A DOSE DEPENDENT RESPONSE AMONG YOUNG OBESE WOMEN

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Objective: The aim of this study is to evaluate the impact of two training programs on body composition, total fat and abdominal fat in obese young women.

Methods: Twenty-one obese women (mean age 27 ± 3 years) participated in the program. This program lasted 12 weeks. These volunteers were trained five times a week. Each training session lasted 60 minutes. Eleven candidates (G1) were trained at a low-intensity (50% peak oxygen uptake - VO_2 max-) and ten (G2) at a high intensity (75% VO_2 max).

Before and after the training program, abdominal obesity was evaluated by waist circumference. Total body composition and total fat were measured by bioelectrical impedance

Results: The two programs resulted in a very significant weight and total fat reduction. The weight reduction was higher in G2 (- 5.33 Kg) than in G1 (-3.03 Kg).The total fat reduction in G2 (-5.13 Kg) was also higher than in G1 (-3.95 Kg).

Moreover, there was an increase in the total skeletal muscle in G1 (+0,95 Kg)

The reduction in waist circumference was very important in the two groups (- 8.5 cm in G1 and - 9.35 cm in G2).

Conclusion: Physical exercises at 50% and 75% VO_2max were both effective in reducing abdominal and total fat without impairment in total skeletal muscle. These body composition changes are suggestive of reduction in cardiovascular risk.

TRANSCRIPTIONAL AND FUNCTIONAL DEREGULATIONS OF LIPID AND CHOLESTEROL METABOLISM BY ANTIPSYCHOTIC COMPOUNDS ON RAT PRIMARY HEPATOCYTES

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Metabolic side effects such as weight gain, dyslipidemia, impairment in glucose metabolism, and development of diabetes are often associated with antipsychotic drug (APD) treatment. Although a part of these actions involves histamine, muscarinic and serotonin receptors at the CNS level, the main mechanism by which APD provoke such side effects should be a direct action on other tissues. In this study we have investigated the potential role of a large series of antipsychotic agents on the deregulation of lipid and cholesterol metabolism in rat primary hepatocytes.

Results: Our data showed that after a 24 hours-treatment, some APD have the ability to modulate lipid metabolism through transcriptional and functional deregulations. At the transcriptional level, we obtained different signatures with certain molecules highly stimulating expression of genes involved in lipid or cholesterol biosynthesis (clozapine, haloperidol, olanzapine, N-desmethylclozapine, risperidone) and other ineffective or inhibiting compounds (aripiprazole, bifeprunox, quetiapine, paliperidone) correlating with reported clinical metabolic side effects. Moreover, SREBP1 and SREBP2 proteins maturation draw a parallel with these transcriptional deregulations. At the functional level, we showed with the method of [^{14}C] acetate incorporation, that clozapine, haloperidol, olanzapine, NDMC and risperidone are the most powerful inductors of cholesterol, cholesteryl esters, triacylglycerol, FFA and/or phospholipid biosynthesis in rat hepatocyte cells.

Thus, our data are in favour of a putative role of APD-mediated metabolic side effects via direct action at liver level. In the future, we need to explore further this hypothesis and the precise mechanism by which these deregulations take place.

THE EFFICACY AND SAFETY OF VERY HIGH PLANT STANOL ESTER INTAKE

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The efficacy and safety of plant stanol esters in lowering LDL cholesterol has not been studied with a larger dose than 4.0 g/d of plant stanols. Accordingly, we investigated the efficacy and safety of a very high intake of plant stanols (8.8 g/d) as ester (STAEST) for 10 weeks in a randomized, double-blind, parallel study in mildly to moderately hypercholesterolemic subjects (STAEST n=25; controls n=24). Serum and lipoprotein lipids, noncholesterol sterols, safety variables, carotenoids, and fat-soluble vitamins were assayed.

In the STAEST group, serum total and LDL cholesterol concentrations were reduced by 12.8% and 17.3% from baseline, and by 12.0% and 17.1% from controls ($P< 0.01$ for all). STAEST had no effect on HDL cholesterol or serum triglyceride concentrations. The high STAEST dose did not affect the serum vitamin A or D or γ-tocopherol concentrations, or the ratio of α-tocopherol to cholesterol. Serum β-carotene concentration and ratio to cholesterol decreased from baseline and compared with controls. Serum α-carotene concentration and ratio to cholesterol were not different from controls. STAEST decreased the ratios to cholesterol of serum campesterol and sitosterol (markers of cholesterol absorption) by 62% and 48% from controls, and increased serum lathosterol to cholesterol ratio (marker of cholesterol synthesis) by 34% ($P< 0.001$ for all). The high STAEST dose had no effect on liver enzymes, markers of hemolysis or blood cells.

In conclusion, increasing the plant stanol dose to 9 g/d effectively reduces LDL cholesterol values by 17% without having any clinically relevant side effects.

VISCERAL FAT EXPRESSION OF ANGIOTENSIN II RECEPTOR TYPE 1 IS ASSOCIATED WITH DYSLIPIDEMIA AND INFLAMMATION IN HUMANS

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Background and aims: Adipose tissue is a source of renin-angiotensin system (RAS) components that are supposed to contribute to metabolic alterations and local inflammation.

Material and methods: We investigated the relation between mRNA expression of the RAS genes in visceral (VAT) and subcutaneous adipose tissue (SAT), adipose tissue secretion of inflammatory proteins (pentraxin 3, tumor necrosis factor α, interleukin -6) and metabolic alterations. VAT and SAT was obtained from 17 (4 normal weight and 13 obese) patients during surgery. Angiotensinogen (AGT), angiotensin II receptor type 1 (AT1), angiotensin converting enzyme (ACE) mRNA were measured by RT-PCR.

Results: Renin gene was not expressed in adipose tissue. AGT was more expressed in SAT ($p< 0.05$) and AT1 in VAT ($p< 0.01$). VAT AT1 mRNA levels were correlated with triglycerides, fasting glucose and uric acid. In the multivariate analysis triglycerides remained independently related to VAT AT1 (b 0.644, $p< 0.005$). Subjects with dyslipidemia ($p< 0.01$ for high tryglicerides and $p< 0.05$ for low HDL) and hypertension ($p< 0.05$) had higher VAT AT1 mRNA levels than those without metabolic alterations. VAT AT1 expression was positively associated with the secretion from VAT of pentraxin 3. None of the previous observations were recorded in SAT.

Conclusions: AT1 expression in VAT but not SAT is associated with

dyslipidemia and hypertension. Locally or peripherally released angiotensin could exert autocrine/paracrine effects to regulate lipolysis and release from adipose tissue of pentraxin 3 which is involved in the development of atherosclerosis.

ROSIGLITAZONE TREATMENT RESULTS IN REDUCED LEVELS OF OXIDIZED LDL IN DIABETES PATIENTS

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Background: Oxidized LDL (oxLDL) is believed to be involved in the atherosclerotic process. High levels of plasma oxLDL have been shown to be an independent predictor for future cardiac events in type 2 diabetic patients.

Animal studies have shown that treatment with rosiglitazone, a widely used insulin-sensitizer, induces the endothelial receptor for oxidized low-density lipoprotein (OLR1) and therefore could reduce serum oxLDL levels. Studies on humans have shown divergent results probably since measurement of oxLDL has methodological barriers, which have limit its use in epidemiological studies.

Methods: Ten diabetes patients without previous medication were treated with rosiglitazone for eight weeks. We evaluated the effect on plasma oxidized LDL concentration, glycemia and plasma lipids.

Results: Rosiglitazone treatment resulted in reduced ox LDL levels in all patients ($p = 0{,}001$) and reduced glucose concentrations ($p = 0.02$). In contrast, we observed increased LDL-cholesterol concentrations ($p=0.01$).

We measured Ox LDL by a novel commercially available ELISA-kit (Immundiagnostik AG, Germany). The reproducibility of the ELISA method was investigated by determination of the intra- and total-assay-coefficients of variation. The intra-assay variation was 4,5% (mean value 38,6 ng/mL) and the total-assay variation was 5,2%.

Summary: Oxidative modification of LDLs is generally believed to play a pathogenic role in the development of atherogenic lesions. In a small number of patients we show that rosiglitazone treatment was strongly associated with reduced plasma oxidized LDL levels which theoretically would lead to reduced atherosclerosis. To our knowledge this has not been described earlier.

RESPONSE TO LIPANTHYL TREATMENT IS ASSOCIATED WITH APOLIPOPROTEIN A5 AND METHYLENETETRAHYDROFOLATE REDUCTASE POLYMORPHISMS IN TYPE 2 DIABETES

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Background: Fenofibrate improves lipid levels in type 2 diabetes. Then, it is particularly well suited for use in atherogenic dyslipidaemia. Unfortunately, fenofibrate use is associated with increase in total homocystein (tHcy) level which is associated with progression of coronary artery disease. Apolipoprotein A5 (apo A5) and methylenetetrahydrofolate reductase (MTHFR) are two candidate genes related to lipoprotein and homocystein metabolism.

Objective: Response to fenofibrate treatment according to apo A5 and MTHFR polymorphisms in type 2 diabetes.

Methods: tHcy was measured by GC-MS with isotopic dilution and plasmatic lipid and lipoprotein concentrations by enzymatic methods, before and after 4 weeks of treatment with lipanthyl® 200M. The apo A5 and MTHFR polymorphisms were determined by PCR-RFLP.

Results: Our results showed that fibrates decreased TG levels and increased HDL-C and tHcy concentrations. But these variations are dependant of apo A5 and MTHFR polymorphisms. After 4-week treatment, apo A5 homozygous (TT) displayed better decrease in TG and increase in HDL-C levels relative to their basal values in the fasting state when compared with heterozygous (TC) (a TG reduction of -46.1 % vs. -26.6 % and HDL-C increase of 23.5 % vs. -1.3 %). Also, the MTHFR homozygous (CC) displayed lower increase in tHcy than the homozygous (TT) after lipanthyl treatment (39 % vs. 24.7 %).

Conclusion: This preliminary study suggests that apo A5 homozygous (TT) benefited more from the lipanthyl treatment in lowering TG and increasing HDL-C levels, more else, MTHFR homozygous (CC) benefited more from the lipanthyl treatment by minimizing the tHcys increase.

INVERSE ASSOCIATION BETWEEN METABOLIC SYNDROME OCCURRENCE AND THE CONTENT OF NERVONIC ACID IN SERUM PHOSPHATIDYLCHOLINE OF SPANISH DYSLIPIDEMIC SUBJECTS

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Aims: Nervonic acid (C24:1n-9, NA) is a structural component of sphingomyelin in brain myelin. The physiologic role of this fatty acid is controversial. One study reported a positive association of the NA content of serum phospholipids with adipose tissue depots in obese adolescents. In contrast, two studies found that the serum NA content in subjects free of cardiovascular disease was inversely associated with coronary risk factors and positively associated with insulin sensitivity. In a cross-sectional study, we evaluated the association between plasma NA content and metabolic syndrome (Met Syn) status in Spanish subjects with primary dyslipidemia.

Methods: The fatty acid composition of phosphatidylcholine was determined by gas-chromatography in fasting serum samples of 475 dyslipidemic subjects. Cardiovascular risk factors, including smoking, waist circumference, blood pressure, fasting blood glucose and untreated serum lipid levels were available for all patients. MetSyn was defined per National Cholesterol Education Program Adult Treatment Panel III criteria.

Results: 139 patients (29.3%) met the criteria for MetSyn. NA accounted for 0.23±0.12% of total fatty acids in serum phosphatidylcholine. After adjusting for gender, age and smoking history we found that subjects in the top tertile of NA had a 51% lower risk of MetSyn occurrence compared to those in the bottom tertile (95% CI, 0.289 - 0.837; P=0.009).

Conclusion: The results reinforce the novel hypothesis that an increase of serum NA content is inversely associated with MetSyn but offer no insight on the mechanisms of this protective effect.

DIFFERENTIAL EFFECTS OF PIOGLITAZONE AND ROSIGLITAZONE ON THE CATABOLISM OF HDL-CHOLESTERYL ESTERS *IN VIVO*

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Aims: To determine the effect of thiazolidinediones (TZDs; i.e. rosiglitazone and pioglitazone) on the HDL-cholesteryl esters (CE) turnover and its relationship with the HDL cholesterol plasma levels.

Methods: New Zealand White rabbits received 1.75 mg/kg/day of pioglitazone (PIO, n=6) or 0.34 mg/kg/day of rosiglitazone (ROS, n= 6) during 6 weeks. Control group (n=6) received only vehicle. For the CE turnover, animals received $1.0x10^6$ cpm of [^{3}H]-CE-HDL intravenous. Blood samples were obtained 5min after injection and at different intervals up to 5h. VLDL/LDL and HDL fractions were separated by ultracentrifugation. [^{3}H]-CE curves were constructed for HDL and for apo B containing lipoproteins, considering 5min HDL sample as 100% of the initial radioactivity.

Results: Pioglitazone increases de HDL-C plasma levels in comparison with the control group while ROS group had no significant changes (20.1±5.5 and 15.3±5.7 vs 11.7±4.8 mg/dL; respectively, $p< 0.001$). In the HDL-CE turnover studies, PIO group showed shallower radioactivity decay curve in the HDL fraction than ROS and control groups, suggesting a lower catabolism of HDL-C in pioglitazone treated animals. CE transfer from HDL to VLDL/LDL fraction is delayed in PIO group, compared to the control and ROS groups.

Conclusion: The different effects on the HDL-C plasma levels between pioglitazone and rosiglitazone treatments, may be the result of their differential effects on the HDL-CE metabolism, since pioglitazone delays the catabolism and transfer to the pro-atherogenic lipoproteins and rosiglitazone does not alter this turnover. Supported by CONACyT grant No. 47275.

HIGH TRIGLYCERIDES, LOW HDL CHOLESTEROL, AND SMALL LDL PARTICLES INDEPENDENTLY PREDICT INCIDENT TYPE 2 DIABETES IN NON-DIABETIC CORONARY PATIENTS

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Aims: Patients with type 2 diabetes mellitus (T2DM) exhibit a typical pattern of dyslipidemia with high triglycerides, low HDL cholesterol, and small LDL particles which is also frequently observed in pre-diabetic patients. We therefore aimed at investigating whether these lipid abnormalities predict incident T2DM in the high-risk population of angiographied coronary patients.

Methods: The incidence of T2DM was recorded over 6 years in a population of 503 consecutive non-diabetic patients undergoing coronary angiography for the evaluation of stable coronary artery disease.

Results: During follow-up, T2DM was newly diagnosed in 86 (17.1%) of our patients. In logistic regression analysis adjusting for age, gender, BMI, hypertension, and smoking the standardized odds ratio (OR) for fasting glucose as a predictor of T2DM was 1.72 [95% CI 1.36-2.18]; $p < 0.001$ and, in line with our hypothesis, also the serum levels of triglycerides (OR = 1.57 [1.25-1.98]; $p < 0.001$) and HDL cholesterol (OR = 0.62 [0.45-0.86]; $p = 0.004$) as well as the LDL particle diameter (OR = 0.57 [0.44-0.75]; $p < 0.001$) proved significantly predictive of incident T2DM. Importantly, triglycerides (OR = 1.49 [1.18-1.88], $p = 0.001$), HDL cholesterol (OR = 0.66 [0.47-0.91], $p = 0.012$) and the LDL particle diameter (OR = 0.61 [0.45-0.80], $p < 0.001$) still significantly predicted T2DM after additional adjustment for the baseline fasting glucose values.

Conclusions: High triglycerides, low HDL cholesterol, and a small LDL particle diameter significantly and independently predict the 6-year incidence of T2DM among non-diabetic coronary patients.

MEDIUM CHAIN FATTY ACIDS HAVE TISSUE-SPECIFIC EFFECTS ON LIPID METABOLISM AND INSULIN SENSITIVITY

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Objective: To investigate the effect of medium chain fatty acids (MCFA) on insulin sensitivity and fatty acid metabolism in rodents.

Methods: C57BL/6J mice and Wistar rats were fed a high-fat diet rich in MCFA or long chain fatty acids (LCFA) for 4-5 wk. Insulin sensitivity and markers of fatty acid oxidation and synthesis were examined in skeletal muscle and liver.

Results: Despite equivalent caloric intake, rodents fed the MCFA diet displayed reduced adiposity compared to LCFA-fed animals. Triglyceride levels were ~30% lower in muscle of MCFA-fed animals compared to LCFA-fed animals. The reduced intramuscular lipid accumulation following MCFA feeding, was associated with elevated (30-50%) enzymatic activity and expression of key oxidative proteins (e.g. CPT1) compared to LCFA-fed animals. In contrast to muscle, liver triglycerides were higher in MCFA-fed animals. The increased lipid deposition in MCFA-fed animals was not due to differences in hepatic oxidative capacity, but was related to upregulation of lipogenic pathways. MCFA-fed mice displayed improved glucose tolerance compared to LCFA-fed mice (40% lower area under curve, $P< 0.01$). Utilising euglycemic-hyperinsulinemic clamps in rats we observed that the MCFA and LCFA diets had similar effects on liver insulin sensitivity (i.e. hepatic glucose output). However, peripheral insulin sensitivity, as assessed by the Rd during the clamp and insulin-stimulated glucose uptake into muscle, was 30-40% higher ($P< 0.01$) in rats fed the MCFA diet compared to LCFA-fed animals.

Conclusion: MCFA have potent tissue-specific effects on fatty acid metabolism and protect muscle against lipid-induced insulin resistance.

HIGH LEVELS OF APOB, LP(A), HSCRP AND LEUCKOCYTE COUNTS IN DIABETES MELLITUS AMPLIFY THE PREDICTIVE VALUES FOR CORONARY ARTERY DISEASE

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Background: Interactions between risk factors have been proposed to cause high risk for CAD.

Objectives: To examine the potential interactions between diabetes and lipids and nonlipids risk factors.

Methods: Markers of inflammation, electrolytes, the profiles of serum (apo)(lipo)proteins as well as classical risk factors were determined in 270 clinically stable angiographically documented subjects. The subjects were classified as CAD cases and controls according to the results of coronary angiography.

Results: The frequency and severity of CAD, Framingham CAD scores, relative and absolute risks for CAD were higher in diabetes than non-diabetes. Diabetic relative to non-diabetic subjects had higher levels of LDLc, apoB, Lp(a), BUN, measured osmolality, potassium, ESR, hsCRP, and leukocyte and platelet counts. Bivariate correlation analyses showed significant associations of diabetes with LDLc, apoB, Lp(a), BUN, measured osmolality, potassium, ESR, hsCRP, and leukocyte and platelet counts. On multiple logistic regression analysis, diabetes was among the major risk factors and showed multiplicative interactions with correlated risk factors.

By constructing dummy combined variables, diabetes accompanied with

high apoB Lp(a), hsCRP and leukocyte counts exhibited amplified high risk for CAD.

Conclusions: The results show that, elevated levels of apoB, Lp(a), hsCRP and leukocyte counts in diabetic patients have synergistic effects that promotes CAD. This synergistism warrants aggressive risk factor intervention in diabetic patients with elevated interactive risk factors.

EFFECTS OF PITAVASTATIN ON HIGH DENSITY LIPOPROTEIN CHOLESTEROL, OTHER LIPOPROTEIN PROFILES AND CHOLESTEROL ESTER TRANSFER PROTEIN IN PATIENTS WITH METABOLIC SYNDROME

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Objective: Statin increased high density lipoprotein cholesterol (HDL-C) level by 5-10%. But in some patients, HDL-cholesterol level decreased with statin. This study was designed to investigate the effect of pitavastatin on HDL-C level, predictive factors of HDL-C increase and its association with cholesterol ester transfer protein (CETP) in patients with metabolic syndrome.

Methods: This was mono-arm study with pitavastatin in patients with metabolic syndrome. After 4 weeks' therapeutic lifestyle change, patients received pitavastatin 2mg/day for 8 weeks. Primary parameter was change of HDL-C level after 8 weeks' treatment. Secondary objectives were changes of other lipoproteins, apolipoprotein B/A1, high sensitivity C-reactive protein (hsCRP) and CETP.

Results: 66 patients were screened and 63 patients (59.4 years of age, male 38.9%) were treated. After 8 weeks´ pitavastatin treatment, HDL cholesterol increased 5.4% from mean 41.5 to 43.5 mg/dL (p=0.037). Pitavastatin significantly decreased LDL cholesterol by 38.8%, total cholesterol by 26.1%, apolipoprotein B/A1 ratio by 36%. HsCRP level decreased insignificantly with treatment. CETP decreased 26.3% with treatment, but CETP increase was not associated with HDL-C increase. Predictive factors for HDL-C increase were male, absence of diabetes, BMI < 30 kg/m^2, old age.

Conclusion: Pitavastatin significantly increased HDL-C, decreased total cholesterol, LDL-C, triglyceride levels, apolipoprotein B/A1 ratio, CETP in patients with metabolic syndrome. CETP change was not associated with HDL-C increase in this study.

SERUM LEVELS OF MCP-1 ARE STRONGLY ASSOCIATED WITH HIGHER RATIO OF LDL- TO HDL-CHOLESTEROL LEVELS AND LOWER ESTIMATED GFR IN A GENERAL POPULATION

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Background: Monocyte chemoattractant protein-1 (MCP-1) has been shown to contribute to macrophage infiltration into adipose tissues and vascular wall cells, thereby playing a role in the pathogenesis of insulin resistance and atherosclerosis. Recently, it is suggested the ratio of LDL-C to HDL-C (L/H ratio) predicts progression of atherosclerosis in insulin resistant patients. Chronic kidney disease (CKD) is also known as a risk factor for insulin resistance and atherosclerotic disease.

Objective: We investigated whether serum MCP-1 levels are associated with the risks for atherosclerosis, including L/H ratio and CKD, in a general population.

Methods: A total of 860 residents (318 men and 542 women, mean age 65.4±9.8 years) underwent a complete history and physical examination, determination of blood chemistries, including serum levels of MCP-1.

Results: Mean levels of MCP-1 were 281.4±7.3 pg/ml. Elevated MCP-1 levels were associated with higher levels of WBC ($p< 0.05$), hsCRP ($p< 0.05$), γ-GTP ($p< 0.0001$), HbA_1c ($p< 0.05$), BUN ($p< 0.0001$), Cr ($p< 0.0001$), Uric acid ($p< 0.0001$), IMT of carotid arteries ($p< 0.0001$), and L/H ratio ($p< 0.05$). Elevated MCP-1 levels were associated with the lower levels of HDL-C ($p< 0.05$) and estimated GFR ($p< 0.0001$) by analysis of co-variance adjusted for age and sex. The hierarchical model demonstrated that the serum MCP-1 levels were the highest in the group with higher L/H ratio and lower estimated GFR.

Conclusion: The present study demonstrated that serum levels of MCP-1 were strongly associated with higher L/H ratio and CKD, thus being involved in accelerated atherosclerosis in these high-risk patients.

EFFECTS OF L-CARNITINE, POLYPHENOLS, AND PHOSPHOLIPID N-3 FATTY ACIDS ON PLASMA LIPIDS AND EXPRESSION OF CATS IN BLOOD CELLS IN HUMAN HYPERLIPIDEMIC SUBJECTS

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Free fatty acids (FFA) play important physiological roles in most tissues like skeletal muscle, heart, liver and pancreas, but chronically increased FFAs have been implicated as an important causative link between obesity and hepatic and peripheral insulin resistance. When the partitioning of FA metabolism towards the secretion of triacylglycerol (TG) is enhanced, the secretion of TG may be raised sufficiently to induce insulin resistance. Substitution of the EPC-complex resulted in a significant ($p< 0.05$) decrease of TG, FFA and cholesterol ($P< 0.001$, $p< 0.05$ and $p< 0.05$, respectively).

The relative mRNA amounts of CPT1A, CPT1B (interestingly, both expressed in peripheral mononucleated blood cells (PMNC)), and CRAT were increased after EPC substitution (2, 2 and 2.5 fold, respectively). Yoghurt drinks enriched with vitamins C and E (control group) had no effects neither on plasma lipid levels nor on gene expression in PMNC. In addition, the results provide convincing, albeit indirect evidence, that long time metabolic effects of dietary supplements on gene expression are detectable in PMNC.

In conclusion, the combined effects of the dietary constituents (EPC-complex) on reduction of plasma lipid levels and stimulation of the expression of regulatory enzymes involved in FA oxidation in PMNC were confirmed in the present study. The rational for using mixtures is that the mechanisms and loci of action of different agents vary and they interact in a network and consequently a mixture is more likely to have stronger effects.

PIOGLITAZONE AND ROSIGLITAZONE DECREASE HDL-CHOLESTERYL ESTERS UPTAKE *IN VITRO*

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Aims: Thiazolidinediones (TZDs; i.e. pioglitazone and rosiglitazone) shift HDL size distribution to small HDL3c and modulate the expression of the scavenger receptor BI (SR-BI). HDL/SR-BI interaction modifies the size

and composition of these lipoproteins. Our hypothesis is that TZDs modify HDL structure increasing cholesterol influx (in vitro) from HDL to Fu5AH cells through SR-BI.

Methods: Rat Fu5AH hepatoma cells, expressing SR-BI, were plated at a density of $1x10^5$cell/well and co-incubated with 0.4 or 2.0 µg/mL of rosiglitazone or pioglitazone, respectively, and control cells with vehicle (DMSO), 48 h before the experiment. HDL containing $1.0x10^6$ cpm of [^{3}H]-cholesteryl esters (CE) were incubated with cells for 0.5, 1 or 3 h. Radioactivity was determined in the medium by scintillation counting. Intracellular radioactivity was determined treating the cells with isopropanol. Cholesterol uptake was expressed as percentage of total radioactivity found intracellularly.

Results: Pioglitazone and rosiglitazone-treated cells showed an initial rapid [^{3}H]CE uptake after 0.5 h (1.0±0.4 and 1.0±0.4%, respectively vs control cells 0.6±0.2%). After 3h the [^{3}H] CE uptake was lower in treated cells compared to controls (1.7±0.2 and 1.3±0.3%, respectively, vs 2.5±0.2%, $p< 0.05$).

Conclusion: The present data demonstrate that TZDs treatment decreased the CE uptake by hepatoma cells, suggesting a little effect of SR-BI in the genesis of small HDL particles. These data show that over-expression of SR-BI is not enough to increase the influx, and that the structure of the HDL may have greater impact on the uptake.

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EFFECTS OF COMBINED HYPOLIPIDEMIC THERAPY ON LIPIDS AND THE ATHEROGENIC INDEX OF PLASMA [AIP - LOG(TG/HDL-CH)] IN PATIENTS WITH MIXED DYSLIPIDEMIA AND HIGH CARDIOVASCULAR RISK

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Aim: High risk patients with mixed dyslipidaemia should achieve low target levels of LDL cholesterol (ch) event. non-HDL-ch or apolipoprotein-B. We studied the safety and tolerability of combination therapy (statin + fenofibrate) on lipid parameters in addition to AIP which has been proven earlier to be a predictor of cardiovascular risk (CVR).

Methods: The study took place in six lipid centers. The high CVR was based on patient history or the presence of risk factors: SCORE≥5%. Mixed dyslipidaemia was defined as the existence of two out of the following three lipid abnormalities: LDL-ch ≥ 2,5 mmol/L, HDL-ch < 1 mmol/L in men and < 1,3 mmol/L in women, TG >1,7 mmol/L prior to the initiation of treatment. Following a personal educational session regarding lifestyle, combination therapy was initiated: any statin at the lowest dose and 160 mg of fenofibrate. After three months, the doses could be increased provided the patients did not reach target values. Adverse effects were monitored in addition to creatinine kinase.

Results: A total of 81 patients were included in the study (53 men, 28 women) aged 60±10 years. After 6 months LDL-ch decreased significantly by 29%, TG by 40%, apolipoprotein-B by 27% and non-HDL-ch by 25% ($p< 0,001$), HDL-ch increased by 3% (NS), AIP decreased significantly by 50% ($p< 0,001$). There was no incidence of serious adverse events.

Conclusion: Combination therapy was very well tolerated and significantly improved the lipid parameters and reduced CVR calculated using the AIP.

DIABETES TYPE 2 AND DISLIPIDEAMIA

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Executive summary: Type 2 diabetes association with obesity tend to increase insulino-resistance and hyperinsulinaemia, who are responsible for lipidic disturbances.

Objectives: To evaluate the percentage of diabetics that reach the therapeutic objectives, in accordance with the guidelines recommended by Diabetology Societies.

Patients and methods: The sample was composed by 223 diabetic patients, 123 of which were female (55, 2%) and 100 were male (44, 8%). The sample age average was 60,8 ± 10,9 (20-87) years. They were randomly selected from patients registered in the Endocrinology Consultation of S. João Hospital. We defined the following benchmarks: Total Cholesterol < 175 mg/dl, HDL > 45mg/dl, LDL < 100mg/dl, Triglycerides < 150 mg/dl and Microalbuminurea < 30 mg/day. In order to produce the statistical data analysis we used the SPSS software program.

Results: Regarding the parameters that were analyzed we observed the following mean results: Total Cholesterol - 190,55 ± 44,27 mg/dl; Cholesterol HDL - 50,45 ± 15,79 mg/dl; Cholesterol LDL - 120,61 mg/dl ± 34,78 mg/dl; Triglycerides - 168,22 ± 121,07 mg/dl; Microalbuminurea - 78,93 ± 246,28 mg/day.

Conclusions: The study allowed us to conclude that, 15, 2% of diabetic patients achieved the therapeutic goals, 18 % of which were male and 7, 6 % were female. Apparently women had more lipidic disturbances mainly because of theirs overweight and the type of therapeutic they follow.

APPLICATION OF LIPID CRITERIA IN CAMEROON (SUB-SAHARAN AFRICAN)

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Background: It is well known that obesity is closely related to insulin resistance (IR), the incidence of the development of IR in people with obesity is not known in Cameroon.

Objective: The measurement of the IR by standard methods is expensive and not easily applicable in epidemiologic studies, this study was conduct in order to identify anthropometric as well as metabolic markers of IR and the evaluate prevalence of IR in Cameroon.

Methods: 1189 non diabetic overweight or obese subjects were recruited. Measurements included anthropometrics measurement, blood pressure, plasma lipid and glucose levels The Areas under the receiver operating characteristic curve were used to identify the best predictor of insulin resistance which was the used to assess the prevalence of insulin resistance in our population study.

Results: The Areas under ROC curves for triglycerides (0.956±0.01) level and triglycerides-HDL-C ratio (0.938±0.03), gave an exceptional discrimination. Therefore, they could be used as markers of insulin resistance. Using the lipid ratio, the overall prevalence of insulin resistance was 19.7% and was high among women (20,50%), morbid obese (23.4%) and participants from north part of the country (25%).

Conclusion: In Cameroonian, TG levels and TG-HDL-C ratio are reliable markers of insulin resistance. Although the prevalence of insulin resistance is low compare to westernized countries, hence obese or overweight persons should follow a Healthy diet and increase their physical activity level in order to reduce cardiovascular risk factors.

COMBINED APPLICATION OF EZETIMIBE AND FENOFIBRATE FOR DYSLIPIDEMIA CORRECTION AT PATIENTS WITH METABOLIC SYNDROME

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Research purpose: Analyse efficiency of combined therapy of ezetimibe and fenofibrate for dyslipidemia correction at patients with MS.

Material and methods: 65 patients at the age of 32-65. MS was diagnosed in accordance with NCEP ATPIII criteria (2001). The main criterion for including into research is inefficiency of statin monotherapy. After increase in statin dosage all the examined patients showed more than triple excess of the upper level rate ALT/AST. In addition to low cholesterol diet the patients were taking «Ezetrol» (Schering-Plough) 10 mg and «Lipantyl» (Fournier S.A.) 200 mg per day during 4 weeks. Estimated: changes of lipidic profile, the level of ALT/AST and CPK, tolerance for drug therapy, side effects.

Results: After 4-week complex therapy total cholesterol is down by 28%, VLDL-C - by 33 %, VLDL-C - by 26%, triglycerides - in 1,7 times, HDL-C level went up by 16,5%. All the examined patients noted good tolerance for the combined therapy. During a week two patients complained of stomachache after taking fenofibrate, but this did not require drug withdrawal. No other allergic and dyspeptik disorders were fixed. There was no case of combined therapy application in which CPK or ALT/AST rise was registered.

Outcomes: Combination of ezetimibe and fenofibrate is high efficient at dyslipidemia treatment at patients with MS. Its use makes it possible not only to achieve LDL-C aims, but also to raise HDL-C content. This combination appears to be safe.

Acknowledgement of its equality to statins calls for a wider investigation in population.

SERUM 7-KETOCHOLESTEROL LEVELS MIGHT BE REGULATED BY SEVERITY OF INSULIN RESISTANCE AND SERUM LDL-C LEVELS

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Many oxysterols have been detected in the plasma of humans by gas chromatography with mass spectrometry analysis (GC-MS), but the significance of serum oxysterol levels is not fully understood. In this study, we examined the clinical significance of serum 7-ketocholesterol levels (s-7KCHO) in patients with type 2 diabetes mellitus. The s-7KCHO of 137 patients with type 2 diabetes mellitus and 89 non-diabetic healthy subjects were measured by GC-MS. The s-7KCHO was significantly higher in patients with type 2 diabetes mellitus (33.8 ng/ml) compared to non-diabetic healthy subjects (16.1 ng/ml). The patients with type 2 diabetes mellitus were divided into patients with and without metabolic syndrome, and the significance of s-7KCHO was examined. The s-7KCHO was significantly higher in patients with metabolic syndrome (39.5 ng/ml) compared to those without metabolic syndrome (30.1 ng/ml). Among patients with metabolic syndrome, s-7KCHO was significantly higher in patients with high low density lipoprotein-cholesterol (LDL-C) levels (45.1±5.9 ng/ml) compared to those with normal LDL-C levels (35.3±7.0 ng/ml). Furthermore, s-7KCHO increased according to the number of concurrent coronary risk factors. These results suggest that serum 7-ketocholesterol levels may depend on the severity of insulin resistance and serum LDL-C levels.

DYSLIPIDEMIAS IN TRAFFIC SAFETY EMPLOYEES

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Introduction: Dyslipidemias represent a major cause for the occurrence of atherosclerosis and the diseases associated with it (ischemic cardiopathy, cerebral-vascular ischemic diseases, peripheral vascular diseases).

Objectives: We closely monitored the correlation between the obesity type, the body mass index (BMI) and the presence of dyslipidemia (quantitative, qualitative), as well as carefully studied the prevalence of various complications and morbid associations depending on the type of dyslipidemia.

Material and method: The retrospective study was carried out on a batch of 199 patients, all male, hospitalized in the IVth Medical Clinic Cluj-Napoca, within January - October 2007. Each patient was assessed in what the individual risk factors are concerned, as well a series of mezological factors.

Results: Out of the total of 199 patients, more than half (108 patients) showed isolated hypercholesterolemia, 33 patients having isolated hypertriglyceridemia, and 58 mixed dyslipidemia. As mezological factors, the tobacco and alcohol intake have the highest prevalence among dyslipidemic patients; however, where coffee intake is concerned, it was recorded among patients with hypertriglyceridemia and mixed dyslipidemia. Regarding the co-morbidities, the following had the highest prevalence: high blood pressure, ischemic cardiopathy, liver steatosis, diabetes mellitus.

Conclusions: Life's 4th and 5th decades are the period with the highest frequency of dyslipidemias; work place conditions, in terms of location, do not determine significant differences regarding the prevalence of dyslipidemias; as preferred mezological factors; the co-morbidities remain at a high prevalence in patients with dyslipidemias (obesity, high blood pressure, ischemic cardiopathy, hyperuricemia, liver steatosis, diabetes mellitus).

THE EFFECT OF ATORVASATIN ON THE LIPOPEROXIDATION IN METABOLIC SYNDROME

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Metabolic Syndrome (MeS) has both systemic and coronary endothelial dysfunction with reduced vasodilatatory response. Statins reduce oxidized. low-density cholesterol, a molecule know to increase the production of endothelin-1 and downregulate endothelial Nitric Oxide Synthase. The beneficial effects of statins are thought to be due to lipid-lowering, especial of oxidized low-density lipoprotein and to the pleiotropic effects of those agents.

Aims: We investigated the action of atorvastatin on lipoperoxidation in patients with MeS with a biomarker of oxidative stress.

Methods: We perform a randomized, prospective study, on 20 patients with MeS, who received 10 mg Atorvastatin daily. MeS was defined by the ATP III clinical definition. Study entrants has LDL-cholesterol concentration was 4,6mmol/l or greater, a fasting triglyceride amount over 1,65mmol/l. They were subjected to a submaximal exercise test and compared with a control group. The used marker of oxidative stress was Malondialdehide (MDA) measured as acid thiobarbituric-reactive substances, by Satoh method, in venous blood at 5 and 10 minutes after effort test.

Results: The patients who received treatment with atorvastatin has less exercise-induced ischemic ST-segment depression (22 vs.35%) and a significant reduction of average MDA levels at 5 and 10 minutes after exercise, compared with control group (2,48 ± o,64 vs. 3,18± 0,45 nmol/l).

Conclusions:

1. The use of atorvastatin reduced the average MDA level in venous blood after submaximal exercise test.

2. Atorvastatin 10mg daily reduced a marker of lipoperoxidation in MeS and may contribute to the improvement of endothelial dysfunction and vascular events prevention.

LDL-CHOLESTEROL LEVELS AND THEIR ASSOCIATION WITH MICRO- AND MACRO- VASCULAR COMPLICATIONS IN TYPE 2 DIABETES

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Aims: Type 2 diabetes is not only associated with hyperglycaemia but also with dyslipidaemia. According to American Diabetes Association (ADA) the target level of LDL-cholesterol for diabetics is < 100 md/dl (< 70 mg/dl for those with coronary artery disease). The aim of this study was to investigate the association of dyslipidaemia with micro- and macro-vascular complications in a sample of diabetics over a time period of 2 years.

Methods: The study included 191 patients with type 2 diabetes (mean age: 64.7±9.2 years old, 99 males) visiting for the first time the diabetes clinic of Gennimatas Hospital. Metabolic parameters, as well as vascular complications (both previously undiagnosed and new occurrences) were recorded during a 2-year time period. Microvascular disease was assessed by fundoscopy, microalbuminurea, and clinical examinations, while macrovascular by coronary angiography, electrocardiogram changes and doppler study.

Results: At baseline 20% of the patients had LDL-cholesterol values within the desired levels according to ADA recommendations. At the end of the study the respective percentage was 35%. 55% of the patients were on statin treatment. Macrovascular complications were less frequent in patients with target achieved LDL levels compared to those without (7.6% vs. 23% respectively, p=0.009). On the contrary, no significant differences were observed with respect to the presence of microvascular complications between those who achieved LDL target values and those who didn't (35% vs. 44% respectively, p=0.28).

Conclusions: Aggressive decrease of LDL-cholesterol within the recommended values in type 2 diabetics is crucial for the avoidance of macrovascular disease.

HORMONAL-METABOLIC PROFILES OF DYSLIPIDAEMIAS IN NON-OBESE TYPE II DIABETIC PATIENTS WITH ATHEROSCLEROSIS

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Objective: The aim was to evaluate the hormonal-metabolic profiles of dyslipidaemias in non-obese patients (pts) with type II diabetes mellitus (DM) and documented atherosclerosis (ATH).

Methods:
Group 1 (gr1) was composed of 30 normal subjects (age = 54.50+2.03; means+SEM).

Group 2 (gr2) consisted of 20 non-obese type II DM pts with hypertriglyceridaemia (type IV HLP) and ATH (age = 53.19+1.91).

Group 3 (gr3) consisted of 23 non-obese type II DM pts with mixed hyperlipidaemia (type IIB HLP) and ATH (age = 56.73+1.96).

Following have been determined in serum, in fasting state: total cholesterol (CH), HDL-cholesterol (HDL-CH), atherogenicity coefficient (HAC), triglycerides (TG), lipolytic activity (LA), lipoprotein fractions, prostaglandins A1 and E1, prostaglandin F2alpha(PGF). Following have been determined in plasma, during standard OGTT: glucose, insulin, insulin/glucose index (IGI), glucagon, C-peptide, STH, somatostatin, ACTH, cortisol, aldosterone, beta-endorphin.

Results: Both gr2 and gr3 pts, compared to gr1, had higher body mass, CH, TG, HAC, and lower HDL-CH, LA, insulin (at OGTT hour 1), IGI, STH (hour 2), basal aldosterone. Gr2 pts, compared to gr1, had lower STH (hours 1 and 2). Gr3 pts, compared to gr1, had higher glucagon (hour 2), somatostatin (hours 0 and 1), cortisol (hours 1 and 2), PGF, and lower C-peptide (hour 1), STH (hours 0 and 2).

Conclusions: Altered hormonal-metabolic profiles have been observed in non-obese type II DM pts with ATH and dyslipidaemias, including decreased STH and elevated cortisol.

SIMVASTATIN IN ESCALATION DOSES IMPROVE RENAL FUNCTION IN PATIENTS WITH DIABETES MELLITUS AND MILD-TO-MODERATE PROTEINURIA

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The aim: To exam whether both candesartan cylexitil and simvastatin are superior to candesartan cylexitil alone in patients with diabetic nephropathy and mild-to-moderate proteinuria.

Methods: 62 patients (47 men) with 2nd type diabetes mellitus and mild-to-moderate proteinuria aged 45-62 years were enrollment to the study. During 4 weeks run in period all patients were treated by candesartan cylexitil (target dose was 16-32 mg daily oral) and then they were randomized into group candesartan cylexitil (n=22) and both candesartan cylexitil and simvastatin (n=40) in daily ranged oral doses: 5 mg (n=10), 10 mg (n=10), 20 mg (n=10), and 40 mg (n=10). Course of treatment was 52 weeks.

Results: During treatment period doses escalation of simvastatin from 10 mg to 40 mg per day occurs diminishing of C-reactive protein plasma level (-27% [95%CI = - 9.6% to - 38.2%]; P< 0.05) without negative trend of glomerulat filtration rate (-1.8% [95%CI = - 0.4% to - 3.3%]; P< 0.01). It was verified interrelation between simvastatin dosages and C-reactive protein (r=-0.68; P=0.0012), interleukin-6 (r=-0.45; p< 0.05), TNF-alpha (r=-0.46; P< 0.02) plasma levels. High dose (40 mg daily) of simvastatin is more available to renoprotective and anti-inflammatory effects. There was not a significant changes of interleukins and TNF alpha plasma levels in candesartan cylexitil patients group.

Conclusion: Simvastatin added to ARB candesartan cylexitil in patients with 2nd type diabetes mellitus might be improve renal function dose-dependently.

CALMIDAZOLIUM CHLORIDE (CMZ) INDUCED OXIDATIVE STRESS, MITOSOLIC CALCIUM AGGRAVATION AND APOPTOTIC CELL DEATH IN NEONATAL AND ADULT CARDIOMYOCYTES

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Intracellular calcium concentration ([Ca]i) regulates contractility in myocardial cells. Elevation of [Ca]i level occurs both by entry of Ca2+ through voltage-dependent Ca2+ channels in the plasma membrane and by Ca2+ release from sarcoplasmic reticulum (SR). CMZ blocks L-type calcium channel as well as voltage-dependent Na+ and K+ channel currents.

Accumulation of intracellular calcium occurs as a result of blockage of calcium channels using CMZ. Calcium accumulation leads to the opening of a high-conductance mitochondrial permeability transition pore resulting in collapse of the electrochemical potential for H^+, thereby arresting ATP production and triggers production of reactive oxygen species. Collapse of mitochondrial energy apparatus leads cell death.

Neonatal and adult cardiomyocytes were cultured under standard conditions and effect of various doses of CMZ was studied. Cell viability was assessed using MTT assay. Calcium measurement studies were done using Fluo-3 AM. ROS and RNS levels were determined using specific probes like DCF-DA, DHE, DAF-2DA and DHR 123. Mitochondrial membrane potential was assessed by using DiOC6/TMRM. Cell cycle analysis was done using PI staining by FACS. Western blotting was done to assess cell death pathway.

Increased accumulation of intracellular calcium after addition of CMZ in a dose-dependant manner. There was a dose dependent increase in the formation of $O_2^{-\cdot}$ and H_2O_2 as detected by DHE and DCF-DA with a simultaneous increase in NO and ONOO as detected by DAF-2DA and DHR 123 staining. Apoptotic cell death with low doses and necrosis with high doses of CMZ was observed.

CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY REDUCES OXIDATIVE STRESS MARKERS, REDUCING BLOOD PRESSURE IN SLEEP APNEA-HYPOPNEA SYNDROME PATIENTS

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Introduction: Sleep apnea-hypopnea syndrome (SAHS) is characterized by the presence of recurrent limitation of airflow episodes located in the upper airway during sleep. During hypoxia/reoxygenation phenomenon happened in SAHS, generation of reactive oxygen species is increased.

Objective: Investigate whether continuous positive airway pressure treatment (CPAP) could reduce oxidative stress in patients with SAHS and which metabolic alterations would be associated to redox imbalance.

Methods: Twenty-eight patients with SAHS requiring CPAP treatment were enrolled.

Total antioxidant capacity and the activities of: glutathione peroxidase, glutathione reductase, glutathione s-transferase, catalase and superoxide dismutase were measured in plasma with commercial kit from Cayman Chemical. Lipid peroxidation levels were measured in serum using a commercial kit from Cayman Chemical.

ROS generation, such as superoxide anion and hydrogen peroxide, intracellular glutathione and mitochondrial membrane potential were measured in total leukocytes, lymphocytes, neutrophils and monocytes by flow cytometry.

Analyzed biochemistry variables were: glucose, uric acid, cholesterol, HDL-c, LDL-c, triglycerides, insulin, leptin, adiponectin and Hb1Ac.

Results: Parameters of cellular oxidative stress were notably decreased after treatment. In addition, there was a significant increase of intracellular glutathione and mitochondrial membrane potential. Most of the plasma antioxidants activities showed a significant increase after treatment. There was a significant decrease of Epworth, systolic and diastolic blood pressure. Insulin levels and insulin resistance showed a slightly decrease.

Conclusion: We have observed an obvious improvement of oxidative stress especially at the cellular level and found that is accompanied by an equal evident decrease of blood pressure without insulin resistance modification.

OXIDATIVE STRESS AND METABOLIC MODIFICATIONS AFTER CPAP TREATMENT IN PATIENTS WITH SAHS

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Introduction: Sleep apnoea-hypopnoea syndrome (SAHS) is characterized by recurrent episodes of hypoxia/reoxygenation. This seems to causes an increased reactive oxygen species production and the oxidative stress promotion. SAHS patients are associated with an increase in the prevalence of hypertension, obesity and dyslipidemia. Also, there are evidences that support an increase of oxidative stress in SAHS patients and this could induce the cited diseases.

Objective: Investigate how oxidative stress markers modify after continuous positive airway pressure (CPAP) treatment and the effect that these changes produce on the pathology associated with SAHS**.**

Methods: Seventy-eight patients who required CPAP were enrolled. Patients were classified as a function of hypertension, obesity and dyslipidemia.Serum lipid peroxidation levels, plasma total antioxidant capacity and the plasma activities of: glutathione peroxidase, glutathione reductase, glutathione s-transferase, catalase and superoxide dismutase were measured.Analyzed biochemistry variables: glucose, uric acid, cholesterol, HDL-c, LDL-c, triglycerides, insulin, leptin, adiponectin, hs-CRP and Hb1Ac.

Results: Blood pressure (BP) decreased after treatment but only diastolic BP showed a significant decrease. Moreover, systolic and diastolic BP significantly reduced after CPAP in hypertensive patients.CPAP reduced oxidative stress markers especially in nondyslipidemic and hypertensive patients.

SAHS severity parameters positively correlated with insulin levels and HOMA indexes. Leptin, adiponectin and hs-CRP levels significantly correlated with SAHS severity parameters.

Conclusion: An obvious improvement of oxidative stress is accompanied by an equal evident decrease of BP without significant insulin resistance modification. Consequently, we believe that the oxidative stress decrease is not the central cause to the improvement of insulin resistance in these patients.

SILDENAFIL PROTECTED CARDIOMYOCYTES FROM DIABETES-INDUCED APOPTOSIS: REDUCTION OF OXIDATIVE STRESS AS A POSSIBLE INVOLVED MECHANISM

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Aims: Cardiomyocyte apoptosis, as a result of increased oxidative stress, plays a dominant role in the pathogenesis of diabetic cardiomyopathy. Sildenafil has been demonstrated to have antioxidant effects, but its effects on diabetes-induced cardiomyocyte apoptosis and antioxidant status of diabetic hearts have not yet been investigated.

Methods: TUNEL assay was used to evaluate the effect of sildenafil on cardiomyocyte apoptosis, at its peak value after streptozotocin administration, in diabetic mice. To elucidate the antioxidant activities of sildenafil in cardiac tissues, the levels of Malondialdehyde, by product of lipid peroxidation, and the activities of Catalase, Glutathione peroxidase and Superoxide dismutase have also been studied.

Results: Seven days after streptozotocin administration, diabetic mice showed lower body weight gains, heart weights and heart weight to body weight ratios compared to control ones, and sildenafil treatment (0.71 mg/kg,bid) did not have any effects on these parameters in diabetic mice. While apoptotic rates and malondialdehyde levels were significantly higher in diabetic mice compared to control ones, sildenafil treatment could reduce them in diabetic mouse hearts. In Hematoxylin & Eosin staining of the heart tissues, diabetic hearts displayed structural abnormalities compared to their control ones. These structural abnormalities were prevented by sildenafil treatment. Moreover, there were no significant differences between antioxidant enzyme activities of diabetic and control groups, whereas sildenafil treatment could increase antioxidant enzyme activities in both groups.

Conclusion: Our study indicated that sildenafil was beneficial to hearts of diabetic mice by the reduction of cardiomyocyte apoptosis, partially due to its antioxidant effects in hearts.

AMINOACETONE CAUSES OXIDATIVE STRESS AND DEATH TO INSULIN-PRODUCING RINM5F CELLS

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Aminoacetone (AA) is a threonine and glycine catabolite produced in the mitochondrial matrix, recently implicated as an endogenous source of methylglyoxal (MG) in *diabetes mellitus*. Oxidation of AA to MG, H_2O_2 and NH_4^+ has been reported to be catalyzed by a copper-dependent semicarbazide amine oxidase (SSAO) as well as by Cu(II) and Fe(II) ions. Because MG and H_2O_2 have been found to be toxic to β-cells and AA is a potential source of oxyradicals by metal-catalyzed oxidation, we propose a possible pro-oxidant role of AA in pancreatic β-cells. AA toxicity to RINm5f cells was monitored by the MTT assay at 24 h after AA (0.1-10 mM) treatment. Cytotoxic effects of AA plus Cu(II) ions (5 - 100 uM) in insulin-producing cells (RINm5f) were partially inhibited by added antioxidant enzymes (SOD, 50 U/mL and catalase,5 uM), a copper chelator (bathocupreine, 0.1 mM) and fetal calf serum (FCS). Furthermore, AA was found to promote cellular DNA cleavage, $[Ca^{2+}]_I$ increase, activation of pro-(Bax) and anti-apoptotic (Bcl-2, Bcl-xL) expression proteins, NO production and, ultimately, apoptosis and necrosis. Although the physiological concentration of AA in tissues of diabetics is unknown, considering that AA is produced in mitochondrial matrix and that pancreatic β-cells display low expression of ROS scavenging enzymes, it is tempting to suggest that AA-generated H_2O_2 reacts with Cu(I) to form reactive species, thereby contributing to pancreatic β-cell injury and death.

Support: FAPESP, CNPq, Milênio Redoxoma.

ASSOCIATION BETWEEN FREE FATTY ACID AND INSULIN RESISTANCE, IMPACT OF OXIDATIVE STRESS (SUPEROXIDE DISMUTASE/SOD) AND INFLAMMATION (ADIPONECTIN DAN HS-CRP) AMONG OBESE NON DIABETIC INDIVIDUAL

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Background: Obesity is highly related to insulin resistance. Free Fatty Acids (FFAs) are adipokine secreted from adipocyte. FFA is now recognized as a major link factor between obesity and IR or diabetes.

Objective: To discover the existence of SOD, hs-CRP,TNF-a and adiponectin/hs-CRP ratio towards the occurrence of IR which is caused by elevated level of ALB, and to discover the interaction between SOD, FFA, TNF-a and adiponectin/hs-CRP ratio.

Design: Case control study.

Methods: There were 65 obese non diabetic and 45 non obese non diabetic subjects met the criteria.

Result: Mean fasting FFA levels was 0,61 mmol/L in obese and 0,5 mmol/L in non obese (p = 0,108), SOD levels was 1050 U/g Hb in obese and 1164 U/g Hb in non obese (p = 0,001), hs-CRP levels was 3,94 ng/L in obese and 0,99 ng/L in non obese (p = 0,000), adiponectin levels was 3,47 ng/mL in obese and 5,57 ng/mL in non obese (p = 0,000), and TNF-a levels was 8,38 pg/mL in obese and 3,19 pg/mL (p = 0,007). There were no significant differences between obese non diabetic and non obese non-diabetic in basal FFA concentrations but there was a differences in mean of FFA levels between two groups.

Conclusion: There was negative significan correlation between FFA and SOD levels. SOD and adiponectine levels were decreased in obese IR patiens compare with non obese non IR.TNF-a and hs-CRP levels were increased in obese IR compare with non obese non IR patients.

THE INFLUENCE OF THE COMBINED THERAPY OF LACIDIPINE AND CANDESARTAN ON THE SERUM 8-ISOPROSTANE LEVEL AT OVERWIGHT HYPERTENSIVE PATIENS

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Objective: Obesity is one of the leading risk factor hypertension. Such pathogenic combination relevant for the development oxidative stress (OS).

The aim of the study was to investigate the level 8-isoprostane as a marker oxidative stress at overweight hypertensive patients on the dynamics with combined lacidipine and candesartan therapy.

Design: 14 overweight hypertensive patients (II - stage, 2-3 degree of arterial hypertension, mean age - 55,3±1,33 years) and 10 practically healthy persons have were examined.

Blood serum content of 8-isoprostane had been determined by enzyme-linked immunosorbent assay («8-isoprostane ELISA» firms " US Biological ", USA). The obtained data were expressed in pg/ml.

Results: Overweight patients with arterial hypertension manifested the increase of 8-isoprostan blood serum content (12.67±2.57 pg/ml versus (1.41±0.25 pg/ml) in controls, $p< 0.0001$. After 14 days of treatment of the lacidipine in a combination with candesartan we observed the decrease of 8-isoprostane blood serum content by 25% (9.51±1.98 pg/ml), $p< 0,05$ in comparison with the baseline level. After 2 month of treatment we observed the decrease of 8-isoprostane blood serum content by 80.09% (2.42±0.74 pg/ml), $p< 0.05$ in comparison with the baseline level.

Conclusions: The treatment with lacidipine in a combination with candesartan is accompanied by significant decrease of a level 8-isoprostane and related to the depression of the features oxidative stress at obesity-associated hypertension.

EFFECTS OF EXPERIMENTAL METABOLIC SYNDROME ON OXIDATIVE STRESS AND ENERGETIC METABOLISM IN RAT CARDIAC TISSUE

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Aims: Recently investigation associated inadequate food intake (IFI) with incidence of cardiovascular damage, however cardiac biochemical pathway was unclear. The present study evaluated the energetic metabolism (EM) and the oxidative stress (OS) in rat cardiac tissue.

Methods: Male *Wistar* rats, 12 animals, were divided into two groups (n=6): (A) group received basal diet and (B) received high sucrose intake (30% in water solution) *ad libitum*. After 30 days animals were sacrificed and the left ventricle (200mg) used to determination of hydroperoxide (HP), total antioxidants substances (TAS) and the activity of catalse (CAT), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), lactate dehydrogenase (LDH),citrate synthase (CS) and hidroxiacil CoA dehydrogenase (OHCoAD). The plasma also used to determination of HP, LDL-ox, TAS, Oxide nitric sintetase (ONS), fasting glucose (GLU), HDL, LDL and triglycerides (TG). Statistical analysis: T-test, $p< 0.05$.

Results: In serum was observed decrease in HDL (27%), TAS (22%), ONS (36%), and an increased in GLU (27%), TG (75%), LDL (26%), HP (24%), LDL-ox (70%). Cardiac tissue shows decrease in TAS (28%), increased in HP (39%) and LDH (17%). Wasn´t observed difference in CAT, GSH-Px, SOD, OHCoAD.

Conclusion: The IFI induced alteration in the balance antioxidant/oxidant in all parameters of the study, inducing physiological cardiovascular alterations in EM and OS in rat cardiac tissue, associated with shift of cardiac metabolism.

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ROLE OF REACTIVE OXYGEN SPECIES IN DNA-BINDING ACTIVITY OF C/EBPB AND MITOTIC CLONAL EXPANSION DURING ADIPOCYTE DIFFERENTIATION

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Aims: Growth-arrested 3T3-L1 preadipocytes rapidly express CCAAT/enhancer binding protein-b (C/EBPb) upon hormonal induction of differentiation. However, DNA-binding activity of C/EBPb is not achieved until the cells synchronously reenter S-phase, thereby mitotic clonal expansion (MCE). In this period, C/EBPb is sequentially phosphorylated by MAPK and glycogen synthase kinase (GSK) 3b, giving rise to DNA binding activity and transcriptional activation. Because DNA-binding activity of C/EBPb is further enhanced by oxidation *in vitro*, we investigated how redox state affects the C/EBPb binding and MCE during adipogenesis.

Methods: 3T3-L1 preadipocytes were treated with H_2O_2 or antioxidant as well as hormonal stimuli, and the differentiation as well as C/EBPb binding was investigated.

Results: When 3T3-L1 cells were treated with H_2O_2 as well as hormonal stimuli, differentiation was accelerated with increased expression of PPARg. Interestingly, cell cycle progression (S to G_2M phase) was markedly enhanced by H_2O_2 on FACS analysis, while antioxidant caused "S-phase arrest" during the MCE. H_2O_2 treatment resulted in early appearance of punctate pattern on immunofluorescent staining of C/EBPb, which is a hallmark for C/EBPb-binding activity to regulatory elements, whereas short treatment (4h) of anti-oxidant rapidly dispersed the centromeric localization of C/EBPb. The binding of C/EBPb to PPARg promoter was also enhanced by H_2O_2 treatment in chromatin immunoprecipitation assay. During standard differentiation, reactive oxygen species (ROS) production was increased during MCE in 3T3-L1 cells.

Conclusions: Our results indicate that redox-induced DNA-binding, as well as the dual phosphorylation of C/EBPb, is required for the MCE and terminal differentiation of adipocytes.

SERUM MYELOPEROXIDASE AS A MARKER OF OXIDATIVE STRESS IN DIFFERENT CATEGORIES OF GLUCOSE TOLERANCE

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Aim: The aim of the present study is to evaluate serum myeloperoxidase (MPO) as a novel marker of oxidative stress at the fasting and post-challenge state in subjects with different categories of glucose tolerance - normal glucose tolerance (NGT), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and newly-diagnosed diabetes (NDD).

Material and methods: 87 subjects (44 males and 43 females), of mean age 54.4±9.4 years and mean BMI 32.2±5.1 kg/m^2 - 23 with IFG, 24 with IGT, 20 with NDD and 20 with NGT were enrolled. Glucose tolerance was studied during OGTT, applying 2006 WHO criteria. Plasma glucose was measured by a dehydrogenase method. Serum MPO was assessed at 0 and 120 min during OGTT by ELISA method.

Results: The NDD group presented with significantly higher fasting MPO level as compared to NGT (120.3±82.3 ng/ml vs 62.3±38.1ng/ml, $p=0.006$) and IFG (120.3±82.3 ng/ml vs 74.8±31.3 ng/ml, $p=0.02$). Similar results were found when analyzing post-challenge MPO levels - the diabetic patients demonstrated significantly elevated MPO when compared to NGT (168.8±130.6 ng/ml vs 102.8±52.4 ng/ml, $p=0.04$) and IFG (168.8±130.6 ng/ml vs 93.6±65.4 ng/ml, $p=0.02$). The difference between NDD and IGT did not reach statistical significance neither at the fasting, nor at the post-challenge state.

Conclusions: Our results demonstrate that diabetes even at the time of diagnosis is associated with increased oxidative stress as assessed by MPO at both fasting and post-challenge state. IGT appears to have similar MPO levels to those of NDD, pointing out the cardiovascular risk associated with this prediabetic state.

RELATION BETWEEN PLASMA ANTIOXIDANTS AND INDICATORS OF OXIDATIVE STRESS IN METABOLIC SYNDROME IN IRANIAN POPULATION

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Aim: The aim of this study was to test the hypothesis that metabolic syndrome (MetS) is associated with increased oxidative stress in adult subjects in Iranian population. MetS was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria.

Methods: The study population consisted of Fifty-nine Metabolic syndrome subjects (mean age 62.5±8.7years) and 42 ages- and sex-matched nonobese normolipidemic controls. Plasma vitamin E and malondialdehyde were determined using high-performance liquid chromatography. Plasma levels of hydroperoxides were measured by the ferrous oxidation in Xylenol Orange, version 2 (FOX2). Glutathione, vitamin C and superoxide dismutase (SOD) were spectrophotometrically measured.

Results: Plasma levels of malondialdehyde and hydroperoxide, as markers of oxidative stress, were increased in the MetS patients as compared to control subjects. Vitamin C and glutathione concentrations and vitamin E-to-lipid ratio were significantly decreased in the MetS patients compared to the controls (all P< 0.05). No significant differences were seen in plasma levels of SOD and absolute vitamin E between the MetS patient and control group.

Compared with the control group, the MetS group had significantly higher levels of total cholesterol and LDL-cholesterol. LDL/HDL and TG/HDL were correlated with the number of components of the MetS (*P*< 0.001). There were significant negative correlations between both markers of oxidative stress and vitamin E-to-lipid ratio or C in MetS patients.

Conclusions: Our results show that MetS patients have a greater oxidative status than healthy persons. Our results support the oxidative stress hypothesis for metabolic syndrome.

IMPAIRED PLASMA LIPID PROFILE AND ANTIOXIDANT STATUS IN PATIENTS WITH METABOLIC SYNDROME

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Patients with metabolic syndrome (MS) are at increased cardiovascular risk.

The aim of this investigation was to evaluate whether plasma lipid profile and antioxidant status were affected by MS. Inclusion criteria of MS were: men and women age > 50 and < 70 as defined by the presence of at least 3 of 4 abnormalities: waist circumference: ³ 95 cm in men and ³ 85 cm in women, fasting glycemia::³1.10 g/L, blood pressure:³140/90 mmHg, TG::³ 1.5 g/L and/or HDL-C < 0.40 g/L in men and < 0.5 g/L in women.

Patients displaying MS (56: M/W 7/49) and healthy subjects (18: M/W 5/13) were recruited. Plasma insulin, fibrinogen, lipid profile and oxidative stress were evaluated.

In MS, a significant increase in body weight, waist circumference, body mass index (BMI), glycemia, systolic and diastolic blood pressure was observed compared to controls. Subjects with MS showed higher levels of plasma insulin (46%), triglyceride (119%) total cholesterol (21%), fibrinogen (29%) and HbA_1C (57%) and lower phospholipid (64%) and albumin (22%) concentrations *vs* controls. Plasma urea and creatinine contents were 1.81-and 2.43-fold higher in MS *vs* controls. In plasma, carbonyls, thiobarbituric acid-reactive substances (TBARS) and hydroperoxide concentrations were respectively, 2.8-, 1.50- and 1.51-fold higher in MS *vs* controls. A positive correlation was obtained between plasma TBARS and HbA_1C ($r = 1$, $P < 0.05$) in MS patients.

This study shows that MS is characterized by impaired plasma lipids and increased oxidative stress compared to healthy subjects. These abnormalities might contribute to increased risk of cardiovascular diseases.

PECULIARITIES OF THE OXIDATIVE STRESS IN MEN WITH THE DEVELOPMENT OF TYPE II DIABETES MELLITUS WITH THE METABOLIC SYNDROME

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We studied 113 men 49,91±0,95 years old with hypertension and dislipoproteinemia, 61 from them were with abdominal obesity. Normoglycemia was registered in 97 men, 16 were with diabetes mellitus; control group include 20 healthy men. In group with manifested carbohydrate metabolism disorder malondialdehyde levels remain 1,9 times higher than control group parameters (4,78±0,67; p< 0,05), however, there is a tendency for decrease of average parameters compared with normoglycemia patient group. Decompensation of antioxidative potential of β-lipoproteins is also observed. Concentration of major antioxidant - vitamin E is slightly higher than control parameters (0,842±0,248 mg/mg protein, and 0,738±0,149 respectively; p>0,05). Insufficiency of vitamin A is forming on early stages. The LDL retinol concentration is maximal in men with abdominal obesity that is significantly higher than control group parameters (0,069±0,015 mg/mgr LDL protein and 0,019±0,002; p< 0,05). Minimal levels of vitamin A are registered in men with diabetes mellitus. Retinol levels in this group is 1,73 times lower than control parameters, (0,011±0,001; p>0,05), that is significantly lower, p< 0,05, than in men with abdominal obesity.

Obtained data show the necessity of complex study of prooxidative and antioxidative LDL potential for estimation of oxidative stress intensity. Decrease of malondialdehyde levels in patients with carbohydrate metabolism disorder shows possibly the depletion of prooxidative LDL potential after its hyperergic functioning. However this phenomena doesn't deny maximal oxidative stress intensity in this group of patients. Evidently, that such peroxidation products concentration is enough for cytotoxic effect realization under the condition of absolute insufficiency of antioxidative potential.

OXIDATIVE STRESS AFTER FAT OVERLOAD IN PERSONS WITH BASELINE HYPERTRIGLYCERIDEMIA WITH OR WITHOUT THE METABOLIC SYNDROME

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Introduction: The metabolic syndrome is a constellation of anthropometric and physiologic abnormalities occurring together more often than expected by chance. Oxidative stress is thought to play an important role in the pathogenesis of cardiovascular disease and diabetes and in the pathogenesis of the metabolic syndrome. Hypertriglyceridemia is a component of the metabolic syndrome that is associated with increased oxidative stress.

Objective: We compared the levels of biomarkers of oxidative stress before and after a fat overload in three groups.

Material and methods: 17 controls and two groups with

hypertriglyceridemia: 43 without the metabolic syndrome (TG-non-MS) and 29 with the metabolic syndrome (TG-MS). All subjects underwent a 60 g fat overload. Baseline measurements included glucose, BMI (body mass index), waist circumference and HOMA IR (homeostasis model assessment insulin resistance). Cholesterol, triglycerides, HDL (high density lipoprotein) cholesterol, TNF-alpha (tumor necrosis factor) and IL-6 (interleukin-6), lipoperoxide (LPO), carbonylated proteins, reduced glutathione (GSH), oxidized glutathione (GSSG), glutathione peroxidase (GSH-PX), glutathione reductase (GSH-Rd), catalase and glutathione transferase (GST) were measured at baseline and 3 h after fat overload.

Results: Compared to the controls, the two patient groups had higher plasma levels at baseline and after overload of cholesterol, triglycerides and apolipoprotein B, LPO, carbonylated proteins and GSSG, and lower levels of antioxidants at baseline and after the fat overload.

Conclusion: The two patients groups had the same degree of oxidative stress.

OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN TYPE 2 DIABETES WITH AND WITHOUT CORONARY ARTERY DISEASE IN IRANIAN ADULT SUBJECTS

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Aims: The aim of this study was to investigate the relationship between antioxidant status and oxidative stress in type 2 diabetics with and without coronary artery disease (CAD).

Methods: We studied 112 non-smoking type 2 diabetic patients 52 with CAD and 60 without CAD. We also studied 51 non-diabetics, 30 with CAD, and 21 without CAD. To evaluate the oxidative status, we measured circulating malondialdehyde (MDA), plasma levels of superoxide dismutase (SOD), glutathione (GSH), as well as vitamin E and C.

Results: Malondialdehyde concentrations were significantly increased in both groups of diabetic patients and also in non-diabetic patients with CHD, compared to those in control subjects. In diabetics, MDA positively correlated with the total cholesterol, LDL-C, total lipid, and the relations between LDL/HDL and TG/HDL ($P< 0.001$). In non-diabetic with CAD group, MDA positively correlated with total cholesterol ($P< 0.05$). There was significant difference in the SOD, glutathione, vitamin E / total lipid and vitamin C between the groups of diabetics and were lower in the diabetes group with CAD. There were significant negative correlations between MDA and vitamin E and C in groups with T2D, but it was statistically significant in the non-diabetic with CAD ($P< 0.05$).

Conclusion: Type 2 diabetes is associated with excess risk of CAD and primary therapy should be directed first at lowering oxidative stress. CAD and T2D alone and combined carry similar atherosclerotic burden concerning lipid profile, enzymatic and nonenzymatic antioxidative status and oxidative stress.

MENAQUINONE-4, A VITAMIN K2 ANALOGUE, SUPPRESSES INFLAMMATION THROUGH THE INHIBITION OF NFKB ACTIVATION

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Introduction: The metabolic syndrome has been associated with chronic inflammation as overnutrition and ageing are shown to induce cytokine hypersecretion and eventual insulin resistance. Recent studies found vitamin K modulates cytokines in bone turnover, and associates low vitamin K status with higher circulating proinflammation cytokine. Here we investigated the effect of menaquinone-4 (MK4), vitamin K2 analogue, on the signaling cascade of LPS stimulated macrophagic THP-1 cells.

Methods: We activated THP-1 cell with 1,3-phorbol-myristate-acetate for 48 hours followed by MK4 incubation, then 3 hours LPS stimulation and assayed for mRNA and protein expressions. *In vivo* investigation used male Wistar rats fed Harlan Teklad TD97053 with or without MK4 supplementation. Each rat was intraperitoneally administered 0.5 mg/kg bw. LPS (*E.coli* O111:B4) and fasted 18 hours before sacrifice. Plasma from abdominal aorta was assayed for inflammatory cytokines and hepatic injury markers. mRNA expressions were assayed from liver samples.

Results: LPS stimulated Macrophagic THP-1 cells preincubated for 24 hours with MK4 showed significant IL-6 mRNA decrease congruent with EIA test results and IL-6 plasma levels of rats fed MK4. Western immunoblotting indicated MK4 inhibits IkBa degradation after LPS stimulation and increased its basal level, thus inhibiting NFkB activation. In its application, supplementation of MK4 was effective in suppressing hepatic injury caused by LPS challenge *in vivo*.

Conclusion: We observed menaquinone-4 as a potent anti-inflammatory compound, both *in vitro* and *in vivo*, suppressing IL-6 expression by repressing NFkB activation. This novel function of MK4 further correlates vitamin K and inflammation associated metabolic syndrome.

ISOMER-SPECIFIC EFFECTS OF CONJUGATED LINOLEIC ACID ON EX VIVO GENE EXPRESSION IN HUMAN MONOCYTES

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Background and aim: Conjugated linoleic acids (CLAs) refer to a group of dienoic derivatives of linoleic acids. Various beneficial effects including decreasing body fat, cancer, atherosclerosis, diabetes and inflammation were described in vivo and in vitro, although findings of different studies have not always been consistent. The aim of our study was to investigate effects of CLA supplementation on gene expression in monocytes and to elucidate the mechanisms involved.

Study design and methods: In a cross-over study, 34 men (45-65y) underwent four intervention periods (4w) receiving either cis-9, trans-11 CLA, trans-10,cis-12 CLA, of 1:1 mix of both isomers or a reference oil equivalent to 3.4g active substance per day. After each intervention monocytes were separated, gene expression microarrays were performed, and several regulated genes of interest were verified by a real-time PCR.

Results: Compared to control the effect of c9t11 CLA intervention was weak. Only IL-1β (fold change (fc) =-1.59, $p=0.046$) and IL-8 (fc=-1.55, $p=0.017$) were less expressed. After 1:1 mix intervention the effect was similar (IL-1β fc=-1.59, p=0,009; IL-8 fc-1.30 $p=0.041$) other genes were regulated, too.

The strongest effect showed t10c12 CLA. Among other genes IL-1β (fc=-2.60,

$p< 0.001$), IL-8 (fc=-3.12, $p< 0.001$) and COX-2 (fc=-1.43, $p=0.01$) were less expressed after intervention compared to control.

Conclusion: To our knowledge this is the first human ex vivo study demonstrating in a comprehensive expression screening anti-inflammatory isomer-specific effects of CLA. Suggesting that t10c12 CLA had the strongest anti-inflammatory effect in monocytes.

RELATIONSHIP BETWEEN VISFATIN, INSULIN RESISTANCE (HOMEOSTASIS MODEL ASSESMENT OF INSULIN RESISTANCE) AND INFLAMMATION (HIGH SENSITIVE C-REACTIVE PROTEIN) IN INDIVIDU WITH VISCERAL OBESITY

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Backgrounds: Visfatin is a novel adipokine secreted from visceral adipose tissue and has insulinomimetic properties. Visceral obesity is risk factor for metabolic syndrome. Insulin resistance and inflammation are linked to visceral obesity and metabolic syndrome. Dysregulation of visfatin as an adipokin plays an important role in metabolic syndrome through insulin resitance and inflammation. However, this need more evidence.

Aims: Analysis the relationship between visfatin, hs CRP (high sensitive C-Reactive Protein) as a marker of inflammation and HOMA-IR (Homesotasis Model Assesment of insulin Resistance) as marker of Insulin resistance in individu with visceral obesity.

Methods: The study was crossectional in 40 Indonesian obese men and 40 Indonesian obese women. Age: 30-60 years in men and 50-60 for women. Sampling in Jakarta City, Indonesia at February - March 2008.

Results: The measurement is conducted on the concentration of visfatin, HOMA-IR and hs-CRP. No correlation between visfatin and hs-CRP (r : 0,190; P >0.001), or HOMA-IR (r:-0,020; P>0.001). Suprisingly visfatin concentration is correlated with HDL Cholesterol (r : 0,416(**); P< 0.001).

Conclusions: Its Expected that visfatin plays important role in metabolic syndrome trough lipid metabolism. Positive correlation between visfatin and HDL cholesterol as a part of beneficial lipid profile, it is assumed that visfatin had the protective effect. Visfatin as a NAMPT (nicotinamide phosphoribosyltransferase) assumed as a link between NAD (Nicotinamide Adenine Dinucleotide) metabolism and raising of HDL Cholesterol. But the role still unclear and still need a lot of study to remain it.

CENTRAL SYMPATHOLYTIC AGENT MOXONIDINE INCREASES INSULIN SENSITIVITY AND DECREASESBINFLAMMATION

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Numerous studies demonstrate the connection between inflammatory mediators and cardiovascular events especially demonstrated in female gender. In this multicenter, multinational (Finland, Sweden, Lithuania), double-blind, prospective study we compared the effect of two sympatholytic antihypertensive drug treatments, the centrally acting imidazoline receptor-1 agonist moxonidine and peripherally acting β-blocking agent atenolol, on sensitive inflammatory markers in 87 hypertensive postmenopausal overweight women who were not taking hormone therapy. After a four-week placebo run-in phase the patients were randomly assigned for eight weeks to moxonidine (0,3mg twice daily) or atenolol (50mg once daily) treatments. Insulin sensitivity was determined by insulin sensitivity index (Matsuda-ISI) assessed using oral glucose tolerance test.

Mean BP decreased significantly in both groups. Insulin sensitivity increased only in moxonidine group (p=0.0262) and reached near significance between the groups (p=0.054). The mean changes in sCRP and IL-6 did not differ between the groups. TNFα increased in atenolol and decreased in moxonidine group (P=0.0004). Adiponectin concentration decreased dramatically in atenonol but did not change in moxonidine group (P< 0.0001).

As a conclusion, in contrast to the effect of peripheral sympatholytic effect of atenolol, central inhibition of sympathetic outflow with moxonidine resulting vasodilatation, could explain the increase in insulin sensitivity in moxonidine group and favorable effect of inflammation. Markedly reduced adiponectin in the atenolol group most probably led to higher TNFα levels. We believe that centrally acting sympatholytic agents are beneficial in the treatment of postmenopausal overweight women with hypertension with favorable effects to insulin sensitivity and inflammation.

INFLAMMATION-SENSITIVE BIOMARKERS TO REVEAL POTENTIAL GENDER DIFFERENCES IN RELATION TO LOW GRADE INFLAMMATION IN INDIVIDUALS WITH THE METABOLIC SYNDROME

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Aim: Gender differences exist in the expression of different inflammation-sensitive biomarkers in relation to the metabolic syndrome (MetS). We have presently explored these differences in relation to commonly used inflammation-sensitive biomarkers including the high sensitivity C-reactive protein (hs-CRP), quantitative fibrinogen, erythrocyte sedimentation rate (ESR), white blood cell count (WBCC) and the absolute number of polymorphonuclear leukocytes (ANPMN).

Methods: A cross sectional analysis of a group of apparently healthy men (n=5,560) and women (n=3,049) in whom the results of the above mentioned inflammation-sensitive biomarkers were analyzed in relation to the different components of MetS.

Results: The concentration of hs-CRP increased pari-pasu with the number of components of the MetS, the differences between the genders being significant regarding any number of components of the MetS. Regarding fibrinogen, te influence of gender turned significant for waist only, similarly to the results of the ESR. None of these interactions was found to be significant for both the WBCC and the ANPMN.

Conclusion: High sensitivity CRP, but not quantitative fibrinogen, ESR, WBCC as well as the ANPMN, is sensitive enough to reveal the potential gender differences in relation to the various components of the MetS and the expression of the low grade inflammation.

DOMINANCE OF WAIST AMONG THE DETERMINANTS OF THE METABOLIC SYNDROME IN RELATION TO THE PRESENCE OF MICROINFLAMMATION: FROM REGRESSION ANALYSIS TO CLINICAL PRACTICE

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Objective: To analyze the inter-relations between each of the components of the metabolic syndrome (MetS) and four inflammatory biomarkers, namely high sensitivity C-reactive protein (hs-CRP), the erythrocyte sedimentation rate, the concentration of fibrinogen as well the white blood cell count.

Design: A cross sectional study in a group of apparently healthy individuals.

Subjects: A cohort of 7269 apparently healthy individuals. There were 4978 men and 2291 women at the respective mean±SD age of 42±11 and 45±9 years.

Results: A significant correlation was noted between most components of MetS and these 4 biomarkers, the best one being with hs-CRP. In a regression analysis, waist was the main determinant of hs-CRP in both women and men and it remained significant for the other biomarkers as well, although not necessarily as the predominant one.

Conclusion: We conclude that it is essential to perform waist circumference measurements in apparently healthy individuals, if an estimation of the intensity of microinflammation is of interest.

HIGH SATURATED FATTY ACIDS MEAL INDUCED AN INCREASE IN INFLAMMATORY RESPONSE COMPARED TO HIGH MONO UNSATURATED FATTY ACIDS MEAL

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The presence of low grade, internal inflammation is one of the main causes for development of insulin resistance, type 2 diabetes mellitus and atherosclerosis. Consumption of long lasting diets with various compositions affects the inflammatory response. However, the effect of a single meal on the immediate inflammatory response was poorly studied.

Aim: To investigate the effect of a single meal, composed of different type of fatty acids (saturated; SFA vs. mono-unsaturated fatty acids; MUFA) on the development of inflammation in healthy subjects.

Methods: 50 subjects, half of them have normal BMI, and the others are overweight were randomly chosen to eat two isocaloric meals with similar amounts of fat, either high in SFA or in MUFA, given as breakfast. Following three weeks each participant was given the alternate meal. Blood samples were taken following an overnight fast, and 2, 4 hours following the meal.

Results: Both meals induced an increase in triglyceride levels after 2 hours. However, triglyceride levels continued to rise 4 hours after high SFA meal, but stayed stable following high MUFA meal. High SFA meal, but not MUFA increases erythrocyte sedimentation rate, fibrinogen, leukocytes and CRP concentration. In addition, the results indicate that high BMI subjects are less sensitive to the effect of SFA meal, and the increase in the inflammatory response is more moderate.

Conclusion: A single high SFA meal induces immediate postprandial inflammatory response. This study emphasizes the importance of consuming diet with anti-inflammatory effects, showing the harm influence of a single unfavorable meal.

EFFECTS OF A LIFESTYLE MODIFICATION PROGRAM ON INFLAMMATORY MARKERS AND ARTERIAL STIFFNESS IN WOMEN WITH METABOLIC SYNDROME

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Purpose: This study was to examine the effects of a six-month therapeutic lifestyle modification (TLM) program on inflammatory markers and arterial stiffness in women with metabolic syndrome (Mets).

Methods: A randomized controlled design was used. 53 women (mean age=62.9) with Mets were recruited from three rural community health centers and randomly assigned to the TLM or control groups. The program was a six-month supervised weekly TLM session consisted of health monitoring, education, aerobic exercise, and a low calorie diet. Inflammatory markers (CRP, MCP1, RBP4) and arterial stiffness (baPWV) were measured at baseline, completion (month 6), and after completion of the TLM program (month 12).

Results: At baseline, means of MetS criteria in both groups were above normal range. Changes of the CRP, MCP1, and PWV in the TLM group were greater than that of the control group, however, no statistically significant group by time interaction was observed (all $P > .05$). In the TLM group, difference of PWV at baseline and at month12 was significantly correlated with difference of MCP1 at baseline and at month 12 ($r = .447$, $P < .05$).

Conclusion: The results indicate that the improvement of arterial stiffness with TLM is correlated with reduced MCP1 level in women with MetS. This result suggests that TLM program may result in blood inflammation and this can play an important role in improving arterial stiffness in women with MetS.

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INFLAMMATORY, OXIDATIVE AND NUTRITIONAL STATUES OF TUNISIAN OLD CORONARY ARTERY DISEASE PATIENTS

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Aging is an important risk factor for the development of cardiovascular disease which due to an increase of pro inflammatory and oxidative statues with advancing age.

Objective: We study the inflammatory, oxidative and nutritional parameters of Tunisian old coronary artery disease patients.

Patients and methods: A total of 93 patients with coronary artery disease were divided into two groups; younger group (36-65 years; n=59) and older group (>65years; n=34). Oxidized LDL was measured in plasma using an enzyme-Linked immunosorbent assay kit. The evaluation of the nutritional habits was assessed by a validated food frequency questionnaire.

Results: The older patients had a decreased BMI (Body mass index) and an increased level of creatinin. In this study we found significant alterations in inflammatory and oxidative system in older group as compared to younger group. In fact, increasing age is associated with increasing of the levels of ox-LDL (170.33 ± 78.67 vs 213.04 ± 130.31 U/ml; p = 0.065). More else, a significant reduction in the amount of haemoglobin (13.88 ± 1.62 vs. 12.08 ± 2.15 ; $p < 0.001$) with an increase in the amount of plates ($2.33.10^5 \pm 0.65.10^5$ vs. $2.90.10^5 \pm 0.11.10^5$) were shown in older patients.

Despite these perturbations, we noted an increase of the micronutrient fed in older patients compared to younger ones, such as vitamin (p = 0.048) and iron (p = 0.018).

Conclusion: Such results showed that aging process is a major factor that contributes to perturbations seen in the cardiovascular disease in older patients.

CORRELATION OF TUMOR NECROSIS FACTOR-ALPHA AND INSULIN RESISTANCE IN TYPE 2 DIABETES PATIENTS (T2DS) WITH ESSENTIAL HYPERTENSION OR ITS ASSOCIATION WITH CARDIOVASCULAR DISEASE

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We evaluated circulating levels of tumor necrosis factor-alpha (TNF-α) and its relationship with insulin resistance (IR) parameters in T2Ds with essential hypertension (EH) alone or combined with cardiovascular disease (CVD). 29 middle-age T2Ds (M/F: 11/18) with dysglycaemia and metabolic syndrome (NCEP ATP III criteria) were observed. Patients with acute cardiovascular events, high-grade inflammation and renal failure, treated with thiazolidinediones or lipid lowering therapy were excluded. Blood samples were collected repeatedly within 6 months: 26 samples belonged to T2Ds with EH, 34 - to T2Ds with EH+CVD. Eight healthy volunteers served as controls. IR-index was calculated by Homeostasis Model Assessment (HOMA). The unpaired Student's t test, Wilcoxon-Mann-Witney U test, χ^2 test and Spearman's rank order were used.TNF-α levels were increased in T2Ds vs controls (ð< 0.001). They were more pronounced in T2Ds with EH compared to EH+CVD group (7.62±1.98 ng/l vs 4.11±0.35 ng/l, ð=0.045). There were many correlations between TNF-α and metabolic (fasting glycaemia, triglycerides, ferritin, HDL-cholesterol (-)) or hormonal (HOMA-IR, HOMA-IR/adiponectin) parameters of IR. But we did not found any link between TNF-α and such acute phase proteins as haptoglobin and C-reactive protein or oxidative stress markers. We suggest possible modulating effect of poor glycaemic control on association of low-grade inflammation evaluated by TNF-α and IR in T2Ds with hypertension and CVD.

OXIDATIVE STRESS AND INFLAMATION IN OBESE SUBJECTS

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Aims: Cardiovascular disease (CVD) and diabetes type 2 are leading causes of death in Mexico. Obesity, the main risk factor is associated with a state of chronic low-grade inflammation and oxidative stress; both processes are involved in the pathophysiology of diabetes and CVD. The aim of the present study was to determine the association of plasma levels of lipid peroxides and immunoglobulines as indicators of oxidative stress and inflammation in obesity.

Methods: A cross sectional comparative study was performed in 100 subjects (30 men and 70 women), mean age of 37.4 years. Subjects were divided in 5 groups according to body mass index (BMI) in: normal weight, overweight, obese I, obese II and obese III. Obesity was diagnosed by BMI and central adiposity was evaluated with waist/hip (W/H) index. A general clinical health examination was performed. Fasting plasma levels of lipid peroxides (LP), and immunoglobulines (IgG, IgM, IgA) were determined. Additionally, plasma levels of triglycerides (TG) and total cholesterol (TC) were determined. ANOVA and linear regression were carried out to analyze our results.

Results: Plasma levels of lipoperoxides increased significantly as BMI rose (p< 0.001). We found a significant positive correlation between LP level and the degree of obesity (r= 0.54). Fasting levels of immunoglobulines were not significantly different among studied groups. Central adiposity as well as plasma TG increased in parallel to BMI.

Conclusions: Our results indicate that obesity is associated with oxidative stress, but we could not observe significantly changes in plasma levels of immunoglobulins related to obesity.

DISCOVERY OF POTENT AND SELECTIVE N-ACETYL-B-HEXOSAMINIDASE INHIBITORS THAT EXHIBIT IN VIVO EFFICACY BY INHIBITING THE LYSOSOMAL TARGET

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Human N-acetyl-**β**-hexosaminidase (Hex) isozymes are important drug targets because they are directly linked to osteoarthritis and lysosomal storage disorders. We report the rapid discovery of potent and selective Hex inhibitors by diversity-oriented synthesis in microplates and subsequent high throughput screening without product purification. The developed inhibitors were found to have K_i values at a range of sub-nano molar against human Hex and were several thousand times more selective for Hex than for a similar enzyme O-GlcNAcase. A number of factors affecting the inhibition potency and selectivity will be discussed.

Furthermore, the inhibitors were shown not only to target lysosomal Hex but also to modulate intracellular ganglioside GM2 levels as demonstrated by immunofluorescence and immunoprecipitation studies.

CONCOMITANT ELISA MEASUREMENTS OF RAT INSULIN, RAT C-PEPTIDE AND RAT PROINSULIN FROM RAT PANCREATIC ISLETS - EFFECTS OF PROLONGED EXPOSURE TO DIFFERENT GLUCOSE CONCENTRATIONS

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Aim: Until now, there have been few assays to measure C-peptide and proinsulin in the rat. We used a well-established rat insulin ELISA, and two novel ELISAs for rat C-peptide and proinsulin, to examine secretion and content from islets exposed to different glucose concentrations.

Methods: Rat islets were precultured in RPMI medium/11.1 mM glucose for 6 days, and thereafter transferred to RPMI with 2.8, 5.6, 11.1 or 28 mM glucose for 72 h. A glucose-stimulated release experiment was then performed in KRBH buffer, 5.6 mM, 1.7 mM and 16 mM glucose, 30 + 60 + 60 min respectively. Rat insulin, proinsulin and C-peptide in RPMI, KRBH, and in islet extracts were analyzed by ELISA.

Results: The higher glucose concentration used during the 72h period, the higher insulin, C-peptide and proinsulin were obtained in the release experiment. The mean ratio of insulin/C-peptide after glucose-stimulation from islets pre-exposed to 11.1 mM glucose was higher after 16.7 mM than 1.7 mM glucose (1.10 ± 0.22 vs. 2.41 ± 0.06 $p < 0.005$, paired t-test). The insulin/C-peptide content was 2.25 ± 0.19. Similar insulin/C-peptide ratios were also found from islets exposed to 5.6 and 28 mM glucose, but not 2.8 mM.

Conclusion: We found the ratio of insulin/C-peptide to be higher than one within islets, and in KRBH after glucose-stimulation. We speculate that this may be due to a more extensive intracellular degradation of C-peptide than insulin within the beta-cells and/or differences in transport/cellular uptake of insulin and C-peptide within the islet.

IMPACT OF POLYMORPHISMS WITHIN THE ANGIOPOIETIN-LIKE 6 (*ANGPTL6*) GENE IN THE FRENCH MONICA STUDY

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Aim: Although it has recently been shown that the *ANGPTL6* gene product (angiopoietin-like 6) is involved in the regulation of fat mass and insulin sensitivity in mice, its physiological functions in humans are yet to be determined.

Methods: The French MONICA population-based Study (n=3402) was genotyped for SNPs (single nucleotide polymorphisms) in *ANGPTL6* and associations with anthropometric or biochemical phenotypes were looked for.

Results: We evaluated the frequency of 17 *ANGPTL6* SNPs in 100 randomly selected subjects and, on the basis of the linkage disequilibrium map, showed that four SNPs (rs6511435, rs8112063, rs11671983 and rs15723) covered more than 95% of *ANGPTL6*'s known genetic variability. These four SNPs were then genotyped in the whole sample. We found that the *G* allele of rs8112063 was associated with lower plasma glucose levels (*P*=0.009). Moreover, obese subjects carrying the *G* allele of rs6511435 had higher plasma insulin levels than AA subjects (*P*=0.0055). No significant association could be detected for rs11671983 and rs15723.

Conclusion: These results suggest that ANGPTL6 genetic variability could modify glucose and insulin homeostasis, an effect that could be emphasized by obesity.

INVOLVEMENT OF CYTOSOLYC PHOSPHOLIPASE 2 IN INSULIN-STIMULATED PROLIFERATION OF VASCULAR SMOOTH MUSCLE CELLS

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Aim: This investigation used primary cultured rat vascular smooth muscle cells (VSMC) to examine the role of the phosphatidil inositol-3 kinase(PI3K) and p42/44 mitogen-activated protein kinase (ERK1/2) in the insulin (INS) -dependent phosphorylation of cytosolic phospholipase 2 ($cPLA_2$) and proliferation induced by INS.

Methods: VSMC were tretaed with INS (100nM, 10min) or pretreated with the inhibitors: $cPLA_2$ M; 15 min) and then treated with INS for an addditional 10 min. Western blot method was used for measuring cPLAinhibitor MAFP (10μM; 15 min), PI3K inhibitor LY294002 (10μM; 15 min) and ERK1/2 inhibitor PD98059 ($20\mu_2$ and ERk1/2 phosphorylation while and BrDu assay was used for measuring VSMC proliferation.

Results: Exposure of VSMC to INS increased the phosporylation of cPLA2 by 1.5-fold ($p< 0.01$), which was blocked by MAFP . Similarly, the LY294002 and PD98059 abolished the INS-mediated increase in cPLA2 phosphorylation by 59% ($p< 0.001$), and by 75% ($p< 0.001$), respectively. Further, inhibition of cPLA2 with MAFP abolished the INS-stimulated ERK1/2 phosphorylation by 65% ($p< 0.01$). Incubation of rat VSMC with INS resulted in an increase of VSMC proliferation by 85% ($p< 0.001$). The effect of INS on VSMC proliferation was significantly ($p< 0.01$) reduced by pretreatment with MAFP.

Conclusions: Results from this investigation suggest that INS stimulates VSMC proliferation *via* a mechanism involving the PI3K-dependent activation of cPLA2 and release of arachidonic acid (AA) which activates ERK1/2 and further amplifies cPLA2 activity.

POSTPRANDIAL POTENTIATION OF INSULIN ACTION IS DEPENDENT ON PARASYMPATHETIC TONUS

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Following a mixed-meal, insulin sensitivity is reported to increase. We tested the hypothesis that meal-induced insulin sensitization (MIS) involves hepatic parasympathetic activation both in an animal model and human subjects, and is triggered at the intestine.

Fasted (24-hr) Sprague-Dawley rats (n=22) were divided into two groups:

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animals received the mixed-meal (10 ml/kg) via an intragastric catheter (IG), either with or without previous hepatic parasympathetic denervation; or

an intestinal band (next to pylorium) was placed and the mixed-meal was administered (10 ml/kg), either IG or intra-enterically (IE).

Healthy human subjects were submitted to a single-blinded study. Insulin sensitivity was assessed in the fasted and after a meal in both humans and rats, and after an intravenous infusion of a low dose of 0.5mg atropine in humans. MIS is expressed in terms of insulin sensitivity potentiation (%) from the fasted to the post-meal state.

In rats, IG mixed-meal administration induced a 60.7±11.0 % increase in insulin sensitivity from the fasted state ($p< 0.001$); this MIS was prevented by previous hepatic parasympathetic denervation. The intestinal band placement also prevented the MIS when the meal was administered via IG (13.7±14.1 % potentiation; ns); but not when the meal was injected IE (105.4±6.8 % potentiation; $p< 0.001$), despite the intestinal band placement. Likewise, in humans, MIS was potentiated by 232.1± 46.3%, and atropine abrogated MIS to fasted values.

These data suggest a prominent role of the hepatic parasympathetic nerves on the insulin sensitization following a mixed-meal.

GSPE MODIFY INSULIN SYNTHESIS AND SECRETION IN B-CELL

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Procyanidins are a class of flavonoids that are common in fruit, chocolate and also found in beverages like red wine. It has been reported that procyanidins have clear and well-defined beneficial effects against several pathologies including cardiovascular heart disease. Previous studies realized by our research group, suggested that the procyanidins could affect insulin secretion of pancreas. The present work was designed to evaluate the effects of grape seed procyanidin extract (GSPE) on the insulin synthesis and secretion. Firstly, *in vitro* study, with a mouse β-cell line (MIN-6), revealed that GSPE at 1mg/l significantly inhibited insulin secretion, in basal conditions. Phenolic acids and monomers were the main responsible of this inhibition. By contrast, under glucose stimulation conditions, 10 mg/l of GSPE produces a slightly activation of the insulin secretion, in the same cellular line. *In vivo* experiments, with cafeteria feed animals we also showed that chronic GSPE treatment reduces insulin gene expression. This effect depends on the concentration and time of treatment of the extract. Preliminary studies to determine the GSPE action mechanism showed that

these molecules modulate Pancreatic duodenal homeobox-1 (Pdx-1) expression, a transcription factor that activates insulin gene expression.

In conclusion, our results suggest that GSPE modify insulin synthesis and secretion in β-cell. Now we are working at describing with more detail the effects and also to describe the molecular mechanism that explain it.

HEPATITIS B VIRUS X PROTEIN IMPAIRS HEPATIC INSULIN SIGNALING THROUGH DEGRADATION OF IRS1 AND INDUCTION OF SOCS3

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Hepatitis B virus (HBV) is a major cause of chronic liver diseases, and frequently results in hepatitis, cirrhosis, and ultimately hepatocellular carcinoma (HCC). The role of HCV in associations between insulin signaling and HCV infection has been previously elucidated. However, the pathogenesis of HBV-associated insulin signaling remains to be clearly characterized. Therefore, we have attempted to determine the mechanisms underlying the HBV-associated impairment of insulin signaling. The expressions of insulin signaling components were assessed in HBx-transgenic mice, constitutively expressing cells, and transiently transfected cells. HBx induced a reduction in the expression of insulin receptor substrate (IRS) 1, and a potent proteasomal inhibitor blocked the downregulation of IRS1 in HBx-transfected cells. Additionally, HBx enhanced the expression of suppressor of cytokine signaling (SOCS) 3 and induced IRS1 ubiquitination. Also, C/EBPalpha was required for the HBx-induced expression of SOCS3. HBx interfered with insulin signaling activation via the inhibition of the insulin-induced phosphorylation of the p85 subunit of PI3K and Akt, as well as the tyrosine-phosphorylation of IRS1. Finally, HBx recovered the insulin-mediated downregulation of gluconeogenic genes. These results provide direct experimental evidence for the contribution of HBx in the impairment of insulin signaling in the context of HBV infection.

IMMUNOREACTIVE INSULIN AS A RISK FACTOR FOR ATHEROSCLEROSIS

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Aims: To find the relationship between abnormal serum levels of immunoreactive insulin (IRI) and C-peptide and different forms of atherosclerosis and to evaluate the incidence rate of these changes in the general population.

Methods: Authors have examined 2 500 individuals with different forms of atherosclerosis and 5 000 individuals from general population group. The following parameters were measured: IRI, C-peptide, oGTT, parameters of glucose metabolism and basic parameters of lipid metabolism. Results of both groups were correlated with survival from 5-year follow-up period. IRI and C-peptide curves were characterized as hypo- and hypersecretory.

Results: Authors have proved that patients with different forms of atherosclerosis represent abnormal serum levels of IRI and C-peptide during oGTT test at 74% in case of ischemic heart disease, at 65% in case of clinical manifestation of brain atherosclerosis and at 47% in case of peripheral artery atherosclerosis. Abnormal serum levels of IRI and C-peptide were accompanied with impaired oral glucose tolerance test. Abnormal serum levels of IRI and C-peptide were found at 25% of general population group. 60% individuals with abnormal serum levels of IRI have developed manifest diabetes mellitus during the follow-up period. 80% individuals from general population group with abnormal serum level of IRI have developed some of the form of atherosclerosis and 40% suffered from clinical manifestation of diabetes mellitus.

Conclusion: Abnormal serum levels of IRI and C-peptide seem to represent an independent risk factor for atherosclerosis and a serious prognostic factor.

TERMINALIA BELLERICA (BELLIRIC MYROBALAN) STIMULATES THE SECRETION AND ACTION OF INSULIN AND INHIBITS STARCH DIGESTION AND PROTEIN GLYCATION

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Traditional plant treatments have been used throughout the world for the therapy of diabetes mellitus. The aim of this study was to investigate the efficacy and mode of action of *Terminalia bellerica* Roxb. (Combretacea) used traditionally for treatment of diabetes in India. *Terminilia bellerica* aqueous extract stimulated basal insulin output and potentiated glucose-stimulated insulin secretion concentration-dependently in the clonal pancreatic beta cell line, BRIN-BD11 ($p< 0.001$). The insulin secretory activity of plant extract was abolished in the absence of extracellular Ca^{2+} and by inhibitors of cellular Ca^{2+} uptake, diazoxide and verapamil, ($P< 0.001$, n=8). Furthermore, the extract did not increase insulin secretion in depolarised cells and did not further augment insulin secretion triggered by tolbutamide or glibenclamide. *Terminilia bellerica* extract also displayed insulin mimetic activity and enhanced insulin-stimulated glucose uptake in 3T3 L1 adipocytes by 300%. The extract doses also produced 10-50 % ($P< 0.001$) decrease in starch digestion *in vitro* and inhibited protein glycation ($p< 0.001$).

In Streptozotocin (125mg/kg body weight) diabetes-mice, long term administration of *T.bellerica* (5mg/ml) reduced ($p< 0.01$) diabetic polydepsia, with no parallel improvements of glucose homeostasis parameters.

This study has revealed that components in *T. bellerica* extract stimulate insulin secretion, enhance insulin action and inhibit both protein glycation and starch digestion. The former actions are dependent on the active principle(s) in the plant being absorbed intact. Future work assessing the use of *Terminalia bellerica* as dietary adjunct or as a source of active antidiabetic agents may provide new opportunities for the treatment of diabetes.

EFFECT OF *CUMINUM CYMINUM* L. ETHANOLIC EXTRACT ON INSULIN RELEASING FROM PANCREATIC BETA CELLS IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Cuminum cyminum (Apiaceae) is an annual herbaceous plant with fruits each one contains a green seeds which has aromatic characteristics. It is applied in Iranian folk medicine since more than 200 years ago. It has been shown that its fruits have medicinal application in treatment of diarrhea, toothache and epilepsy. Major constituents in Cumin are gamma-terpinene, 2-methyl-3-phenyl-propanal, myrtenal and glucopyranosides. In the present study, the ethanolic extract was investigated for insulin releasing from pancreatic beta cells in streptozotocin-induced diabetic rats. Male adult Wistar rats were injected (i.p.) with streptozotocin. Before administration and 1.5, 3 and 5 h after administrations of ethanolic extract of cumin seeds, the blood samples were drawn from retro-orbital sinus. Serum glucose

levels were determined by glucose oxidase method. To determine the insulin releasing activity of extract, after extract treatment, animals were anesthetized by high dose of ether, the pancreas were excised, fixed in 10% formaldehyde and embedded in paraffin for sectioning. Sections of 5- mm of pancreases were processed for insulin-releasing activity by using immunocytochemistry kit. The results showed that administration of the ethanolic extract exhibited a significant reduction in serum glucose. The results showed that administration of streptozotocin decreased number of beta cells with insulin secretory activity in comparison by intact rats. Treatment of the alcoholic cumin extract increased significantly active beta cells in comparison by diabetic control rats. It is concluded that the extract decreased serum glucose in streptozotocin- induced diabetic rats. Also, the extract can increase insulin releasing from beta cell of pancreas.

INSULIN RESISTANCE AND SECRETION DURING ORAL GLUCOSE TOLERANCE TEST AND MIXED MEAL CHALLENGES IN INDIVIDUALS WITHOUT DIABETES

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Objective: To evaluate the capacity of meal test in predict insulin resistance and insulin secretion and to classifify the individuals.

Methods: 116 healthy subjects, aged 33,3 years, 51% male with body mass index (BMI)of 24,8 Kg/m^2 were submitted to a 75g glucose load (OGTT) and a mixed meal challenge (317Kcal; 55.7% carbohydrates, 14.8% proteins and 29.5% fat) with a maximum interval of ten days apart. According to OGTT the subjects were stratified as normal tolerant (NGT) or intolerant groups [IG: (IFG/IGT)]. Area under curve for glucose (AUCg), insulin(AUCi)and C-pepetide (AUCp) and indexes: insulin, (AUCi/AUCg) and C-peptide, AUCp/AUCg were analysed. To evaluate insulin secretion we used insulin and C-peptide indexes and to evaluate insulin resistance HOMA-R was used.

Results: In our sample,97(83.6%) NGT and 19(16.4%) IG were identified by OGTT. The kappa coefficient agreement between both tests to diagnose IG was 0.49 ,p=0.000. We observed a difference between NGT and IG group respectively in C-peptide index in OGTT (p=0.001) and meal test (p=0.02); insulin index in OGTT (p=0.006) ; AUCg in OGTT (p< 0.001) and meal test (p< 0.001) and HOMA-R in OGTT (p=0.03). No difference between groups was found in AUCi and AUCp.

Conclusions: Mixed meal test was not able to classify IG properly. To evaluate integrated insulin secretion C-peptide index seems to be more faithful to discriminare NGT and IG groups than insulin index during either OGTT or mixed meal.

PREVALENCE OF METABOLIC SYNDROME AND INSULINE RESISTANCE IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Polycystic Ovarian Syndrome (PCOS) is the most common cause of anovulation and hyperandrogenism. Obesity, gloucose intolerance, dyslipidemia and hypertension that are characteristic features of the metabolic syndrome (MS) are frequently observed in these patients. Peripheral insuline resistance (IR) has a crucial role in the pathogenesis of this disorder. The aim of this study was evaluation of the incidance of Metabolic Syndrome and IR in females with PCOS.

Patients and methods: 50 premenopausal adult PCOS women (mean age=27±5.7) presenting to Endocrine clinic of Ghaem university hospital in Mashhad were selected due to Rotterdam workshop criteria. They underwent assessments clinically and by laboratory exams for the evidence of MS (due to criteria laid down by International Diabetes Federation) and IR (fasting G/I ratio of< 4.5 (mg/10(-4)U).

Results: MS was found in 56% of PCOS women. 44% of women with PCOS were insulin resistant. There was statistical correlation between body mass index,Ir and Metabolic Syndrome occurrence.

Conclusion: There is high prevalence of MS and IR in women with PCOS. It seems mandatory that females with PCOS should undergo periodic screening for MS and diabetes.

ADIPONECTIN CONCENTRATIONS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND ITS RELATIONSHIP WITH BODY MASS INDEX AND INSULIN RESISTANCE

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Objective: Insulin resistance has been demonstrated to be implicated in the development of polycystic ovary syndrome (PCOS). To explore the potential contribution of adiponectin , which associates with Insulin resistance, in the etiology of PCOS, and its relationship with obesity this study was designed.

Subjects and methods: In this cross-sectional study serum adiponectin, Insulin and Plasma fasting glucose levels were compared between 103 newly-diagnosed PCOS cases and 73 female controls that were matched for their age and Body Mass Index (BMI). Women were classified as: Group I (n = 69) with PCOS + body mass index (BMI) ≥25 kg/m^2; group II (n = 34) with PCOS + BMI < 25 kg/m^2; group III (n = 34) normal women and BMI ≥25 kg/m^2; and group IV normal women and BMI < 25 kg/m^2 (n= 39).

Results: Adiponectin levels were significantly decreased in women with PCOS (8.4± 2.7 Vs 13.6± 5 in control group, p: 0.00). There was no significant difference between Adiponectin concentrations of women in group I compared with group II (8.1 ± 2.8 Vs 9.2± 2.6 respectively, p: 0.1).Adiponectin levels were significantly decreased in group III compared with group IV.A significant negative correlation was found between Adiponectin and Insulin in all the subjects. Multiple regression analysis showed that existence of PCOS was the only significant determinant of serum adiponectin levels.

Conclusion: Serum adiponectin levels are reduced in all the women with PCOS. There seems to be an interaction between adiponectin and PCOS pathogenesis without considering the effect of BMI.

METABOLIC AND ENDOCRINE ASPECTS IN POLYCYSTIC OVARY SYNDROME

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Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting about 6-10% of women during their reproductive age. This disorder is characterized by hyperandrogenism, oligo- or anovulation, and polycystic ovaries. PCOS is frequently associated with insulin resistance, creating an increased risk for the development of metabolic and cardiovascular abnormalities.

Patients and methods: We evaluated 70 women for PCOS phenotype and performed endocrine functional and metabolic tests (oral glucose tolerance

test, dynamic insulin determination), hirsutism scores, and questionnaires. Insulin resistance was estimated using the HOMA-index (homeostatic model assessment).

Results: 59 women, aged 18 to 41 years, were affected by PCOS. Nineteen percent of women with PCOS were overweight. Obesity was present in 30%. We observed increased waist circumference (92.1±19.0cm) and waist : hip-ratio (0.88±0.1) in PCOS patients. Overt pathological glucose tolerance tests were found in 14% of PCOS patients, but only 50% of these women were obese. A total of 88% of PCOS women with pathological glucose tolerance test showed normal fasting glucose levels. 37% of all PCOS patients demonstrated insulin resistance (HOMA-Index >2). 54% of PCOS women were hirsute. Hirsutism-score correlated significantly with testosterone and C-peptide.

Conclusion: Insulin resistance and impaired glucose tolerance are common findings in PCOS patients despite normal body weight. Screening for glucose intolerance should be performed in all patients by an oral glucose tolerance test. Increased waist circumference and waist : hip-ratio emphasize the increased risk for the development of metabolic disorders in PCOS women.

PREVALENCE OF METABOLIC VARIABLES AND PREDICTORS OF INSULIN RESISTANCE IN POLYCYSTIC OVARY SYNDROME PATIENTS IN SOUTHERN BRAZIL

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Aims: Insulin resistance (IR) is a common feature in Polycystic Ovary Syndrome (PCOS). However, recognizing IR is difficult: the euglycemic hyperinsulinemic clamp isn't suitable for clinical practice and the diagnosis of Metabolic Syndrome (MBS) is too specific to identify all patients in future risk for CV diseases. The lipid accumulation product (LAP) index [waist (cm) - 58] x triglyceride concentration (mmol/l)] is a new marker for estimating CV risk.

Methods: 56 PCOS patients and 44 control women were analyzed to determine the prevalence of MBS and its individual components (NCEP/ATP III), and to verify the association of LAP index with IR in PCOS patients. We performed a ROC curve for LAP index using a HOMA index ≥ 3.8 as the reference value to define IR.

Results: PCOS women were younger than controls and instead having the same BMI (PCOS: 31 ± 8.8 x C: 29.5 ± 5.4) they showed higher total cholesterol, LDL-c and triglyceride levels. MBS was about 5 times more frequent in PCOS. The more prevalent individual risk factors in PCOS group were waist circumference (60%) and low HDL-c (47,3%). Only HAS was more prevalent in PCOS (26.8% vs. 9.8%, p=0.042). Considering LAP index ≥ 34.4 (sensitivity: 84%; specificity: 79%) as a cut off point for IR, we could identify 61.2% PCOS patients in risk for CVD.

Conclusion: these data confirm that PCOS women have a worst metabolic profile in younger ages and LAP index could be useful to discriminate patients in higher risk for metabolic disorders.

ADDITION OF MILK PRODUCTS IN THE DIET OF OVERWEIGHT SUBJECTS HAS SMALL EFFECTS ON METABOLIC VARIABLES

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Aims: Epidemiological studies have suggested an inverse relation between intake of dairy products and components of the metabolic syndrome. The aim of the present study was to investigate the effects of introducing dairy products into the diet of subjects who habitually consume a low amount of dairy products on body composition and disorders related to the metabolic syndrome.

Methods: Middle-aged subjects (n=120) with risk factors of the metabolic syndrome were recruited in Finland, Norway and Sweden. The subjects were randomised into Milk and Control groups for the 6-month study. The Milk group was instructed to include 3-5 portions of dairy products daily in their diet. The Control group continued their ordinary diet with a low intake of dairy products. Anthropometric, clinical and laboratory analyses were conducted in the beginning and end of the study.

Results: There was a modest increase in serum cholesterol levels during the Milk period (p=0.042), associated with increased intake of milk fat. The HOMA index, a marker of insulin resistance, was decreased in the Milk group (p=0.037). Leptin increased only in women during the Milk period (p=0.045) and a significant decrease in VCAM (p=0.001) was also seen only among women during the same period. No significant differences between groups were seen in body composition, blood pressure, markers of inflammation (IL-6, CRP, TNFα, complement C3 and C4), endothelial function (vWF, E-selectin) or adiponectin.

Conclusions: This study gives no clear support to the hypothesis that increasing dairy products in the diet beneficially affects aspects of the metabolic syndrome.

TYPE OF DIETARY FAT INFLUENCES DEVELOPMENT OF METABOLIC SYNDROME AND THE INTESTINAL EXPRESSION OF RELATED POTENTIAL BIOMARKERS

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Aims: Excessive intake of dietary fat is known to contribute to the metabolic syndrome, but the influence of fat-type is still unclear. In this study, we determined the effect of different types of dietary fat, varying in unsaturated/saturated fatty acid (P/S) ratio's, on the development of metabolic syndrome. Additionally, we analyzed gene expression changes in the small intestine, as there is growing evidence that this endocrine organ contributes to the etiology of metabolic syndrome.

Methods: Male C57Bl/6J mice were fed purified high fat diets containing palm oil (HF-PO; P/S1.0), olive oil (HF-OO; P/S4.6) or safflower oil (HF-SO; P/S10.1) for 2 weeks. Microarray analysis was performed on mucosal scrapings of proximal, middle and distal parts of small intestine.

Results: Mice fed the HF-OO and HF-SO diet showed significant lower body weight gain, liver triglyceride content and HOMA-IR index compared to mice on the HF-PO diet. The most pronounced effect of fat-type on gene expression was found in the distal small intestine. Especially lipid metabolism-related genes were elevated on a HF-PO diet, indicating an enhanced fat absorption. Furthermore, fat-type induced changes in intestinal gene expression of potential biomarkers of metabolic syndrome corroborated the differential effects of the high fat diets on development of metabolic syndrome.

Conclusions: Taken together, our data indicate that dietary fat with a low P/S ratio has a more stimulatory effect on development of metabolic syndrome than fat with a high P/S ratio. Differential fat absorption and secretion of signaling molecules related to metabolic syndrome are potential intestinal contributors.

A SATURATED FATTY ACID RICH DIET CAN INDUCE AN 'OBESE GENE EXPRESSION PROFILE' IN ADIPOSE TISSUE OF SUBJECTS AT RISK FOR METABOLIC SYNDROME

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Aims: To investigate the effect of a saturated (SFA) and monounsaturated fatty acid (MUFA) rich diet on insulin sensitivity, serum lipids and gene expression profiles of adipose tissue of subjects at risk for metabolic syndrome.

Methods: A controlled feeding trial of 8 weeks was performed with 20 abdominally overweight subjects. Subjects received a SFA-rich diet or a MUFA-rich diet. Blood and subcutaneous adipose tissue samples were obtained, insulin sensitivity was measured by hyperinsulinemic-euglycemic clamp and serum lipid levels were determined. Microarray analysis was performed on the adipose tissue samples.

Results: Consumption of a SFA-rich diet resulted in increased expression of genes involved in inflammation processes in adipose tissue, without a change in insulin sensitivity or serum lipid levels. Consumption of the MUFA-rich diet led to a more anti-inflammatory gene expression profile, accompanied by a decrease in cholesterol levels.

Conclusions: Consumption of a SFA-rich diet resulted in a pro-inflammatory 'obese like' gene expression profile while consumption of a MUFA-rich diet seems to result in a more anti-inflammatory expression profile. This suggests that the type of fat may be important in the etiology of adipose tissue inflammation. Gene expression is affected without changes in insulin sensitivity. Adipose tissue expression changes of inflammation-related genes might be one of the first hallmarks in development of metabolic syndrome.

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GENE EXPRESSION PROFILING OF 3T3-L1 ADIPOCYTES EXPOSED TO PHLORETIN, A DIETARY FLAVONOID DISPLAYING THIAZOLIDINEDIONE-LIKE EFFECTS

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Adipocyte dysfunction plays a major role in the outcome of obesity, insulin resistance and related cardiovascular complications. Thus, considerable efforts are underway in the pharmaceutical industry to find molecules that target the now well documented pleiotropic functions of adipocyte. We previously reported that the dietary flavonoid phloretin enhances 3T3-L1 adipocyte differentiation and adiponectin expression at least in part through PPARγ activation *(Hassan et al, BBRC 2007)*. A further study was designed to characterize the molecular mechanisms underlying the phloretin-mediated effects on 3T3-L1 adipocytes using microarray technology.

We show that phloretin positively regulates the expression of numerous genes involved in lipogenesis and triglyceride storage, including GLUT4, ACSL1, PEPCK1, lipin-1 and perilipin (more than 2-fold). The expression of several genes encoding adipokines, in addition to adiponectin and its receptor, is positively or negatively regulated in a way that suggests a possible reduction in systemic insulin resistance and obesity- associated inflammation. Improvement of insulin sensitivity is also suggested by the over- expression of genes associated with insulin signal transduction, such as CAP, PDK1 and Akt2. Many of these genes are PPARγ targets, confirming the involvement of PPARγ pathway in the phloretin effects on adipocytes.

In light of these microarray data, it is reasonable to assume that phloretin may be beneficial for reducing insulin resistance, in a similar way to the thiazolidinedione class of anti-diabetic drugs.

HESPERETIN STIMULATES GLUCOSE UPTAKE THROUGH PI 3-KINASE/AKT AND P38 MAPK PATHWAYS IN C2C12 SKELETAL MUSCLE CELLS

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Aims: Hesperetin, a major flavonoid present in citrus fruits is reported to exhibit various biological functions including anti-inflammatory and anti-oxidant effects. In this study, we investigated effects of hesperetin on glucose uptake and signaling mechanism involved in C2C12 skeletal muscle cells.

Methods: Glucose uptake of C2C12 myotubes was analysed by the [3H]deoxyglucose uptake assay. Phosphorylations of Akt and P38 were analysed by Western blotting. IRS-1 tyrosine phosphorylation was measured by immunoprecipitation and western blotting.Glut1 expression was assayed by RT-PCR.

Results: Hesperetin increased 2-deoxyglucose uptake and this increase was inhibited by LY294002 (an inhibitor of PI 3-kinase) and SB203580 (an inhibitor of p38 MAPK) but not by compound C (an inhibitor of AMPK). We found that hesperetin increased phosphorylation of Akt and p38 MAPK. Moreover, hesperetin appears to increase IRS-1 tyrosine phosphorylation and expression of GLUT1 in C2C12 muscle cells.

Conclusions: These results show that hesperetin stimulates glucose transport via PI 3-kinase/Akt and p38 MAPK signaling pathways in C2C12 myotubes and suggest that hesperetin can be developed as a potential drug for the anti-diabetic therapy.

EFFECTS OF A LOW-FAT, HIGH-FIBER DIET COMPARED WITH A LOW-CARBOHYDRATE DIET ON INSULIN SENSITIVITY AND ENDOTHELIAL FUNCTION IN ADULTS WITH METABOLIC SYNDROME

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Aims: We compared the effects of a low-fat, high-fiber (LoFat-HiFiber) diet compared to a low-carbohydrate (LoCarb) diet on insulin sensitivity and endothelial function in adults with the metabolic syndrome.

Methods: Twenty-three women and men (32-62yrs) with the metabolic syndrome completed a randomized crossover comparison of two, non-calorically restricted, 4-week diets. All meals [LoFat-HiFiber: 55-60% carbohydrate, 20-25% fat, 15-20% protein, 38-48g fiber/day; LoCarb: 15-20% carbohydrate, 55-60% fat, 25-30% protein, 9-11g fiber/day] were prepared by a research dietician at the General Clinical Research Center (GCRC), and consumed *ad libitum*. Before and after each diet, fasting blood

was drawn and endothelial function was assessed via brachial artery flow-mediated dilation (FMD).

Results: Insulin [mean (SEM), uU/ml] was reduced (P< 0.05) similarly after LoFat-HiFiber [12.6 (1.6) vs. 9.9 (1.2)] and LoCarb [11.8 (1.2) vs. 9.8 (1.0)]. A trend for reduced glucose (mg/dl) was observed after LoFat-HiFiber [100.1 (2.4) vs. 96.9 (2.2); P=0.07]. Insulin sensitivity (QUICKI) was improved (P< 0.05) after LoFat-HiFiber [0.315 (0.006) vs. 0.326 (0.006)] and LoCarb [0.315 (0.006) vs. 0.326 (0.007)]. Although FMD was unchanged after LoFat-HiFiber [9.5 (1.3)% vs. 10.4 (1.5)%; P=0.61)], a strong trend (P=0.06) for reduced FMD was observed after LoCarb [10.1 (1.4)% vs. 7.2 (1.1)%], thus producing a significant diet interaction (P=0.01).

Conclusions: Because LoCarb appears to impair endothelial function, we conclude that a low-fat, high-fiber diet is preferred to a low-carbohydrate diet as an intervention strategy in adults with the metabolic syndrome.

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PROLONGED LEUCINE SUPPLEMENTATION IN OLD RATS DOES NOT IMPAIR GLUCOSE TOLERANCE, BUT INCREASES WHITE ADIPOSE TISSUE MASS

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Leucine is a potent activator of protein synthesis notably by activating mTOR signaling, in synergy with insulin. However, the mTOR pathway is also a negative regulator of insulin action by inducing a negative feedback loop at the level of IRS-1. This process could play a role in the development of insulin resistance and lead to perturbations of glucose homeostasis. The aim of this study was to determine in old rats the effects of a prolonged leucine supplementation on whole body insulin sensitivity. Two groups of 18 month-old male Wistar rats were fed *ad libitum* with a diet enriched either with leucine (Leu group, 36 rats) or with glycine (Control group, 35 rats) during 22 weeks. OGTTs, performed before and after the supplementation period, were similar between the Leu group and the Control group. Insulinemia measured during OGTTs were not different in both groups. Total body weight of rats from the Leu group was significantly higher than that of control rats (719 ± 17g *vs* 678 ± 14g, p< 0.05). The leucine-rich diet did not change the weight of muscles and liver. Importantly, perirenal adipose tissue mass was 40% higher (p< 0.001) in the Leu group compared to the control group. In conclusion, prolonged leucine supplementation in old rats did not affect whole body insulin sensitivity, but induced a marked increase in white adipose tissue mass, probably due to hyperplasia. Our data support the concept that increased body weight due to hyperplastic adipose tissue is compatible with unchanged insulin sensitivity.

EXPLOITING NEW FOOD CONCEPTS IN THE COMBAT OF OBESITY AND INSULIN RESISTANCE

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Our hypothesis is that administration of plant-associated polyphenols (antioxidants and prebiotics), alone or in combination with dietary bacteria (probiotics), can prevent or alleviate the low-grade systemic inflammation considered to be one of the underlying causes to insulin resistance and type 2 diabetes.

In this study, C57BL/6J mice were used as a model for early human type 2 diabetes. Different combinations of polyphenols and probiotics were administered together with a high-fat diet for 22 weeks. Body weight, food intake, body fat and metabolic blood parameters were registered throughout the study. At the time of sacrifice, plasma and tissues were collected.

Supplementation of a plant polyphenol to a high-fat diet, inhibited the body weight gain significantly already after two weeks, primarily as a result of reduced adiposity. In addition, liver weight and liver fat content were significantly reduced in mice offered the polyphenol-enriched diet, and in this case, a synergistic beneficial effect was observed after addition of probiotics. In plasma, we observed decreased fasting insulin and fasting glucose compared to control mice, indicating a beneficial glucose control, as a result of polyphenol supplement and with a synergistic effect of probiotics. The reduced weight of the spleen together with decreased plasma IL-6 and PAI-1 indicate an inhibited inflammatory activity in mice getting either the polyphenol or the probiotics, although no synergistic effect was observed.

In conclusion, supplementation with this specific polyphenol and/or probiotics give beneficial effects on body weight, adiposity, inflammatory activity and glucose control in mice provoked with a high-fat diet.

HIGH FAT DIET INDUCED CHANGES IN THE EXPRESSION LEVELS OF GENES INVOLVED IN ENERGY METABOLISM

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The key regulator of cellular energy metabolism is the peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α). The muscle-enriched orphan nuclear receptor ERRα has been identified to be required for PGC-1α - mediated activation of the PDK4, which is a negative regulator of glucose oxidation. Our aim was to investigate the effect of high fat (HF) feeding and physical activity in the gene expression level.

The mRNA expression levels of the genes PGC-1α, ERRα and PDK4 were measured with quantitative RT-PCR. In this experiment we used C57BL/6J mice as a model for high fat diet induced type 2 diabetes.

In addition being more insulin resistant, the HF animals had altered blood lipid profile, indicating some changes in the overall lipid metabolism. The expression level of PGC-1α was slightly down-regulated after HF feeding, although running restored the levels. However, the HF feeding had up-regulating effect on the expression levels of ERRα. Furthermore, clear up-regulating effects of HF feeding could be seen in the expression level of PDK4 and combined running had even more profound effects on the expression levels.

Although HF diet in general did not have up-regulating effects on PGC-1α mRNA levels, the results indicate that the regulation of energy metabolism after HF feeding leads to a situation where PDK4 inhibits the glucose oxidation coincident with the increased mitochondrial fatty acid oxidation. Whether the fatty acid oxidation is reduced *de facto* after HF feeding, as the hypothesis on accumulation of ectopic lipids might suggest, remains to be further clarified.

EFFECTS OF OMEGA 3 FATTY ACIDS ON GENE EXPRESSION IN THE FRUCTOSE FED RAT, A MODEL OF METABOLIC SYNDROME

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Aim: To study the effect of a diet enriched in omega-3 polyunsaturated fatty acids on the expression of genes involved in lipid metabolism and inflammation processes in the fructose-fed rat model.

Method: 42 male "Wistar Han" rats received for 8 weeks, either a standard chow food or an isocaloric 67% fructose diet. In each group animals were given either a normal lipid intake, or enriched in alpha-linolenic acid (ALA), or DHA and EPA (LC3). After sacrifice, heart (apex), periepididymal adipose tissue and liver were analyzed for the expression of 22 genes involved in metabolic and inflammatory processes by "on demand" TaqMan® low density arrays method.

Results: No difference in body weight was observed but fructose-fed rats exhibited an increase in liver weight, plasma triglyceride and cholesterol levels that were prevented by LC3 supply. In liver, the fructose diet increased the stearoyl-CoA desaturase and fatty acid synthase (FAS) and decreased PPAR gamma and delta expressions. In heart, FAS and PPAR delta expressions were increased. The addition of ALA and LC3 resulted in a protection against fructose diet effects on plasma (triglycerides and cholesterol), and expression of lipogenic genes. However, the omega 3 supply did not counterbalance the alterations in PPAR delta expression in liver and heart, but decreased this expression in liver of control rats.

Conclusion: Our results cast a new light on the role played by LC3 fatty acids on PPAR delta expression at the onset of the metabolic syndrome in the fructose-fed rat.

EFFECTS OF FISH OIL (FO) ON METABOLIC ALTERATIONS INDUCED BY CARBOHYDRATE (CHO) OVERFEEDING (O) IN HEALTHY VOLUNTEERS

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Aim: Does FO prevent metabolic alterations induced by CHO overfeeding?

Methods: 32 subjects randomized into 2 groups: one without O (C) (44.1±1.5y, BMI: 22.30±0.42 kg/m²) and one with O (44.1±1.6y, BMI: 22.95±0.31 kg/m²). Group C was studied once while absorbing usual diet; group O was studied 6-w apart while absorbing over 4-d prior to each experiment 75% energy from CHO/d in addition of their daily energy expenditure. Over these 6 w, 8/16 subjects absorbed 3g/d FO (Epax 6000 QualitySilver®); 8/16 received 3g/d paraffin oil (P). Parameters studied: Glucose Infusion Rate (GIR) (euglycaemic hyperinsulinaemic clamp: insulin infusion rate = 1 mU/kg/min), mean arterial blood pressure (MBP), plasma FFA, HDL, triglycerides (TG) and insulin concentrations.

Results: mean±SEM (ANOVA and Student´s t-test). O *vs.* C (n=16): O increased basal insulinemia (5.5±0.6 vs. 4.7±0.3 mU/L; p< 0.05) and TG (2.11±0.29 vs. 0.72±0.07 mmol/L; p< 0.0001), decreased HDL (1.02±0.08 vs. 1.46±0.09 mmol/L; p< 0.001) and FFA (176±35 vs. 446±44 µmol/L; p< 0.0001). Clamp: O decreased GIR (9.71±0.47 vs. 11.45±0.60 mg/kg/min; p< 0.05). FFA were less inhibited (48±6 vs. 17±4 µmol/L; p< 0.0001). MBP increased (90.4±1.4 vs. 87.0±1.4 mmHg; p< 0.05). O+FO vs. O+P (n=8): P had no effect. FO decreased basal TG (1.58±0.41 *vs.* 2.12±0.58 mM; p< 0.05) and MBP (84.0±6.8 *vs.* 86.4±2.0 mmHg; p< 0.0001). Clamp: FO increased GIR (10.1±0.7 *vs.* 8.8±0.7 mg/kg/min; p< 0.01) and decreased MBP (85.3±2.9 *vs.* 89.4±1.7 mmHg; p< 0.0001).

Conclusions: 6-w FO supplementation (1.7 g/d EPA+DHA) prevents most of metabolic alterations induced by a 4-d CHO overfeeding.

DOES LEGUMES CONSUMPTION IN A REAL LIFE CONTEXT CAN IMPROVE COMPONENTS OF METABOLIC SYNDROME? A RANDOMIZED CONTROLLED TRIAL

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Context: People with metabolic syndrome are at increased risk of cardiovascular disease, the leading cause of mortality and morbidity in women in Canada. Emerging evidence suggests that legumes may have protective effects on components of metabolic syndrome by improving lipid profile and glycemia.

Objective: To investigate the effect of consumption of legumes on the components of metabolic syndrome and fat mass on women with abnormal metabolic profile, through a "real life" randomized controlled trial.

Method: Between February and September 2007, 134 participants were randomized to consume during 16 weeks:

1) 750 ml of legumes per week or

2) control meals without legumes.

Primary components of the metabolic syndrome (HDL-C, TG, blood pressure, glycemia, waist circumference) and fat mass were measured at the weeks 0, 8, 16 and 24.

Secondary components of the metabolic syndrome (insulin, apo A1, apo B, Lp (a), fibrinogen, CRP, IL-6, TNF-α) were measured at weeks 0 and 16.

Results: A total of 132 participants were included in the analysis. At week 16, both legumes and control diet reduced significantly waist circumference (p< 0.05), apo B and fibrinogen. Fat mass was significantly reduced only in the legumes diet group. However, there was no significant difference in primary and secondary components of metabolic syndrome and fat mass between the two groups.

Conclusion: In a "real life" context, legumes consumption produced a favourable effect on dietary intakes and on anthropometric variables but the magnitude of the change achieved during 16 weeks is too modest to modify metabolic risk factors.

DIETARY PATTERNS AND MORTALITY IN ELDERLY SWEDISH MEN

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The health impact from long-term adherence to the officially recommended diet, advocated in most western countries, has been questioned and alternative dietary patterns have been suggested as more advantageous. Therefore, we investigated the relation between 12-year mortality and the adherence to

1) the officially recommended diet,

2) a Mediterranean-like diet and

3) a low-carbohydrate diet in 70-year-old Swedish men.

In this study, composite scores previously used in the literature to discriminate degree of adherence to above dietary patterns were applied in 1138 men (all 70-years) included in a longitudinal study. All participants underwent a detailed physical and biochemical examination and dietary habits were determined by 7-day records. Dietary mis-reporters were identified with the Goldberg cut-off.

High adherence to the officially recommended diet was associated with lower waist circumference and higher inflammatory biomarkers (CRP and IL-6), but no association to total mortality was found. In turn, high adherence to Mediterranean-like diet was associated with lower CRP and cystatin C and a lower estimated risk of total mortality compared with low-adherent individuals (HR 0.60; 95% CI 0.42-0.85). Finally, high adherence to a low-carbohydrate diet was associated with elevated BMI, waist circumference, PAI-1 and CRP and lower insulin sensitivity compared with low-adherent individuals. In addition, the estimated risk for total mortality was higher in individuals consuming a low-carbohydrate diet (HR, 1.54 95% CI 1.02-2.30) compared with high-carbohydrate consumers.

The results from this study indicate that total mortality is decreased in individuals with a Mediterranean-like diet, but increased in individuals with a low-carbohydrate diet.

HIGH FAT DIET INFLUENCES *N*-ACYLETHANOLAMIDE FORMATION IN THE INTESTINE

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Oleoylethanolamide (OEA) and palmitoylethanolamide (PEA), both members of the *N*-acylethanolamides (NAEs) family, have shown to be implicated in peripheral appetite regulation. Administration of OEA and PEA decreases food intake and body weight gain, and endogenous OEA and PEA produced in the intestine seems to be a physiological regulator of food intake through PPARα.

Rats consuming a high fat diet (37energy% from fat) for 7 days had significantly lower levels of OEA and PEA in the intestine compared to regular chow fed animals. Currently, we are conducting a time-course study on the effect of high fat diet (chow supplemented with olive oil to give 37 energi% from fat) on intestinal levels of OEA, PEA and total NAE.

Using LC-MS techniques we have found that intestinal levels of PEA and total NAEs is significantly reduced (30% and 25%, respectively) after only one day of high fat diet. This reduction was evident throughout the entire experimental period of 7 days. Activity measurements of fatty acid amide hydrolase (FAAH), the primary enzyme responsible for NAE degradation was significantly decreased on day 1 and 7. Thus changes in FAAH levels may not be responsible for the lower levels of NAE. Currently, we are investigating whether NAPE-PLD, a NAE-synthesizing enzyme, is down regulated during the high fat diet regime, and whether the expression of genes (qPCR) related to the function of OEA (e.g. PPARα, GPR119 and FAT/CD36) are changed.

DIETARY GLYCEMIC LOAD IS ASSOCIATED WITH THE METABOLIC SYNDROME IN AUSTRALIAN ADOLESCENTS

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Aims: Diets with a high postprandial glycemic response, as measured by the daily glycemic index (GI) and glycemic load (GL), have been associated with the metabolic syndrome (MetS) and development of diabetes in adults. However, there is limited research in younger populations to determine if a similar relationship exists. Our aim was to evaluate cross-sectional associations between GI, GL, and the prevalence of the MetS in a population based cohort of adolescents.

Methods: Participants were 697 males and females aged 13-15 years, free of diabetes, participating in The Western Australian Pregnancy Cohort (Raine) Study. Three day diet records were analysed using a customised GI database to determine energy adjusted daily GI and GL. MetS was defined using the International Diabetes Federation Age-Specific Adolescent Criteria and included waist circumference, blood pressure, HDL-cholesterol, triglycerides, and glucose.

Results: A total of 3.6% of adolescents met the criteria for the MetS. Mean±SD daily GI and GL were significantly higher in adolescents with the MetS compared to those without (GI 60.2±3.9 vs 58.1±3.8, P=0.005; GL 165.3±24.2 vs 150.8±23.5, P=0.002). In a logistic regression model, an increase in daily GL of 10 units was associated with increased odds of the MetS (OR=1.55, 95%CI 1.23-1.96, P< 0.001) and elevated triglycerides (OR=1.22, 95%CI 1.06-1.40, P=0.002) after adjustment for potential confounding variables including body mass index, lifestyle and dietary factors.

Conclusion: Results of this study support the concept that diets with a high postprandial response are associated with a higher prevalence of the MetS in adolescents.

EFFECT OF A HIGH MUFA-DIET AND A MEDITERRANEAN TYPE OF DIET ON SERUM LIPIDS AND INSULIN SENSITIVITY IN ADULTS WITH MILD ABDOMINAL OBESITY

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Background: Diets high in monounsaturated fatty acids (MUFA) such as the Mediterranean diet may reduce the risk of cardiovascular diseases by improving insulin sensitivity and serum lipids. Besides high in MUFA, the Mediterranean diet also contains abundant plant foods, moderate wine and low amounts of meat and dairy products, which may also play a role.

Objective: To compare the effects of a MUFA-rich diet with a diet high in saturated fatty acids (SFA) and the additional effect of a Mediterranean diet on insulin sensitivity and serum lipids.

Design: Randomized parallel controlled feeding trial, in 60 non-diabetics (40-65y) with mild abdominal obesity. After a two week run-in diet high in SFA (19 energy-%), participants were allocated to a high MUFA-diet (20 energy-%), a Mediterranean diet (MUFA 21 energy-%), or the high SFA-diet, for eight weeks.

Results: The MUFA-rich diet and the Mediterranean diet did not affect fasting insulin concentrations. The high MUFA-diet reduced total and LDL-cholesterol compared with the high SFA-diet, but not triglyceride concentrations. The Mediterranean diet increased HDL-cholesterol concentrations (+0.09 mmol/L, 95%CI 0.0, 0.18) and reduced the ratio of total cholesterol/HDL-cholesterol (-0.39, 95%CI -0.62, -0.16) compared with the high MUFA-diet.

Conclusions: Replacing a high SFA-diet with a high MUFA or a Mediterranean diet did not affect insulin sensitivity, but improved serum lipids. The Mediterranean diet was most effective, because it reduced total and LDL-cholesterol, and also increased HDL-cholesterol and reduced the total cholesterol/HDL-cholesterol ratio.

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HETEROGENEITY OF DIETARY PROFILES IN HIGHLY SEDENTARY YOUNG GUADELOUPEAN WOMEN

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Aims: Our aim was to examine the relationship between the physical activity pattern and the dietary profile. Although some clustering of the variables related to these major determinants of cardiovascular risk has been demonstrated, they have not been extensively studied together.

Methods: Two hundred and two female university students from the main Guadeloupe (French West Indies) campus participated. They self-administered a validated food frequency questionnaire and the 1-year recall Modifiable Activity Questionnaire. Principal component factor analysis was performed with scores and variables related to the dietary pattern and variables related to the physical activity pattern.

Results: A model including ten variables explained 84.9% of the total variance. The physical activity pattern was not associated with the dietary pattern, apart from the fruit intake. The physical activity level was homogenously low (median 1.58, first and last cutoff 1.54 and 1.66, respectively). There was no correlation between the physical activity level and the food frequency questionnaire score (r=-0.005).

Conclusions: The absence of strong relationship between the food and physical activity profiles in this study is consistent with the view that no regulation of the quality of the food intake is possible below a certain threshold of physical activity.

DIFFERENCES IN OMEGA-3 AND OMEGA-6 FATTY ACID INTAKES IN ADOLESCENTS WITH AND WITHOUT THE METABOLIC SYNDROME

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Background: Dietary intake of anti-inflammatory omega-3 fatty acids may help prevent low-grade inflammation associated with development of the metabolic syndrome (MetS). It has been proposed that a high intake of omega-6 fatty acids may reduce the beneficial effects of omega-3 fatty acids, however some studies suggest a combination of both types is associated with the lowest level of inflammation.
Aim: Examine associations between the MetS and omega-3 and omega-6 fatty acid intakes in non-diabetic Australian adolescents.

Subjects and methods: Fatty acid intakes in 766 males and females aged 13-15yrs were evaluated using 3-day diet records and an updated Fatty Acid Compositional Database. MetS was defined using International Diabetes Federation Age-Specific Adolescent Criteria and included waist circumference, blood pressure, HDL-cholesterol, triglycerides, and glucose.

Results: Energy adjusted daily intakes of omega-3 and omega-6 fatty acids were lower in adolescents who met the criteria for the MetS (n=27) compared with those who did not (n=739), with medians and interquartile ranges (IQR) of 0.97 (0.79-1.25) vs 1.12 (0.91-1.4) g, P=0.14; and 6.54 (4.68-8.21) vs 7.54 (6.14-9.60) g, P=0.01, respectively. After adjustment for potential confounding factors, adolescents in the lowest quartile of omega-3 fatty acid intake had higher odds of MetS compared with adolescents in the highest quartile (OR=5.5, 95%CI 1.43-20.8, P=0.013). A similar pattern was observed for the lowest compared to highest quartile of omega-6 fatty acid intake (OR=17.6, 95%CI 1.9-160.9, P=0.011).

Conclusion: Higher intakes of both omega-3 and omega-6 fatty acids may be associated with a decreased risk of the MetS in adolescence.

MAJOR DIETARY PATTERNS AND THEIR RELATIONSHIP WITH GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS IN TEHRAN, IRAN

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Objective: To detect major dietary patterns and their association characterized by factor analysis with glycemic control in type 2 diabetic patients in Tehran.

Subjects: In a cross-sectional study, 301 men and women aged 30-65 years were selected by simple sampling method. Factor analysis was conducted to ascertain the major dietary, and multiple regression models were fitted to assess the relationship between glycemic control and the adherence to major dietary patterns.

Results: 2 major dietary patterns were extracted: Healthy (all kinds of vegetable, fruits, olive, fish, low fat diary products and nuts) and unhealthy (mayonnaise, processed meats, hydrogenated fats, snacks, pizza, refined grains, red meat, fried potato, soft drink, egg, butter and whole fat dairy products). After control for potential confounders, subjects in the highest tertial of unhealthy dietary pattern scores had a higher odds ratio for the fasting serum glucose (odds ratio: 3.11; 95% CI: 1.57, 6.16; P for trend < 0.01) than did those in the lowest tertial. Compared with those in the lowest tertial, diabetic patients in the highest tertial of unhealthy dietary pattern scores did not have greater odds for HbA1c.

Conclusion: Significant associations exist between dietary patterns identified by factor analysis, and fasting blood glucose.

EFFECT OF DIETARY CHOLESTEROL ON GALLBLADDER BILE LITHOGENICITY AND GENE EXPRESSION PROFILE IN THE ENTEROHEPATIC AXIS OF NON-OBESE GALLSTONE AND CONTROL WOMEN

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Cholesterol (Ch) absorption and insulin resistance may play a pivotal role in gallstone development.

Aim: To investigate the role of dietary *Ch* and insulin resistance on lithogenic state and gene expression profile in the gut-liver axis.

Methods: 7 *Ch*GD and 9 healthy women received a high and low *Ch* diet for 14 days. Blood samples, duodenal biopsy and bile were obtained after each diet. Gallbladder epithelial cells (GBEC) were harvested from patients who underwent cholecystectomy. Liver biopsies were obtained in *Ch*GD patients. cDNAs were used for qRT-PCR.

Results: *Ch*GD and control patients were non-obese and normoglycemic. $HOMA_{IR}$ index, insulin and triglycerides were higher in *Ch*GD ($p \leq 0.05$). Campesterol to lathosterol ratio was 30% lower in *Ch*GD ($p < 0.05$). Bile from *Ch*GD showed higher cholesterol saturation (CSI >100%) under both diets. In the gut, transcripts for LXRα, β and SREBP2 were 3 to 4-fold higher in *Ch*GD. Genes controlling *Ch* synthesis (HMGCoA-r/-s) and lipid traffic (ABCG5, ABCG8, NPC1L1, ABCA1, SR-BI, ACAT, FAT/CD36) were 1.5- to 4-fold higher in *Ch*GD ($p \leq 0.01$), and were down-regulated by *Ch* feeding. Genes regulated by insulin (Foxo1, PEPCK, IRS-1) were down regulated in the gut of *Ch*GD under high Ch diet. Similar differential expression profile of genes was observed in GBEC. A positive correlation of transcripts was observed between gut and liver ($r=0.5$, $p < 0.005$).

Conclusions: Dietary *Ch* did not influence lithogenicity indexes. Gene expression of NR and genes controlling lipid metabolism and insulin signaling varied widely in *Ch*GD and controls. (Supported by grant FONDECYT 1080325).

DIFFERENT CAPACITY OF CARDIOVASCULAR RISK SCORES, FRAMINGHAM, SCORE AND PROCAM, TO REVEAL EARLY ATHEROSCLEROSIS, IN PATIENTS WITH METABOLIC SYNDROME FROM TRANSYLVANIA

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The carotid intima-media thickness(IMT) is an accepted parameter for the assessment of early systemic atherosclerosis. The presence of metabolic syndrome(MetS) represent a risk for the development of both type 2 diabetes and cardiovascular diseases. The purpose of study was to determine how cardiovascular risk, assessed by FRAMINGHAM, SCORE and PROCAM scores, reflects carotid atherosclerosis in a specific group: patients with MetS from Transylvania.

We included 152 patients who fulfill the IDF 2005 criteria for the diagnosis of MetS, men and postmenopausal women. Cardiovascular risk was calculated using specific diagrams(SCORE,FRAMINGHAM,PROCAM). IMT was determined by high resolution ultrasonography, at the level of common carotid arteries (including bifurcation), bilaterally. We used overall single maximum IMT. For each risk scores we split patients in groups using the median value.

Increased FRAMINGHAM score is associated with significant increase in carotid IMT (1.12±0.24mm vs.0.98±0.18mm,p=0.005, for men with scores≥20% vs.< 20%; 1.02±0.13mm vs.0.9±0.12mm,p< 0.001, for women with scores≥6% vs.< 6%). In men, IMT was significant higher at PROCAM score≥8% comparing with score< 8%(1.13±0.17mm vs.0.88±0.19mm,p< 0.001). Same results were obtained for women with PROCAM score≥2%vs.< 2%(0.98±0.15mm vs.0.88±0.14mm,p=0.003). There isn't signifficant variability of IMT with SCORE system.

At these patients with MetS, high cardiovascular risk assessed by FRAMINGHAM and PROCAM scores is associated with significant increase in carotid IMT. Increase of IMT with rise of cardiovascular risk assessed by SCORE system was not significant. These results could be explained by different number of common cardiovascular risk factors found both in cardiovascular risk scores and IDF 2005 definition of MetS.

EFFECTS OF ´ORUJO´ OLIVE OIL ON HYPERLIPIDEMIA

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Hyperlipidemia is the presence of raised or abnormal levels of lipid in the blood. Lipid abnormalities are regarded as an important risk factor for cardiovascular disease due to the influence of cholesterol, one of the most clinically relevant lipid substances, on atherosclerosis. The clinical complications of atherosclerosis could be improved when plasma lipid level was lowered by hypocholesterolemic agents, but many of promising agents have serious side effects. In the present study, we have examined the hypocholesterolemic effect of ´orujo´ olive oil, which is an olive sub-product and possesses potential beneficial components (e.g. pentacyclic triterpenes: oleanolic and maslinic acids). Identification and quantitation of pentacyclic triterpenes in ´orujo´ olive oil were carried out by applying HPLC methods. The content of maslinic acid and oleanolic acid in pomace oil was 81.23mg·g^{-1} and 30.31 mg·g^{-1}, respectively. Hyperlipidemia was induced in male Sprague-Dawley rats by feeding them with a high cholesterol diet (HCD) for 30 days. ´Orujo´ olive oil was supplemented (200 mg / kg body wt / day) during the last 15 days. The levels of serum total cholesterol (TC), triglyceride (TG), high density lipoprotein - cholesterol (HDL - C), low density lipoprotein-cholesterol (LDL - C) increased in hyperlipidimia rats. Treatment with ´orujo´ olive oil significantly modulated the abnormalities induced by hyperlipidimia. Lipid accumulation was decreased in histological findings. The pentacyclic triterpenes in 'orujo´ olive oil may hold great promise as a natural and almost non-toxic therapeutic agent for treatment hyperlipidemia.

DIAMEL INTERVENTION TRIAL ON METABOLIC SYNDROME: BASELINE DATA

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Aim: To set up a clinical trial to assess whether Diamel (Food supplement made of lettuce and oligoelements) could diminish any of the clinical and metabolic parameters of metabolic syndrome according to the definition given by the Word Health Organization (WHO).

Subjects and methods: The Diamel intervention trial is a randomized, doubled-blind, placebo-controlled intervention trial undertaken in Cuba. Entry criteria were the clinical definition of the Metabolic Syndrome (MS) according to WHO. Subjects the study group was further studied for the presence of acanthosis nigricans, as well as for free cholesterol, creatinine and uric acid concentrations.

Results: SM screening was carried out in 179 overweight or obese subjects. A total of 78 individuals fulfilled MS criteria for eligibility and all of them were randomized to treatment. Of these, 41 were aged less than 45 years (75,6% female) and 37 were 45 years of age or more (70,3% female). Free cholesterol (p=0,036) and Uric acid concentrations (p=0,043), were higher in subjects with MS and ages over 45 years.

Conclusions: Diamel intervention trial has shown that the use of natural products together with indications for lifestyle improvement aiming at

diminishing risk factors for future development of type 2 diabetes or cardiovascular disease is feasible and has high acceptance levels on obese or overweight subjects informed to be "labeled" as persons with MS. Uric acid but not cholesterol appears to be associated with age only on MS individuals indicating that this marker could be useful for the screening of MS.

HIGH PROCESSED MEAT CONSUMPTION IS A RISK FACTOR OF TYPE 2 DIABETES IN THE ATBC COHORT

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Relatively small lifestyle modifications related to weight reduction, physical activity and healthier diet has been shown to decrease the risk of type 2 diabetes. Connected with diet, low consumption of meat has been suggested as a protective factor of type 2 diabetes.

The aim was to examine the association between the consumption of total meat or the types of meat and the risk of type 2 diabetes.

This cohort study included middle aged male smokers from the ATBC Study, a joint project between US and Finland. During up to 12 years of follow-up (1985-1997), 660 incident cases of diabetes were diagnosed from 25,505 participants through the nationwide register. Food consumption was assessed by a validated food frequency questionnaire.

In the age-adjusted model, high total meat consumption was a risk factor of type 2 diabetes (relative risk (RR) 1.59, 95% confidence interval (CI): 1.20, 2.13, highest vs. lowest quintile), but the risk attenuated slightly and was no longer statistically significant in the multivariate model adjusted for environmental and dietary factors. The RR of type 2 diabetes was 1.57 for processed meat (95% CI: 1.19,2.07) in the multivariate model. No association was found between red meat (beef and pork), poultry and the risk of type 2 diabetes. In general, the results were not explained individually by intakes of fat, protein, heme iron, nitrates or nitrites, and were not modified by obesity.

In summary, it may help to prevent the global epidemic of type 2 diabetes by reducing the consumption of processed meat.

SWITCHING HIGH-FAT DIET TO HIGH-CARBOHYDRATE DIET SIGNIFICANTLY DECREASED BODY FATS AS WELL AS SERUM ADIPOKINE LEVELS IN MICE

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Aims: The purpose of this study was to investigate the effects of dietary changes from high-fat diet (45% of total calories from fat) to high carbohydrate diet (70% of total calories from carbohydrate) on the body weight, and serum levels of lipids and adipokines.

Methods: Five weeks-old male C57BL/6 mice were fed high-fat diet for 9 weeks (baseline) then switched to a high-carbohydrate diet or continued the high-fat diet for 3 weeks. Body weight, adipose tissue, serum and hepatic lipid levels were measured. Levels of adipokines (leptin, adiponectin and resistin) were also analyzed.

Results: The results showed that after the high-fat diets were switched to high-carbohydrate diets, body weight, epididymal and retroperitoneal fats were significantly reduced compared with those of high-fat diet group($p< 0.05$). The levels of serum total cholesterol and HDL-cholesterol were not different between the two groups however, TG concentration of high-carbohydrate group was significantly lower than that of high-fat diet group. The levels of adiponectin were not different between the two groups however, leptin and resistin levels of high-carbohydrate group were significantly lower ($p< 0.05$). The levels of resistin were negatively correlated to body weight ($p< 0.05$).

Conclusions: High-carbohydrate diet after switched from high-fat diet significantly decreased body weight, epididymal and retroperitoneal fat and the serum levels of TG as well as leptin and resistin.

DOES COFFEE MODIFY POSTPRANDIAL GLYCEMIC AND INSULINEMIC RESPONSES?

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Background: Epidemiological studies have shown inverse association between coffee consumption and risk of type 2 diabetes. On the other hand, in postprandial studies caffeine has impaired glucose tolerance.

Objective: To study the effect of coffee on glycemic and insulinemic responses.

Methods: Twelve healthy volunteers (age 34.8±10.4 yrs, BMI 21.9±2.5 kg/m^2) were served each test food once (small coffee containing 150 mg caffeine with glucose solution; large coffee containing 300 mg caffeine with glucose solution; large coffee with sucrose and milk; and large coffee with bun) and the reference food (glucose solution) twice, each containing 50 g available carbohydrate, after an overnight fast at one-week intervals in random order. Capillary blood samples were drawn at intervals for 2 h after each food for analysis of blood glucose and insulin. The incremental area under the curve (IAUC) and glycemic index (GI) were calculated to estimate glycemic and insulinemic responses.

Results: Coffee portion produced slightly smaller average IAUC than the reference glucose solution. The caffeine content of the coffee portions had no effect on the GI value, 92 for both portions. Both portions yielded a similar insulin IAUC that was about 89% of that of glucose solution. When sucrose and milk or bun were used together with the large coffee portion, lower GI values and insulin responses were found reflecting the carbohydrate quality and protein content of the accompaniments.

Conclusions: Coffee has only modest effect on glycemic and insulinemic responses.

CHANGES IN CARDIOVASCULAR DISEASE RISK FACTORS FOLLOWING A 3 MONTH DIETARY INTERVENTION PROGRAMME COMBINED WITH A PHYTOSTEROL ENRICHED MILK

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Aim: Many studies have shown that adherence to the dietary guidelines or the use of plant-sterol enriched products can induce favorable changes on the lipid profile. Still whether the use of phytosterol-enriched products provide additional benefits to subjects complying to the dietary guidelines has not been thoroughly examined.

Methods: A sample of 108 modestly hypercholesterolemic subjects (40-60 years old) were randomized to a phytosterol enriched milk intervention group (IG :n=40),a placebo milk group (PG: n=37) and a control group (CG: n=31). Subjects consumed 450ml/d of placebo or plant sterol milk (2.25gr plant sterols/d) for 3 months. IG and PG subjects attended 7 nutritional sessions during the interventional period.

Results: IG had significantly more favorable changes compared to CG regarding serum total cholesterol (−25.4±4.1 vs -9.6±4.7 mg/dl, P< 0.023), LDL-cholesterol levels (−21.8±3.5 vs -7.9±4.1 mg/dl, P< 0.014) and apo-lipoprotein B (-13.2±2.4 vs -3.3±2.8 mg/dl, P< 0.020). There were no differences among groups regarding HDL-cholesterol, triglycerides, glucose and apo-lipoprotein A concentrations.

Conclusion: Although both IG and PG attended nutritional sessions only the IG had significantly favorable changes in serum total, LDL cholesterol, and apo-lipoprotein B levels compared to the control subjects.

ENERGY INTAKE OF BEVERAGES

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Object: Intake of energy in beverages is usually underestimated. The results of our study show different situation.

Method and group: One day diet recalls of 1240 volunteers were analysed (671 males, 569 females, 18-55 years, permanent address in Central or South Bohemia).

We ascertained: total energy intake, intake of beverages, energy of beverages, energy intake of saccharides markers of metabolic syndrome.

Statistical methods: χ^2, Mann-Whitney analyse were used.

Results:

Average daily intake of beverages is very variable 651 - 5320 ml

Daily intake of : sweet waters (lemonades) - cca 692 ml , 615 kJ

beer is cca 755 ml (males more than females p p< 0,01) ,979 kJ

milk beverages (milk, cacao, chololate) - cca 256 ml, 569,3 kJ

coffee - cca 282 ml

tea cca 697 ml (energy depends on quantity of sugar, 75% of our volunteers drink coffee and tea without sugar)

Drinks - wine cca 292 ml , brandy 53 ml daily, (females without MS drink more wine p< 0,001 and brandy p< 0,05 than MS +)

Daily intake of energy of beverages is cca 599 kJ, of drinks (wine, beer, brandy) is cca 510 kJ.

Conclusion: Energy intake of drinks is about 20-35% total daily energy , fast glucose was higher in volunteers with daily energy intake of beverages more than 30% of total energy.

Energy intake of beverages affects prevalence of metabolic syndrome, overweight and obesity.

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USE OF MATHEMATICAL MODELS TO ASSESS INSULIN SENSITIVITY AFTER HYPOCALORIC HIGH/LOW GLYCEMIC INDEX DIET INTERVENTION

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Existting methods for laboratory assessment of insulin sensitivity (InsSens), such as glucose clamp, are neither practical nor cost-effective for clinical practice. Mathematical models based on single blood sample (HOMA S, QUICKI), or OGTT curve-points (Cederholm Index-CI) can be useful.

Aim: Identify if these models can reliably detect InsSens induced by weight loss. We treated 41 overweight subjects (19 men;age 34,1±7y ;BMI 30,8±2,8kg/m2) who followed a 4mo hypocaloric diets with high glycemic index (HGI;n=12), low glycemic index (LGI;n=14) and LGI plus metformin (LGI+MET;n=14). We studied InsSens by calculating HOMA S, QUICKI and CI using glucose and insulin values from the OGTT at baseline and after treatment. Metabolic parameters (weight, BMI, waist circumference, %fat mass (%FM), NEFA plasma levels) were measured at basal conditions and after weight loss. Data are presented as mean±SD difference after-before intervention. Wilcoxon test was used (p< 0.05). Subjects obtained significant weight loss (HGI:-3,85±6Kg,p=0,016; LGI:-6,32±5,2Kg,p< 0,0001; LGI+MET:-4,55±2,7Kg,p< 0,0001) accompanied by significant reduction in BMI, waist circumference and %FM in all groups after treatment. NEFA plasma levels remained unaltered. LGI group exhibited significant decrease at the area under glucose (p=0,02) and insulin (p=0,01) curves after treatment and higher CI (p=0,03). Fasting and 120min insulin points decreased significantly (p=0,02;p=0,017,respectively) for LGI+MET group accompanied by significant increase in HOMA S (p=0,03) and CI (p=0,005), suggesting an enhancement of InsSens, although a non-expected significant decrease in QUICKI (p=0,03) was observed. No significant alterations were observed in HGI group. Homa S and CI were capable to detect enhancement in InsSens in subjects treated with LGI diets.

ENERGY RESTRICTION WITH HIGH-PROTEIN DIETS DECREASES VISCERAL FAT MASS BUT NOT FASTING AND POSTPRANDIAL INFLAMMATION IN OVERWEIGHT INSULIN-RESISTANT RATS

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Visceral obesity may worsen the low-grade postprandial inflammatory response to a high-fat meal. To test this hypothesis, we studied the effects of energy restriction in rats with diet-induced overweight. Overweight rats were given free-access to a high-fat diet (HF), or restricted to 60% of the spontaneous intake of HF rats, with either the same diet (HFR) or protein-rich diets (HPR) for 5 weeks. Before and at the end of this period, rats were administered a high-fat meal and plasma insulin, triglycerides and cytokines were monitored after meal. Rats were killed at the end of the experiment and the epididymal fat pads were weighed.

At the end of the experiment, the weight of the restricted rat were similar between HFR and HPR rats and 19%-lower than in HF rats. However, the epididymal fat mass were slightly but significantly lower in HPR rats than in HFR and HF rats (14.5±0.6, 17.4±1.2 and 24.0±2.3 g, respectively). During the 5 weeks, fasting insulin did not change in restricted rats, while almost doubling in HF rats. At the end of the experiment, fasting and postprandial increases in IL-1β, IL-6, MCP-1 and PAI-1 did not differ between groups. Altogether, these results suggest that decreasing visceral adiposity in insulin-resistant overweight rats does not impact fasting and postprandial low-grade inflammation.

EFFECTS OF INCREASED FRUIT AND VEGETABLE CONSUMPTION ON BLOOD MARKERS OF OXIDATIVE STRESS AND INFLAMMATION IN OVERWEIGHT WOMEN

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The endocrine function of adipose tissue plays a central role in the pathogenesis of chronic diseases by regulating cellular redox status and inflammatory responses. This study was performed to examine whether vegetable and fruit consumption is related to biomarkers of oxidative stress and inflammation in overweight women. Subjects (n=22, 19-29 yrs) participated in two-phase intervention composed of low vegetable-fruit diet(LVF) and high vegetable-fruit diet(HVF). Each phase was 2 wks long and apart by 2 wks. The average calorie supply was maintained similar (~2000kcal/d). Blood samples were collected at the beginning and the end of each intervention. Statistical significance was determined for differences within as well as between interventions. Results indicated average anthropometric measurements were not changed by dietary intervention. Between intervention analyses showed HVF diet significantly decreased level of C-reactive protein (p=0.021) and increased total antioxidant status (TAs) (p=0.054). Plasma TAs at the end of HVF intervention was increased compared to the level at beginning. Adiponectin level was significantly lower after LVF intervention compared to the level at beginning. The level of CRP was significantly higher at the end of LVF diet. PGE_2, leptin, IL-1β, IL-6 and IL-8 level, however did not show differences in both within and between intervention analyses. Our results suggest that diet high in fruit and vegetable regardless of total energy intake suppressed selected blood markers of oxidative stress and inflammation therefore, possibly reduce the risk of obesity related metabolic disturbances.

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BLOOD PRESSURE-LOWERING EFFECTS OF MICRONUTRIENTS SUPPLEMENTATION IN TYPE 2 DIABETIC PATIENTS

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Objective: The present study designed to assess the effect of Mg+Zn+ vitamin C+E, and combination of these micronutrients with B vitamins on blood pressure in type 2 diabetic patients.

Materials and methods: In a randomized, double-blind, placebo controlled clinical trial, 76 type 2 diabetic patients were randomly divided into three groups, each group receiving one of the following daily supplement for 4 months; group MV: 250 mg Mg and 20 mg Zn, 200 mg vitamin C and 100 mg vitamin E (n=28), group MVB250 mg Mg and 20 mg Zn, 200 mg vitamin C and 100 mg vitamin E, 10 mg vitamin B1, 10 mg vitamin B2, 10 mg vitamin B6, 10 µg vitamin B12 and 1 mg folic acid (n=23), group P: placebo (n=23). Blood pressure was measured at the beginning and after 2 and 4 months supplementation.

Results: Results indicate that after 4 months of supplementation levels of systolic, diastolic and mean blood pressure decreased significantly in the MV group by 8 mmHg (126±12 vs. 134±16 mmHg), 7 mmHg (77±6 vs. 84±8 mmHg), and 7 mmHg (93±7 vs. 100±9 mmHg), respectively ($p< 0.05$). There was no significant change in the levels of these parameters in the other 2 groups.

Conclusion: In conclusion, the results of the present study indicated that in type 2 diabetic patients, combination of vitamins C and E and magnesium and zinc might decrease blood pressure.

DIET COMPOSITION AND INSULIN RESISTANCE IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Aim: The aim of this study was to estimate the intakes of energy and macronutrients by patients with essential hypertension and to correlate amount of selected nutrients with insulin resistance.

Methods: The examined population consisted of 119 patients with well controlled essential hypertension from Outpatient Clinic of Hypertension at the National Institute of Cardiology in Warsaw. There were 60men/59women, aged 42-75y. All patients were receiving antihypertensive treatment (diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors) and lipid-lowering medicines. Over 70% of hypertensive patients were obese. Abdominal obesity, confirmed by waist circumferences, was found among 79.8% of patients.

Results: The fasting serum insulin ranged from 4.0 to 36.3 mU/ml. The 25th percentile was 9.3 mU/ml, median was 12.8 mU/ml and the 75th percentile was 17.6 mU/ml. The HOMA-IR ranged from 0.89 to 10.1, with the 25th percentile = 2.16, median =3.09, and the 75th percentile =4.35. The average HOMA values were 3.6 ±1.9 and 3.34 ±1.8 in men and women, respectively. HOMA-IR showed a significant positive correlation with BMI ($r =0.47$, $p< 0.000$), energy (($r =0.21$, $p< 0.000$), and fat intake ($r =0.27$, $p< 0.000$), as well as negative correlation with potassium intake ($r = -0.22$, $p< 0.02$).

Conclusion: The nutritional advice should emphasize reducing total and saturated fat and increasing consumption of whole grain products, fruits and vegetables.

ANTIDIABETIC PROPERTIES OF THE FOOD CONSTITUENTS UA AND L7G

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Epidemiological studies have shown that interventions based on diet changes reduce the incidence of diabetes and associated cardiovascular complications in high-risk groups. After a meal, insulin stimulates glucose uptake, blocks glycogenolysis and gluconeogenesis, and stimulates glycogen synthesis in the liver. Rising insulin levels stimulates liver glycogen synthesis by the signaling cascade IR/IRS/PI3K/Akt activation, which promotes the phosphorilation/inactivation of glycogen synthase kinase-3 (GSK3) dephosphorylation/activation of glycogen synthase (GS) and thus increasing glycogen synthesis. There is a growing interest in traditional plant treatments for diabetes and several species of the genus *Salvia* (family Lamiaceae), including *Salvia fruticosa*, are empirically used for this purpose. Luteolin-7-glucoside (flavonoid) and ursolic acid (triterpene) are constituents of *Salvia* genus. With the aim to evaluate the involvement of sage constituents on plasma glucose regulation, ursolic acid (UA) and luteolin-7-glucoside (L7G) were assessed in rats. A significantly decrease on plasma glucose concentration, total cholesterol and LDL was observed after both UA and L7G treatment. UA also significantly increased liver glycogen synthesis (by a mechanism mediated by GSK3) and plasma HLD levels. This study revealed that both UA and L7G, major constituents of this plant genus, may be useful in ameliorating the diabetic condition, especially UA which may contribute to reduce the risk of cardiovascular complications.

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EFFECT OF BRAZIL NUT CONSUMPTION AND HYPOCALORIC DIET ON THE METABOLIC PROFILE AND SKIN NUTRITIVE MICROCIRCULATORY PATTERNS IN OBESE FEMALE ADOLESCENTS

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Excessive body fat is associated with an increase of inflammatory cytokines that compromise blood vessel function. This study aimed to evaluate the effect of Brazil Nut consumption combined with a hypocaloric diet on the metabolic profile and microcirculatory function of obese female adolescents. Twelve obese girls were randomly divided in two groups:

(1) hypocaloric diet and Brazil Nut (n=5) and

(2) hypocaloric diet and placebo (n=7).

Data on body mass, height, waist and hip circumference, insulin, glucose, HOMA, C-reactive Protein (CRP), triglycerides, HDL-C, total cholesterol (TC), and LDL-C were collected on the first visit and after 8 and 16 weeks. The microcirculation was examined by dynamic videocapillaroscopy at the nailfold of the fourth finger. Functional capillary density (FCD), capillary diameters (afferent, apical and efferent), red blood cell velocity at rest (RBCV) and after 1 min of total ischemia, maximum red blood cell velocity ($RBCV_{max}$) and the time taken to reach it ($TRBCV_{max}$) during the reactive hyperemia response were determined. The initial metabolic profile showed insulin resistance (HOMA= 3.2 ± 0.8 and 3.6 ± 0.9, for group 1 and 2, respectively), whereas inflammatory profile was normal in both groups. Group 1 had a significant decrease in TC (152.4 ± 28 vs.140.2 ± 6.5 mg/dl), an increase in RCBV (1.4 ± 0.06 vs. 1.6 ± 0.05 mm/s, $p < 0.05$) and in $RBCV_{max}$ (1.6 ± 0.04 vs. 1.8 ± 0.04 mm/s, $p < 0.05$). This study showed that Brazil Nut consumption can positively influence microcirculatory parameters, possibly due its antioxidant effect.

CHANGES OF NUTRITIONAL STATUS IN PATIENTS WITH TYPE 2 DIABETES

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Aims: The aim of this study was to investigate the nutritional status of type 2 **diabetes patients using modern** techinques of nutrimetabolomica.

Methods: We studied eighty patients with type 2 diabetes mellitus. Average age was 56±0.9 years, body mass index was 38.9±0.7 kg/m^2. 96% patients had abdominal obesity. Nutritional status was assesed by method of indirect calorimetry, bioimpedance analysis, immunoenzyme method, biochemical method, computer-based assessment of food consumption.

Results: Dietary energy redundancy was observed in 80 per cent subjects. Overwhelming majority of these patients had redundant fat consumption 136±5.4 g/day. Average consumption of carbohydrate was 294±7.6 g/day, protein intake - 108±4.7 g/day. The mean fasting glucose plasma concentration was 9.0±0.3 mmol/L, the homeostasis model assessment index was 5.8±0.3. 85% and 93% patients had increased level of total cholesterol and triacylglycerol accordingly. Serum adiponectin was decreased in 63.5% patients. Serum leptin was significantly increased in 95% subjects. All patients had increase the content of fat mass (45.3±0.7% from body mass). Data of indirect calorimetry were shown the decrease metabolism rate and rate of fat oxidation. Rate of carbohydrate oxidation was increased on 44.3±3.5% ($p< 0.01$) as compared with normal value.

Conclusions: Estimation of nutritional status of **patients** with type 2 **diabetes pointed to need individualization of standard dietary treatment for the purpose to** improve clinical and metabolic parameters in this **patients.**

BODY WEIGHT CHANGE AFTER NUTRITION INTERVENTION IN OUTPATIENTS WITH METABOLIC SYNDROME IN SÃO PAULO, BRAZIL

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Metabolic syndrome is becoming common in São Paulo, Brazil.

Objective: To evaluate compliance to nutritional intervention among patients with metabolic syndrome (MS) according to weight change.

Methods: It is a follow-up study including all the patients seen at the Nutrition Ambulatory of MS from the Federal University of São Paulo during 2008. There were included 39 patients that undertook 3 nutrition counsellings during 4 months. The MS diagnosis was defined by the presence of at least 3 of the 5 criteria established by the National Cholesterol Education Program - APT III (2005). The weight was measured at 3 different times (pre intervention, mean of 2 months and after a mean period of 4 months). A food 24hour recall was applied at the 3 follow-up periods. The result of the pre intervention moment served as a basis to create an individualized meal plan, (hypocaloric and adequate in macro and micronutrients).

Results: The age of the group varied from 27 to 76 years old beeing included 13 men and 26 women; 69.23% of the patients lost weight and 73.08% of the women showed weight lost after nutrition intervention. It was not shown any association between weight reduction, gender, school aging and purpose of counselling. The patients reduced a mean of 0.104kg/week.

Conclusion: Although weight loss was not significant to both sexes and far less than what the literature recommends it was observed that women presented bigger compliance to nutritional therapy. The follow-up period was considered a limitation for more significant results.

EFFECT OF CONJUGATED LINOLEIC ACID, VITAMIN E AND THEIR COMBINATION ON LIPID PROFILES AND BLOOD PRESSURE OF IRANIAN ADULTS WITH ACTIVE RHEUMATOID ARTHRITIS

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The aim of this study was to assess the impact of CLAs, Vitamin E, and combination of these nutrients on serum lipid profiles and BP in patients with active RA. In a randomized, double-blind placebo controlled trial, 87 patients with active RA were divided into 4 groups receiving one of the following daily supplements for 3 months: Group C: CLAs 2.5 g. equivalent to 2 g. mixture of cis 9-trans 11 and trans 10-cis12 CLAs in a rate of 50/50; Group E: Vitamin E: 400 mg; Group CE: CLAs and vitamin E at above doses: Group P: placebo. After supplementation, SBP levels decreased significantly in the group C in compare with groups E and P and MAP reduced significantly in groups C and CE. There weren't significant differences in the levels of PGE2, TG, CHO, LDL-c, HDL-c, LDL/HDL, CHO/HDL, FBS, CRP, AEA , PLT count and BMI between groups. CRP dropped non significantly in groups P, C, E and CE (19%, 24%, 55% and 39% respectively). ESR levels decreased in groups C, E and CE ($P \leq 0.05$, $P \leq 0.05$, $P \leq 0.001$, respectively). It is concluded that supplementation of CLAs decreased BP and Vitamin E decreased CRP. So co-supplementation of CLAs and Vitamin E might be profitable for Heart diseases prevention in RA patients.

Abbreviation: CLAs ,Conjugated Linoleic Acids; RA ,Rheumatoid Arthritis; BP, SBP and DBP ,systolic and diastolic blood pressure ; MAP, Mean arterial pressure ; PGE2,Prostaglandin E2;AEA, Arylestrase activity; PLT, Platelet ;BMI, Body Mass Index

THE EFFECT OF GREEN TEA EXTRACT ON SERUM VISFATIN CONSENTRATION IN PATIENTS WITH T2DM

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Background: Visfatin is a novel adipocytocine that highly expressed in visceral fat. Many studies showed insulin-mimetic activities of this cytocine. Its pathophysiologic role in obesity, diabetes and other metabolic complication remains largely unknown. Previous studies showed protective effect of green tea consumption in control of metabolic disease specially diabetes. In this study we examine the effects of green tea extract on circulating visfatin levels in patients with type 2 diabetes.

Methods: Totally 92 patients with type 2 diabetes were randomized in two groups green tea extract or placebo and received these capsules for 8week. Laboratory and anthropometric measurements include FBG, OGTT, HbA1C and lipid Profile, fasting serum Visfatin, Insulin and HOMA-IR, Weight, Hight, BMI and WHR were performed before and after intervention. All of the statistical data were analyzed using the SPSS13 software.

Results: There was no significant difference between Anthropometric measurement, HbA1C levels and lipid profile in two groups of study.We found a significant reduction in fasting plasma glucose and circulating visfatin in green tea extract group (p Values 0.05 and .012 respectively). Insulin levels increased significant in green tea extract group(p Value= 026) and but not significant negative correlation was bound between circulating Visfatin and Insulin levels changes (p Value= .06, r= .290).

Conclusions: This study showed the effects of green tea extract on FPG and serum visfatin and fasting insulin levels. This foundings suggest green tea extract can help to control of T2DM.

Keywords: Visfatin, Green tea extract, T2DM, Insulin Resistanse.

INFLUENCE OF THE NUTRICIONAL SUPPLEMENT DIAMEL ON THE HOMA-B AND HOMA-IR INDEX IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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The food supplement, Diamel contains aminoacids, vitamins, trace elements and lettuce and blueberry extracts, activated by a process of molecular magnetization, and acts in the beta pancreatic cells.

Objective: To evaluate, over a six-month period, insulin sensitivity and function of beta cells with f HOMA-B and HOMA-IR, in patients with type 2 diabetes receiving glibenclamide plus Diamel.

Research design and methods: A 60 type 2 diabetic were randomized to Diamel plus glibenclamide(group A, n=30) or to glibenclamide alone(group B, n=30). Two Diamel capsules were administered 30 minutes before breakfast, lunch and dinner. The patients were between 40 and 65 years old. Those patients with glycohemoglobin(HbA1c) greater 10% or severe chronic complications were excluded. Were followed for 6 months with clinical and laboratory evaluation. Fasting plasma insulin, fasting plasma glucose, 2-hour post-prandial blood glucose, HbA1c, HOMA-IR and HOMA-B, at 0,3, and 6 months.

Results: The group A and the group B presented character clinical similars and received identical recommendations. Fasting blood glucose, post-prandial blood glucose and HbA1c presented a significant diminution in the group A. The correlation between fasting blood glucose with the HOMA-B was positive in both groups at the beginning of the study but it was more positive in the group A at the 6 months. The correlations of HOMA-IR with the BMI and the waist circumference stayed positive in both groups, but were more significative statistical in group A.

Conclusions: The suplement, Diamel seem useful in increase function of cells beta in type 2 diabetes at least during the 6 months of follow-up.

EFFECTS OF CLINICAL NUTRITION EDUCATION ON GLYCEMIC CONTROL OUTCOMES IN TYPE 2 DIABETES

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Aims: The aim of this study was to assess the effectiveness of dietary education in reducing plasma glucose levels in patients with type 2 diabetes.

Methods: We randomly assigned 135 adult patients with type 2 diabetes (mean age 58 years) to the intervention group or the control group. All participants received basic diabetes education. The subjects in the intervention group participated in 11 weekly nutrition classes (90 min each). Glycosylated hemoglobin, fasting plasma glucose, total cholesterol, triglyceride, HDL and LDL cholesterol, height, weight, BMI and blood pressure were measured at baseline and at the end of the study. Two-sided homoscedastic t tests were used to analyze the differences between the intervention and control groups.

Results: The intervention group lost 1.5 ± 2.2 kg as against a weight gain in the control group of 0.5 ± 2.3 kg ($P = 0.01$). Fasting plasma glucose decreased 21 ± 55 mg/dl in the intervention group and increased 19 ± 78 mg/dl in the control group ($P = 0.028$). Glycosylated hemoglobin decreased 1.9 ± 2.1% in the intervention group and 0.2 ± 2.2% in the control group ($P = 0.022$).

Conclusions: Glycemic control of type 2 diabetes patients can be improved with public health intervention addressing nutrition.

THE EFFICIENCY OF NUTRITIONAL EDUCATION IN NEWLY DIAGNOSED DIABETIC PATIENTS

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Background: The risk for diabetes is 31.2 % in Iasi county (FINRISC), as established by the National Health Evaluation Programme; the diagnosis was confirmed by repeating fasting glycaemia or OGTT. All newly diagnosed diabetics undergo individualized nutritional education sessions, based on the Romanian Healthy Eating Guide.

Aims: To evaluate the results of implementing the nutritional education program in Iasi Clinical Centre for Diabetes, Nutrition and Metabolic Diseases, by looking at modifications in food intake at 6 months after the diagnosis of diabetes.

Material and method: 894 persons were registered as new cases of diabetes during 01.08. - 31.10.2007 in Iasi. We evaluated these patients and educated them about diabetes, benefits of a healthy lifestyle, qualities and structure of the diet. We performed a food frequency questionnaire and 24-hour dietary recall to 100 of them randomly selected, at diagnosis and after 6 months.

Results: The general tendency is for applying the recommendations for healthy eating: the majority of subjects reduced the daily calorie intake and divided the food intake in more meals (from 2-3 to 5-6 meals/day). The reduction in calorie intake was done by reducing lipid intake, with minimal changes in the quantity of carbohydrates, but with increase in fiber intake. Weight loss was statistically non-significant. Subjects who understood and performed the recommended diet modifications had better metabolic control.

Conclusions: Nutritional education proves an essential method in managing people with diabetes. There is a need for periodic reevaluation of energy intake and structure of diet to adapt to individual recommendations.

COMPARATIVE EFFECTS OF DIETS SUPPLEMENTED WITH SOLUBLE FIBERS ON METABOLIC ALTERATIONS IN ADULT OBESE ZUCKER RATS

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Aims: The main object of this study was to analyse the effects of chronic intake of a *P. ovata* husks (soluble and fermentable fibre) supplemented diet on the metabolic alterations own to the metabolic syndrome, and to compare them to those produced by a diet supplemented with the same amount of methylcellulose (soluble and non fermentable fibre).

Methods: We use the experimental model of obese Zucker rats. Male obese (O) rats and lean (L) Zucker rats aged 15 weeks were divided into the following groups: L-control (LB) (n = 10); O-control (OB) (n = 10); O-*P. ovata* husks (OP) (n = 10); O-methylcellulose (OM) (n=10). Rats were fed respectively chow diet, 3.5 % P. ovata husk-supplemented diet and 3.5 % methylcellulose-supplemented diet, for ten weeks.

Results: Chronic intake of both fibre-supplemented diets reduced body weight gain, and elevated plasma concentrations of triglycerides, total cholesterol and free fatty acids compared with OB rats. OP rats also showed lower insulin and leptin circulating concentrations, and reduced hepatic lipid content with respect to the OB rats, an effect which was related to the increased phosphorylation of 5´-AMP-activated protein Kinase (AMPK), and acetyl-CoA carboxylase (ACC) and down-regulation of fatty acid synthase (FAS) protein expression in the liver.

Conclusions: In conclusion, both soluble dietary fibres improve obesity and dyslipemia in obese Zucker rats, while only the fermentable fibre ameliorated hyperinsulinemia and hyperleptinemia and reduced hepatic lipid accumulation and production in obese Zucker rats, an effect that seem to be mediated by AMPK activation.

EXCESSIVE GESTATIONAL WEIGHT GAIN PREDICTS RISK OF ABDOMINAL OBESITY AND METABOLIC SYNDROME IN WOMEN WITH NORMAL WEIGHT BEFORE PREGNANCY

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Aim: The aim was to evaluate the association of excessive gestational weight gain (GWG) with development of abdominal obesity and metabolic syndrome (MS) later in life.

Methods: 62 women with postpartum period >5 years were recruited (18-38 y.o.). All had normal weight (BMI< 25kg/m^2) before pregnancy. They were divided into groups: the group of women with GWG≥16 kg (above the recommendations of the Institute of Medicine) (n=27) and group with GWG< 16 kg (n=35). Data of GWGs were collected retrospectively from medical records and self-reported. Anthropometric parameters, blood pressure, serum concentrations of lipids [total cholesterol (TC), low density lipoprotein (LDL-C), high density lipoprotein (HDL-C)] were measured and oral OGTT with insulin were performed.

Results: Mean value of BMI before pregnancy did not differ in these groups. Women with GWG ≥16 kg had significantly higher BMI (29,1±4,59 vs 26,69±4,39kg/m^2), waist circumference (WC) (86,0±13,78 vs 76,31±11,51cm), prevalence of MS (WHO criteria,1999) (37,04% vs 8,57%) and lower HDL-C (1,35±0,28 vs 1,56±0,31mmol/l), if compared with women GWG < 16 kg (p< 0,01). GWG was associated with BMI (r=0,46), WC (r=0,55), waist/hip ratio (W/H) (r=0,41), TC (r=0,33), LDL-C (r=0,32), HDL-C (r=-0,27), hypertension (r=0,26) and MS (r=0,42) (p< 0,05). On multivariate analysis, BMI (beta=0,74), WC (beta=0,52), W/H (beta=0,43) and GWG (beta=0,372) were found to be independent predictors of MS (p< 0,01).

Conclusion: Excessive gestational weight gain is indicator of abdominal obesity and metabolic syndrome later in life. Interventions for managing of GWG should be developed for all women, including women with normal weight before pregnancy.

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COMPONENTS OF METABOLIC SYNDROME (MS) IN WOMEN AFTER GESTATIONAL DIABETES (GDM)

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The aim was to evaluate the risk of MS in females who suffered from GDM.

Material and methods: Out of 153 quarried patients (SG-Study Group) with previous GDM, 74 had already been treated for DM, and in 5 an abnormal glucose tolerance was found. 74 patients had been subjected to a 75g OGTT, as well as the control group (CG) (N=155), in whom GDM during pregnancy was excluded. In all patients lipid parameters, blood

pressure, height, weight, and waist circumference (WC) were measured and BMI was calculated. MS was diagnosed acc. to modified NCEP-ATP III (3 from 5 had to be present).

Results: SG patients were older than CG (P< 0, 05), higher was their BMI during pregnancy, as well as after the observation's time (p< 0, 0001). MS developed in 30, 7% of SG patients vs 5, 2% from the CG (p< 0,001). Abnormal WC presented 57% patients from SG vs 37,6% from CG (p< 0,005), hypertension 18,9% from SG vs 1,9% from CG (p< 0,001), elevated fasting glycemia 79,1% from SG vs 1,9% from CG. Hypertriglyceridemia was found in 21,6% of patients from SG vs in 2,6% from CG (p< 0, 0001), and decreased concentration of HDL- cholesterol in 11, 1% of CG vs 2, 6% of CG (p< 0,005).

Conclusions:

1. Patients after GDM are at high risk for carbohydrate disturbances and MS later in life.

2. Patients after GDM should be under control that would enable early detection metabolic disturbances.

THE IMPLICATIONS OF GESTATIONAL DIABETES MELLITUS AND PREGNANCY-INDUCED HYPERTENSION SYNDROME ON ADIPONECTIN LEVELS OF BREAST MILK

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Objective: To observe the adiponectin concentrations of breast milk in the gestational diabetes mellitus (GDM) and pregnancy-induced hypertension (PIH).

Methods: The concentrations of adiponectin in maternal serum, cord blood and colostrums (3rd lactation) were determined by enzyme linked immunosorbent assay(ELISA) in health mother (n=28), GDM (n=18) and PIH (n=20). Clinical information about the mothers and newborns were collected using a questionnaire and medical records.

Results: There was no significance difference (p＝0.78) in adiponectin of milk levels at day 3 postpartum between control (37.3 (14.8~82.6) μg /L) and GDM (47.9(15.7~79.2)μg /L). The levels in PIH, adiponectin (70.0(33.5~229.9μg /L) was higher than controls in boarding significant (p=0.056). There was no significance difference in serum adiponectin levels between control group and GDM group (6.8 ±3.1 mg/L vs 6.1±3.0 mg/L, p＝0.39), but in PIH group, the maternal serum adiponectin levels (12.5 ±6.0 mg/L) were higher than that of controls (p＝0.01). The levels of umbilical blood adiponectin were lower in both of GDM (23.1 ±17.1 mg/L, p＝0.019) and PIH group (18.2 ±6.3mg/L, p＝0.013) than that in control (30.8 ±13.8mg/L); Moreover, human milk adiponectin levels correlated positively with the maternal blood (r= 0.38, p=0.003） and the body weight gain during pregnancy (r= 0.26, p=0.048) rather than the umbilical blood (r= 0.08, p＝0.86).

Conclusions: Adiponectin concentrations in umbilical blood are decreased in both of GDM and PIH, whereas in breast milk is unchanged. Breast feeding may play an important role in the infantile metabolic development, especially in the high risk infants.

Keywords: Adiponectin; Gestational diabetes mellitus; Pregnancy-induced hypertension; breast milk.

THE FREQUENCY OF METABOLIC SYNDROM DEVELOPMENT 4 YEARS POSTPARTUM IN WOMEN WITH RISK OF GESTATIONAL DIABETES

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Aim: The aim of the present work was to assess the frequency of metabolic syndrome (MS) development in women who had increased risk of GDM 4 years postpartum.

Materials and methods: Totally 861 pregnant women were supervised, they were selected according to the presence of risk factors for GDM development (family history of DM, BMI>30kg/m2, age>30yrs, hyperglycemia, aggrevated gynecological anamnesis). First (1st) assessment was carried out at 24-28 week of gestation, second (2nd) - two weeks postpartum, third (3rd) - 4yrs postpartum. Each time OGTT with 75g glucose load was performed. MS was defined according to the WHO and IDF criteria.

Results: During 1st examination GDM was revealed in 5.1% and impaired glucose tolerance (IGT) in 4.7% pregnant women. During 2nd examination out of 861 women 69 were diagnosed with impaired glucose metabolism of various degree -2.09% cases of IGT; 2.6% - IFGT, and 3.2% - T2DM. Besides, 47.8% of the 69 women had MS, they had multiple coexisting risk factors for GDM such as family history of DM, obesity and age > 30yrs. 3rd examination showed that 133 out of 861 women had IGT-3.9%, IFGT - 4.6% and T2DM- 6.8%. In 94(70.6%) of those 134 women MS was revealed. These women had second or third pregnancies during previous 4yrs. Besides, multiple risk factors of GDM were present.

Conclusion: Increased risk of GDM in anamnesis may predict to MS development shortly postpartum. Second pregnancy and delivery during 4yrs postpartum still more increases the risk of MS development in these women.

RELATIONSHIP BETWEEN DIET AND PLASMA INSULIN HOMEOSTASIS IN PREGNANT WOMEN

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Insulin resistance is a natural phenomenon of pregnancy that can lead to the development of gestational diabetes. Several dietary compounds may improve insulin sensitivity, such as omega-3 fatty acids and dietary fibers. The aim of this study was to examine the association between the diet and insulin homeostasis measurements in 23 women including 4 women with gestational diabetes and 19 with normal glucose tolerance. Plasma insulin levels were measured fasting and at 15, 30, 60, 90 and 120 min after a 75g oral glucose tolerance test (OGTT). Insulin resistance was estimated using the HOMA-IR index. Dietary intakes were assessed using a food frequency questionnaire at the beginning of the third trimester (27.4±1.8 weeks of pregnancy). No significant correlation was found between insulin measurements and total energy, fat, carbohydrate or protein intakes. However, eicosapentanoic acid (EPA) intakes were inversely related to

fasting and 120 min post-OGTT insulin levels ($p \leq 0.05$). EPA intakes were also negatively associated with HOMA-IR index ($p \leq 0.05$). Docosohexanoic acid (DHA) intakes were inversely related to fasting insulin levels ($p \leq 0.05$) and HOMA-IR index ($p \leq 0.05$). A trend was also observed for an inverse association between DHA intakes and 120 min post-OGTT insulin levels ($p=0.06$). However, no significant association was found between total, insoluble or soluble dietary fiber intake and fasting and post-OGTT insulin measurements. In conclusion, higher omega-3 fatty acid intake is related to a better insulin homeostasis in pregnant women. This may reflect a protective effect of omega-3 fatty acids on insulin homeostasis during pregnancy and reinforce current nutritional recommendations.

EVALUATION OF ENDOCRINE - METABOLIC DISORDERS USING COLPOSCOPIC METHOD OF INVESTIGATION IN WOMEN OF REPRODUCTIVE AGE (PRELIMINARY STUDY)

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Background: There is less data considering the role of endocrine - metabolic disorders in the developmnt of benign changes on uterine cervix. The aim of our study was to evaluate the expression of the endocrine - metabolic disorders on the uterine cervix using colposcopic method of investigation.

Materials and methods: A total of 350 patients with several gynecological problems were involved in the study. The main group consisted from 121 patients of reproductive age with diagnosed metabolic syndrome (MS) according to WHO definition (2002), the control group consisted from the same age 229 patients without MS . TSH, FT4, Anti- TPO, PRL, fasting serum Glucose and Insulin were measured in the serum of the patients. HOMA -IR, HOMA B. and HOMA S were calculated. Digital colposcopy Olympus 500 was used for the evaluation of the uterine cervix. Pap-smear test was done routinely.

Results: The patients in the main group had the following changes on the uterine cervix: endocervical hyperplasia and polyposis were diagnosed in 85,2 % of cases vs. 32,0% of the control group, atrophic changes were observed in 69,7 vs. 21,0% in the control group, keratosis was in the 11,0% of the main group vs. 7,4% of the control group.

Conclusion: In our preliminary study we found that the patients with endocrine- metabolic disorders have significantly increased amount of benign pathology of uterine cervix vs. control group. Thus the evaluation of endocrine -metabolic changes has to be considered in the management and treatment of benign changes of uterine cervix.