
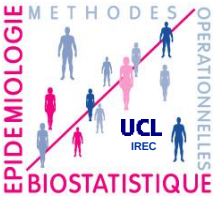

Université catholique de Louvain

External birth defects and neonatal mortality in the Province of Binh Thuan, Vietnam

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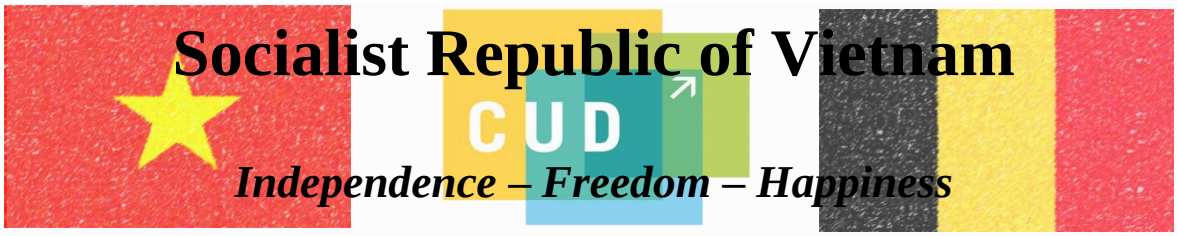

External birth defects and neonatal mortality in the Province of Binh Thuan, Vietnam

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SUMMARY

Out of 4 million neonatal deaths, about 99% occur in low- and middle-income countries, accounting for half of all deaths in under-five children. Worldwide, birth defects are a leading cause of neonatal and infant mortality, and their impact on the future child, on the child's family and on the community is not restricted to mortality. The neonatal mortality and birth defects are therefore of significant Public Health concern. The general objective of this project was to improve the mother-infant health by focusing on birth defect prevalence and neonatal mortality in the Province of Binh Thuan in South of Vietnam.

The findings of our prospective population-based registry study show that the prevalence of external birth defects in the Province of Binh Thuan were generally closed to other registries for most external birth defects, except for spinabifida whose absence requires further investigations. Result of our study clearly shows that neonatal mortality rate was generally lower than in other studies conducted in the North of Vietnam. Our study was able to tract some risk factors for neonatal mortality. Some of them are obviously editable such as mother's education and teenage mothers. Our follow-up study shows a physical growth of infant under 9 months similar to WHO reference population, in this Vietnamese province, but a too low prevalence of heart murmurs was found.

This work provides accurate informations on the burden of congenital anomalies and neonatal mortality. Such data can be useful to identify and prioritise interventions, especially low-cost interventions that can improve perinatal care and outcomes in this population. These are:

- Increase education level in Vietnam, especially in remote areas and in ethnic minorities for reinforcing prenatal care and good mother's attitudes during pregnancy;
- Educate young girls to avoid pregnancy in teenagers;
- Encourage health workers of commune health stations to early well identify birth defects;
- Train health workers of commune health stations to cardiac examination of infant for improving the detection of congenital cardiac anomalies.

LIST OF ABBREVIATIONS

ACE	Angiotensin-Converting Enzyme.
BD	Birth Defect
BMI	Body Mass Index
BPA	British Paediatric Association
CA	Congenital Anomaly
CDC	Centers for Disease Control and Prevention
CHS	Commune Health Station
CNS	Central Nervous System
CUD	Commission Universitaire pour le Développement
CVS	Chorionic Villus Sampling
DALYS	Disability-Adjusted Life Years
EBDS	External Birth Defects
ENMR	Early Neonatal Mortality Rate
EUROCAT	European Registration Of Congenital Anomalies And Twins
GDP	Gross Domestic Product
GPP	Gross Income Per Capita
HDI	Human Development Index
ICBDSR	International Clearinghouse For Birth Defects Surveillance And Research
ICD	International Classification Of Diseases
ICD-10	International Classification Of Diseases 10th Revision
IUGR	Intrauterine Growth Retardation
LB	Live Birth
LNMR	Late Neonatal Mortality Rate
MDG	Millennium Development Goal
MDG4	Fourth Millennium Development Goal
MOH	The Ministry Of Health
NM	Neonatal Mortality
NMR	Neonatal Mortality Rate
NTD	Neural Tube Defect
SB	Still Birth
SD	Standard Deviation
TOP	Termination Of Pregnancy
TOPFA	Termination Of Pregnancy For Fetal Anomaly
U5M	Under-5 Child Mortality
VACTERL	Vertebral, Anal, Cardiac, Tracheoesophageal, Renal, and Limb Anomalies
WHO	World Health Organization

DEFINITION OF TERMS

TERMINOLOGY RELATED TO THE TIMING OF GESTATION AND DELIVERY	
Embryonic period	The first eight weeks after fertilization, during which most, but not all, organs are formed.
Fetal period	The period from the ninth week after fertilization through delivery.
Neonatal period	The first 28 days following delivery of a live-born infant.
Prenatal	Before delivery.
Perinatal	Before, during, or after delivery. The exact time period may vary from 20 to 28 completed weeks of gestation through 7 to 28 days after delivery, depending on the context in which the term is used.
Postnatal	After delivery.
TERMINOLOGY RELATED TO PREGNANCY OUTCOME	
Live birth	Spontaneous delivery of an infant that exhibits signs of life, including a heartbeat, spontaneous breathing, or movement of voluntary muscles.
Fetal death (stillbirth)	Spontaneous delivery of an infant or fetus at least 20 weeks of gestation that does not exhibit signs of life.
Spontaneous abortion (miscarriage)	Spontaneous delivery of a fetus at less than 20 weeks of gestation.
Induced abortion (elective termination)	The purposeful interruption of pregnancy with another intention than to produce a live birth and which does not result in a live birth.
Term infant	An infant born after 37 completed weeks and before 42 completed weeks of gestation.
Preterm infant	An infant born before 37 completed weeks of gestation.
Postterm infant	An infant born after 42 completed weeks of gestation.
Low birth weight	Birth weight less than 2,500 grams, regardless of gestational age.
Very low birth weight	Birth weight less than 1,500 grams, regardless of gestational age.
Neonatal death	Death of a live-born infant within the first 28 days after birth. Early neonatal death refers to death during the first 7 days. Late neonatal death refers to death after 7 days but before 29 days.
Infant death	Death of a live-born infant before 12 months of age.
GENERAL TERMINOLOGY	
Major anomaly	A congenital abnormality that requires medical or surgical treatment, has a serious adverse effect on health and development, or has significant cosmetic impact.
Minor anomaly	A congenital abnormality that does not require medical or surgical treatment, does not seriously affect health and development, and does not have significant cosmetic impact.
Normal variant	A minor anomaly that occurs in approximately 4 percent or more of the population.
Body mass index (BMI)	A measure for human body shape based on an individual's weight in kilograms (kg) divided by height in squared meters (m^2).

CONTENTS

1 INTRODUCTION

1.1 VIETNAM – THE SETTING

Vietnam is a developing country located in Southeast Asia with a surface area of 332,600 km^2, stretching along the 3,260 km eastern coastline of the Indochinese Peninsula. The country, with the shape of an S letter, borders Laos and Cambodia to the West and China to the North. Approximately 80% of Vietnam's land is mountainous, highlands and jungles; only 20% is flat land. Vietnam is usually divided into three parts (North Vietnam, Central Vietnam and South Vietnam) but there are officially 8 different regions, 64 provinces and municipalities, 659 districts and equivalents status, and 10,732 communes.

Vietnam is the second most populous nation in Southeast Asia. Vietnam has a population of over 90 million with 54 different ethnic groups, of which the Kinh represents 87% of the total; the rest are ethnic minorities living scattered all over the country. Table 1 shows some demographic and economic indicators for Vietnam. In term of gross income per capita (GPP) Vietnam is classified as the 164^{th} country over the 225 countries of the world (Belgium is 30^{th}).

Table 1. Statistical information on Vietnam 2013 compared with Belgium

Indicators	Vietnam	Belgium
Total population	90,796,000	11,060,000
Gross national income per capita (GPP international $)	3,250	39,190
Life expectancy at birth m/f (years)	73/77	78/83
Probability of dying under five (per 1 000 live births)	22	4
Probability of dying between 15 and 60 years m/f (per 1 000 population)	128/87	102/59
Total expenditure on health per capita (Intl $, 2011)	231	4,119
Total expenditure on health as % of GDP (2011)	6.8	10.6
Population median age (years)	29.41	42.8
Total fertility rate (per woman)	1.77	1.65
Sex ratio at birth (boys/girls)	1.12	1.05
Number of medical doctors (per 1000 inhabitants)	1.2	3.8
Number of beds (per 100 inhabitants)	3.0	7.0

*Source : WHO: (www.who.int/countries); CIA World Factbook (www.cia.gov/library/publications/the-world-factbook/)

1.1.1 HISTORY OF VIETNAM – A BRIEF SUMMARY

Over the last decades Vietnam has gone through a period of rapid socio-economic development. After reunification in 1975, Vietnam switched its focus to reconstruction and development. However, due to the severe damages caused by many years of war, policy weaknesses and a difficult international environment, Vietnam's economy experienced a long period of crisis during the 1970s and 1980s. To overcome these difficulties, the Doi Moi (renovation) process was initiated in 1986 to open Vietnam to international exchanges. Thanks to these reforms Viet Nam has known a rapid economic growth. Since 1990, Viet Nam's GDP (gross domestic product) nearly tripled based on an average annual GDP growth rate of 7.5% - up until the global economic crisis in 2008. Growth suffered in 2008 (6.2%) and 2009 (5.3%) and is estimated to remain sluggish in 2010. Domestic resources for development have increased and international trade and foreign direct investment have dramatically expanded over the past two decades. The percentage of the population living below the national poverty line, estimated at 58% in 1993 has decreased to under 12% in 2009. Using the international poverty line definition of population living under 1.25 and under 2.0 USD a day, Vietnam was classified 75th over 124 countries with 16.85% and 43.36% of population living under poverty line in 2008.

1.1.2 HEALTH SITUATION

Along with all sectors in the economy, Vietnam's health care system is in the midst of a dramatic transformation. The health service network has been developed covering whole country from grassroots to higher level. The Human Development Index (HDI) increased over the last years. Vietnam HDI value for 2012 was 0.617, in the medium human development category, positioning the country at 127 out of 187 countries and territories. Between 1990 and 2012, Vietnam's HDI value increased from 0.439 to 0.617, an average annual increase of about 1.6 percent, demonstrating progress in education, in health care, and in living standards [1].

The mortality and morbidity patterns have shown major changes in Vietnam over the last two decades. Although significant progress has been made, many health-related issues remain to be addressed. The country is currently facing a double burden of disease. In the past few years, there were important shifts in disease patterns, with declines in the share of morbidity from communicable diseases and malnutrition but with an increase in non-communicable diseases, accidents and injuries. Some communicable diseases such as dengue fever continue

to have high prevalence rates in endemic regions in the Mekong Delta. Malaria is prevalent in the northern mountains and Central Highlands, while tuberculosis is making a comeback in the country. In 2008, the top five causes of burden of diseases, measured in disability–adjusted life years (DALYs) () for men were stroke, road traffic accidents, alcohol use disorders, liver cancer and HIV/AIDS, while for women, the top causes were depression, stroke, vision loss, diabetes and road traffic accidents. Among the five leading causes of mortality, traffic accidents is the highest (21.0 per 100 000 inhabitants). For children under age 15, the top 5 causes of burden of diseases are pneumonia, drowning, falls, road traffic accidents and epilepsy [2, 3].

1.1.3 HEALTH CARE STRUCTURE

The public health care system in Vietnam has four different level, the central, the provincial, the district and communal level. At each level, there is a People's Committee playing a central role in the organization because Vietnam is still a Communist country, even if opened to international exchanges since the Doi Moi in 1986. The Ministry of Health (MoH) formulates and executes health policies and programmes in the health sector in Vietnam. Provincial Health Services are technical agencies administered by the People's Committee of provinces. They assist the Provincial People's Committee in exercising the State management within the province in people's health care. In each province there is at least one general hospital with 500-1000 beds and specialized departments such as obstetric and gynecology, general medicine and surgery. District Health Centers are technical agencies administered by the People's Committees of districts, of provincial capitals or of towns. They are responsible for curative and preventive care as well as health surveillance in the district. The capacity of a district hospital is approximately 100 beds with surgical theatres and laboratory facilities. These hospitals are supported to serve a population of 150,000- 200,000 people in their area. In district hospitals, an obstetrician is always available, but a pediatrician is often lacking. Commune Health Centre also called Commune Health Station (CHS) in communes are the primary health care units accessible to people. As part of the State health system, these health centers have the tasks of providing primary health care services, early detection of epidemic outbreaks, treating common diseases and attending normal deliveries to a population between 5,000 -10,000 people. Other tasks include mobilization of community participation in family planning practices, hygiene and prophylactics and health promotion. It is staffed with at least three trained health professional: a nurse, a midwife and either a medical doctor or an assistant physician. The CHS also supervises the village health workers who operate in the

communes where people live and work. Village health workers, usually a woman (a part-time job with a small monthly allowance), are responsible, especially in remote areas, for conducting health education and communication and collecting essential information related to the community with regard to births, deaths, communicable diseases, accidents and injuries and environment, to report to the CHS. But due to the fact that most of the village health workers work on a part-time basis in this field, they can't address all information on health activities in the village.

One of the strengths of the health sector of Vietnam is the public health service provision network with the even coverage nationwide. In 2006, 100% of communes had a CHS, approximately 70% CHS had a doctor and more than 90% of CHS had midwives or an obstetric assistant doctor. Most of the deliveries in remote rural areas occur at CHSs and only complicated ones are referred to the upper levels [4].Thank to the vast public health network, the health sector has effectively delivered health protective and curative services to people. The National Health programs have brought about enormous results which have contributed substantially to the improvement of people's health.

1.1.4 ANTENATAL CARE IN VIETNAM

The Vietnamese government recommends at least three visits, once each trimester including one or two tetanus injections during pregnancy [5]. Antenatal care is provided by midwives at primary health care level. Antenatal care should include detailed medical and obstetrical history and estimation of date of delivery. About 91% of pregnant women visit an antenatal care clinic at least once, but only 29% visit antenatal care clinic at least three times. There is no official policy on ultrasound examination in prenatal care but technique is readily available [5,6].

Induced abortions are legal until 22 weeks of gestation compared to 12 weeks in Belgium. First trimester abortion is provided at all health care level, while induced abortion at the second trimester is officially only available at central or provincial level. At commune health station and district hospital, induced abortions are performed either with a vacuum aspiration or curettage of uterus up to 12 weeks of gestation. Induced abortion procedures performed in the private sectors are not reported to the official sources. Women seeking in first trimester induced abortion do not need to prove their identity or state a reason for abortion [7, 8].

Vietnam had a strict two-child policy since1998 despite no sanction against non complying families. This policy led the total fertility to decline from nearly five children in 1979 to 1.86 children per women in 2008. Official contraceptive prevalence in Vietnam was 78.5%

population in 2002. The intrauterine device was the most common birth control method (48%) followed by hormone pill (8%) and condom (7%). The rates of unintended pregnancy and abortion have remained high [9]. About 35% of unintended pregnancies in Vietnam that resulted in abortion were due to the non-use of contraception at the time of conception. The strong son preference in combination with the official two child policy has been reported as a contributing factor for abortion in Vietnam[9].

1.1.5 TRADITIONAL CULTURE RELATED TO HEALTH CARE IN VIETNAM

Vietnamese medical practices have been strongly influenced by Chinese medicine and culture. Traditional customs and practices may be carried out before seeking healthcare at a health facility, which may lead to a delay in healthcare seeking behavior as well as possible complications for the mother and newborn.

The concept respecting men and despising women is deeply rooted in rural area. The consequence is that girls in rural areas often discontinue their education at an early age in order to financially support their family or alternatively to became married. One of the deepest rooted Vietnamese rituals is the worship of ancestor. Only the male child can perform the ancestral worship and hence follows the signification of son among the offspring. The son preference has on the fertility decisions of Vietnamese. Vietnam has had an unusual rapid change in the sex ratio at birth in the past few years. Although, in 2000, the ratio was about 106 male births per 100 female births, it increased to 112 in 2008 [10]. Unbalance of sex ratio is a consequence of this preference for sons, coupled with declining fertility, easy and promoted access to abortion, economic development as well as an increasing availability of ultrasonography facilities [11].

In Vietnam, the predominant religion is Buddhism (Taoism and Confucianism, mainly), which promotes spiritual understanding of disease causation. Buddhism has a great influence on the thinking and behavior of Vietnameses people, more as a philosophy than as a religion. For them it is a way of life that emphasizes disconnection to the present. People believe in rebirth and that their present life is a reflection of actions in a previous life. Many Vietnameses regard elderly deaths as "natural" and "deserved" while young deaths are seen as either "good deaths" or "bad deaths." "Bad deaths" are defined as deaths of "dishonorable" persons who led a "bad life". The causes of "bad deaths" and deaths due to stigmatized diseases (e.g., HIV/AIDS, tuberculosis leprosy, birth defects and suicides) are often hidden

by the family. The risk of under-reporting deaths seems to be largest for deaths of infants and "bad deaths" [12].

Many Vietnameses believe that a person's soul lives on after death. One of the most important moral obligations of the living, especially the deceased's children, is to conduct a proper funeral that will facilitate the soul's movement from the world of the living to 'the other world'. In the case of death, it is very important to contact the family and ask them what they would like to do, before the officials come. Some people believe that within the body, the brain may die but the heart is still working. This makes the last minutes of life a very important time for the person to settle, to get ready for rebirth. In the case of death is in a hospital or a residential facility, the family will ask for the monk to come to the bedside to pray. If the monk is not available, the family could bring some elderly people who can do Vietnamese praying.

These practices seem to be deeply rooted in culture and society and there is little evidence of change, especially in rural areas, despite the recent socio-economical and political intervention.

1.1.6 BIRTH AND DEATH REGISTRATION SYSTEMS IN VIETNAM

The reporting of health statistics follows the structure of the health system, with the CHS being the lowest level at which data is recorded in registers. Births and deaths that occur in a commune should all be registered at the CHS through the village health network. Mortality is collected from routine reports based on the death records at the commune level designed by the Ministry of Health of Vietnam, but the form is very simple and designed more for administrative than for medical purpose. Aside from the health system, there are alternate reporting systems through governmental administrative bodies controlled by the Community's People's Committee. After the death of a relative, the family is responsible for going to the Community's People's Committee where the deceased had resided to conduct mortality registration. When a child is born, the family should register at the Community's People's Committee within 30 days of birth (60 days in remote areas). If a neonatal death occurs before the delay for registration, there is no death certificate, and the family seldom may or not register the event at the Community's People's Committee. Nowadays, there is neither incentive for death reporting nor sanctions against the non reporting and many people do not actively report deaths at the Community's People's Committee. These two reporting systems sometimes do not report similar mortality data because of different interests.

Even for alive newborn, there are several reasons why children are late or never registered. In the Vietnamese society the responsibility to register newborns is placed on families, which in many cases have a poor understanding of the necessity to register. Many parents simply don't see an urgent need for the procedure and some in remote areas simply don't have an easy access to registers. Another important aspect, despite not being specific to Vietnam, is that Vietnam's family planning law has implemented fines and other penalties for families having more than two children. Consequently, many families try to avoid extra payments and the third and following children go unreported [13].

1.2 NEONATAL MORTALITY

Known as the neonatal period, the first 28 days of life corresponds to a period where newborns are most vulnerable. Globally, about 3.8 million deaths occur every year during this critical time period. Neonatal deaths now account for more than two-thirds of all deaths in the first year of life and two-thirds of the world's neonatal deaths occur in just 10 countries, mostly in Asia and Africa. Almost all (99%) of neonatal deaths occur in developing countries and constitute an important public health problem with both medical and economical implications (Table 2).

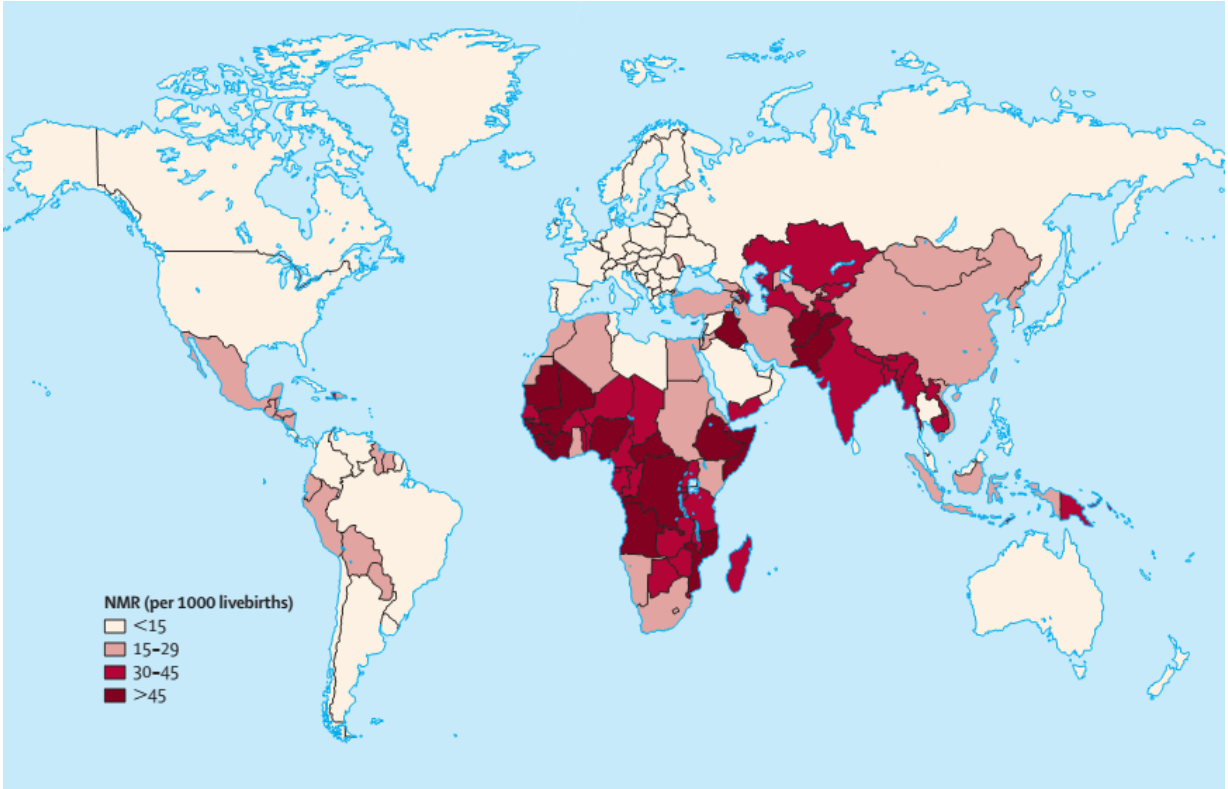
Table 2. Regional or country variations in neonatal mortality rates and numbers of neonatal deaths, showing the proportion of deaths in children under 5 years

	NMR per 1000 livebirths (range across countries)	Number (%) of neonatal deaths (1000s)	Percentage of deaths in children aged under 5 years in the neonatal period	Percentage change in NMR between 1996 and 2005 estimates
Income groups				
High-income countries	4 (1–11)	42 (1%)	63%	-29%
Low-income and middle-income countries	33 (2–70)	3,956 (99%)	38%	-8%
WHO regions				
Africa	44 (9–70)	1,128 (28%)	24%	5%
Americas	12 (4–34)	195 (5%)	48%	-40%
Eastern Mediterranean	40 (4–63)	603 (15%)	40%	-9%
Europe	11 (2–38)	116 (3%)	49%	-18%
Southeast Asia	38 (11–43)	1,443 (36%)	50%	-21%
Western Pacific	19 (1–40)	512 (13%)	56%	-39%
Overall	**30 (1–70)**	**3,998 (100%)**	**38%**	**-16%**

NMR: neonatal mortality rate. *Source:* 4 million neonatal deaths: When? Where? Why? *Lancet* 2005[14].

Of these neonatal deaths, 2.8 million (70%) took place during the first week of life (the early neonatal period), and 1.2 million (30%) occurred between the 8th and 28th days of life (the late neonatal period). More than 40% of neonatal deaths take place within 24 hours after delivery (the very early neonatal period) [14, 15]. Globally, the neonatal mortality rate (NMR) is estimated at 30 deaths per 1,000 live births, but this masks vast differences between countries (Figure 1). While developed countries only experience an average NMR of 5 per 1,000, in developing countries the average rate rises to 42 per 1,000 in 2006 [16].

Figure 1. Variation between countries in neonatal mortality rates.



Source: 4 million neonatal deaths: When? Where? Why? *Lancet* 2005[14].

As overall infant and child mortality fall, the annual neonatal mortality has remained unchanged in the past decades and the neonatal mortality represent an increasing proportion with recent estimates showing that neonatal mortality now accounts for more than 40% of the overall under-5 child mortality (U5M), an increase from the 37% reported in 1990 [17, 18].

Recent data for 2011(www.worldbank.org) show that Vietnam has the 107th rank out of 193 countries, with a NMR of 12 per 1,000 live births (Belgium is ranked 22th with NMR of 2/1,000 live births and Somalia is ranked 193th with NMR of 50/1,000 live birth)[19].

Achieving Millennium Development Goal Nr 4 (MDG4: Reduce child mortality; Target 4A: Reduce by two-thirds between 1990 and 2015 the U5M) will therefore need to include reducing deaths during the neonatal period in high-mortality countries and reducing deaths in the first week of life.

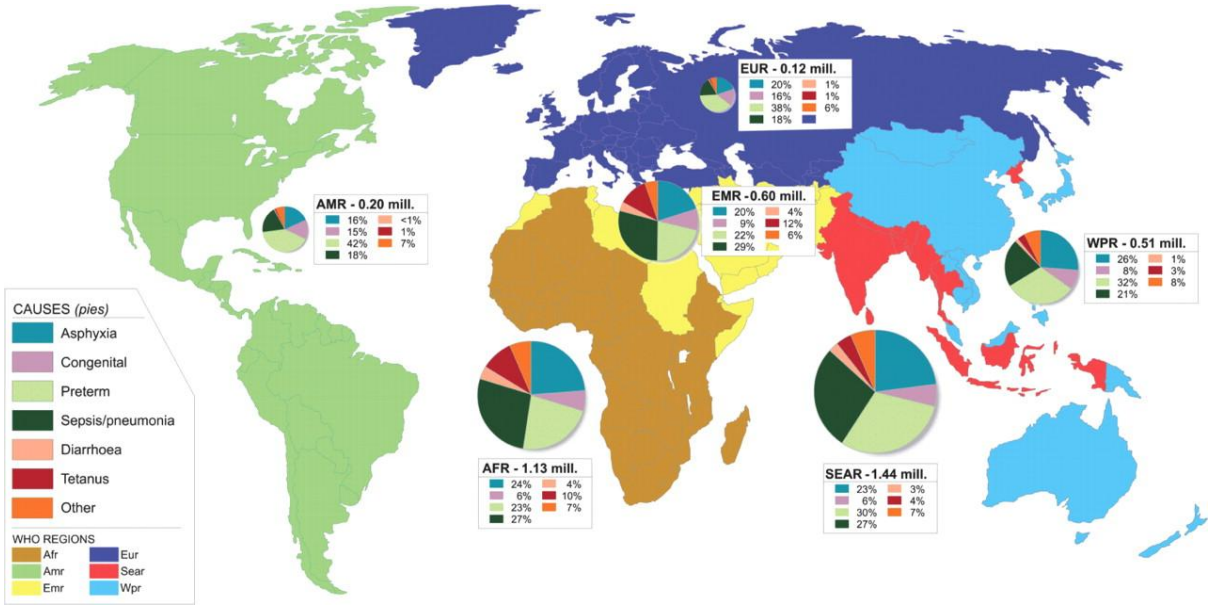
One reason why neonatal deaths have been neglected until recently is that the problem has been to some extent "hidden" due to limited data. Many newborns in developing countries are born and die at home without contact with health care professionals. These deaths usually

go unrecorded by any health information systems. Most developing countries do not have effective vital registration systems, and therefore any estimate of the burden of mortality usually relies on community-based surveys such as Demographic and Household Surveys [13].

1.2.1 CAUSES OF NEONATAL MORTALITY

Data on the causes of neonatal mortality are sparse, because most deaths in developing countries occur at home without any contact with professional health care providers. Probably the best current global estimate is from a study by Lawn et al(2006) who modeled cause of death using multinomial regression techniques based on vital registration data (where available) and both published and unpublished studies. The study estimated that infections are responsible globally for 36% of all deaths (26% attributed to sepsis/pneumonia, 7% to tetanus and 3% to diarrhea) (Figure 2). A further 28% are caused by pre-term birth, 23% by asphyxia and a further 7% result from congenital abnormalities [14, 15].

Figure 2. The estimated distribution of causes for 4 million neonatal deaths for the six WHO regions in the year 2000



Size of circle represents number of deaths in each region. Afr = Africa, Amr = Americas, Emr = Eastern Mediterranean, Eur = Europe, Sear = Southeast Asia, and Wpr = Western Pacific. Source: Estimating the causes of 4 million neonatal deaths in the year 2000. Int J Epidemiol 2006,[20]

1.2.2 DETERMINANTS OF NEONATAL MORTALITY

While probably less is known about the determinants of neonatal mortality than those for older children, there is still a considerable body of evidence on a wide range of factors that affect newborn survival. This section reviews the existing literature on different groups of determinants of neonatal mortality.

1.2.2.1 Socioeconomic determinants

Maternal education has long been established as an important determinant of child mortality. Well educated mothers have better health indicators because of their ability to better understand and use the health system, compared to their less educated peers [21].

Poverty is an underlying cause of many neonatal deaths, either through increasing the prevalence of risk factors such as maternal infection, or through reducing access to effective care [14]. Recent research using data at the family/individual level confirms a wealth gradient in mortality of newborns, with the poorest 20% of households experiencing consistently higher NMRs than the 20% most wealthy [14].

1.2.2.2 Maternal health and intrapartum complications

The health of the mother and newborn are intrinsically linked, and a number of maternal health problems have been shown to have a detrimental effect on newborn survival. The level of female emancipation may decide where the delivery takes place and who is assisting [22]. The death of a mother substantially increases the risk of death for her newborn child. Complications of pregnancy also impact negatively on the newborn. Between 5% and 24% of perinatal deaths are due to hypertensive disorders. Obstructed/prolonged labor and bad presentation were also found to be responsible for about 32% of perinatal deaths [23]. The death of a mother substantially increases the risk of death for her newborn child. In one study reporting on child outcomes for mothers who died in labor, authors show that all the newborn babies died within first year [24].

1.2.2.3 Health care interventions

Health care interventions are as determinants of neonatal deaths. There is a common misconception that neonatal mortality is difficult to prevent, and requires expensive interventions relying on advanced technology. There is also much interest in simple, low technology approaches to managing neonatal health such as tetanus toxoid immunization, diagnosis and treatment of reproductive tract infections during pregnancy, improved maternal nutrition, “kangaroo care” and early initiation of exclusive breastfeeding [25].

1.2.2.4 Birth weight

As well established as a direct cause of mortality, low birth weight (less than 2500 g) is one of the most important underlying factors affecting neonatal mortality. Although these low-birth weight babies constitute only about 14% of children born, they account for 60–80% of neonatal deaths[14].

Low birth weight arises through preterm birth (before 37 weeks), intrauterine growth restriction or a combination of the two. Low birth weight infants are approximately 20 times more likely to die as heavier babies [14, 26].

1.2.2.5 Sex

Neonatal mortality has been shown to be higher in males than in females, a biologically expected difference. The male-to-female ratio in neonatal mortality in developing countries is estimated at 1.3 [27]. In nearly all countries, males have higher mortality than females during infancy. The male disadvantage is particularly marked in the neonatal period [28].

1.2.2.6 Others determinants

Multiple births are also a major risk factor: twins and other higher multiple births are at greater risk of death due to higher rates of congenital abnormalities, low birth weight, preterm labor and complications at delivery. A study found that the relative risk for multiple births was 6 for neonatal mortality, and this dropped to 2.2 for post-neonatal mortality and 1.4 for early childhood mortality [29].

Birth order demonstrated a "U" shaped relationship for neonatal mortality, with high rates of mortality for first births. Mortality began to increase again for births of order five and above [29].

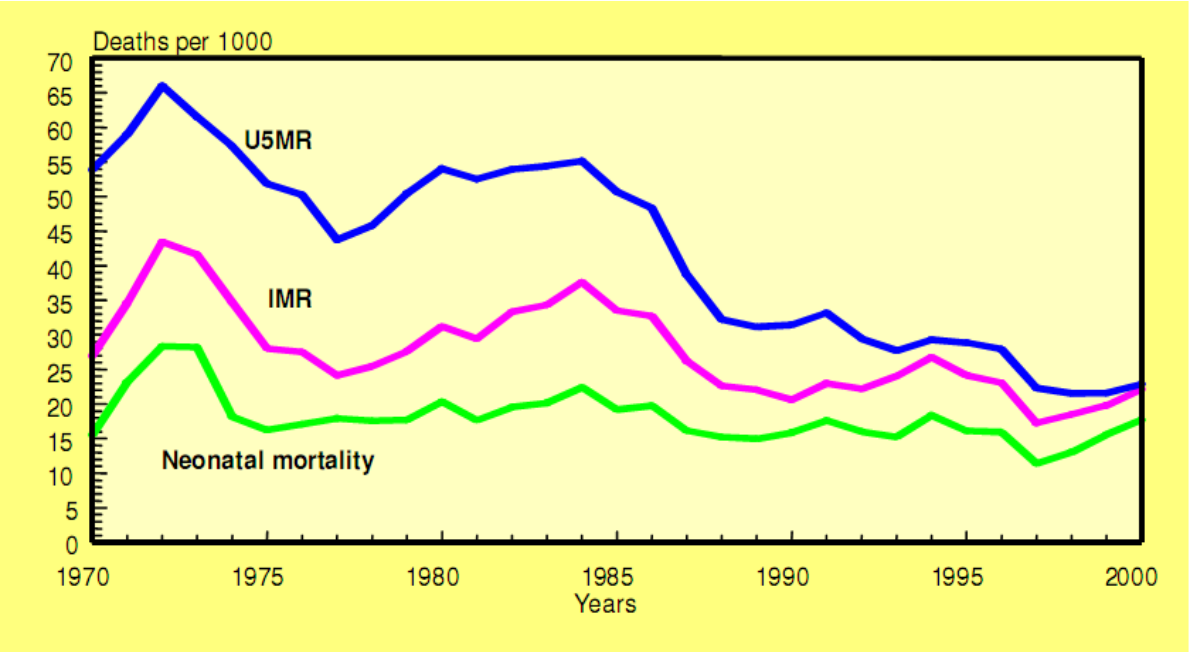
Maternal age is another well-known factor that affects child mortality with children of both younger and older mothers experiencing higher mortality. Again, risks associated with both older and younger mothers are most marked in the neonatal period [29, 30].

1.2.3 NEONATAL MORTALITY IN VIETNAM

Vietnam is also committed to the MDGs. The Vietnamese government has identified perinatal health and neonatal mortality as priority areas and evidence-based guidelines on reproductive health were launched in 2003 for improving newborn care and survival [31].

In Vietnam, the under-five mortality rate has dropped considerably over the last 30 years (55/1,000 to 30/1,000), while neonatal mortality remained basically unchanged in the range of 15/1,000 during the time period 1970–2000 (Figure 3) [32].

Figure 3. Mortality trend in Ba Vi district in Northern Vietnam between 1970 and 2000



U5MR: Under 5 mortality rate; IMR: Infant mortality rate.

Officially, the NMR in Vietnam was 12/1,000 in 2004 [33]. Graner et al reported a NMR of 11.6/1,000 live births over the period 1999-2005 in a rural population in Northern Vietnam [34]. A recent study in Quang Ninh province in Northern Vietnam reported a NMR of 16 /1000 live births over the period 2008-2010 [35]. No data on NMR in communities of Southern Vietnam have been published yet. A survey carried out in 7 central-level pediatric hospitals and 10 provincial hospitals in 2005 show that prematurity/low birth weight is the major cause of mortality in newborns, accounting for 23% all neonatal deaths; other important causes include asphyxia (15%), pneumonia (12%), sepsis (12%) and malformation (13%) [36].

1.3 CONGENITAL ANOMALIES

1.3.1 DEFINITION

Congenital anomalies, congenital abnormalities (CAs), birth defects (BDs) and congenital malformations are all interchangeable terms used to describe developmental disorders of the embryo and fetus. However, it is unfortunate that there are to date no internationally accepted terms for defining congenital anomaly and there is no single universally accepted system of classification[37]. The term is often limited to apparent structural problems, but sometime is expanded to include defects in function, metabolism, or body chemistry that lead to physical or mental problems or death.

According to the March of Dimes, United States nonprofit organization whose mission being to improve the health of babies by preventing birth defects, premature birth and infant mortality , "a birth defect is an abnormality of structure, function, or metabolism (body chemistry) present at birth that results in physical or mental disability, or is fatal" [38].

Another definition (International Classification of Diseases, 10th revision) limits the term to structural malformations and deformations. In the tenth revision of the International Classification of Diseases (ICD-10), the term "congenital anomalies" was replaced by "congenital malformations, deformations and chromosomal abnormalities" to denote structural malformations and exclude conditions such as inborn errors of metabolism [39].

Unlike the March of Dimes, many clinicians and scientists do not consider metabolic abnormalities to be birth defects since many can be explained by recessive genetic inheritance. Minor structural birth defects do not necessarily result in a disability, though they may be unwanted, cosmetically disfiguring, and a sign of abnormal development that signals an underlying cause that should not be ignored.

According to national birth defects prevention network in the United States of America, the general term 'birth defect' may take on a variety of meanings depending on the context in which it is used and the perspective of the person using it. "Congenital abnormality", "congenital anomaly", and "congenital malformation" are terms often used as synonyms for "birth defect". However, the word "congenital" may describe any condition present at birth, regardless of its etiology or timing of occurrence. In the broadest sense, the term birth defect encompasses a diversity of conditions including physical malformations, sensory deficits,

chromosomal abnormalities, metabolic defects, neurodevelopmental disorders, and complications related to prematurity and low birth weight, among others [40] .

Varying definitions of the term "birth defect" add to the challenges of tracking their prevalence and understanding their causes.

1.3.2 PUBLIC HEALTH IMPACT OF CONGENITAL ANOMALIES

Congenital anomalies develop during prenatal life and are present at birth, even if they are not detected until sometimes a couple of years later. Congenital anomalies are important at all levels of health care because they affect all age groups and can involve almost any of the body tissues and organs [41].

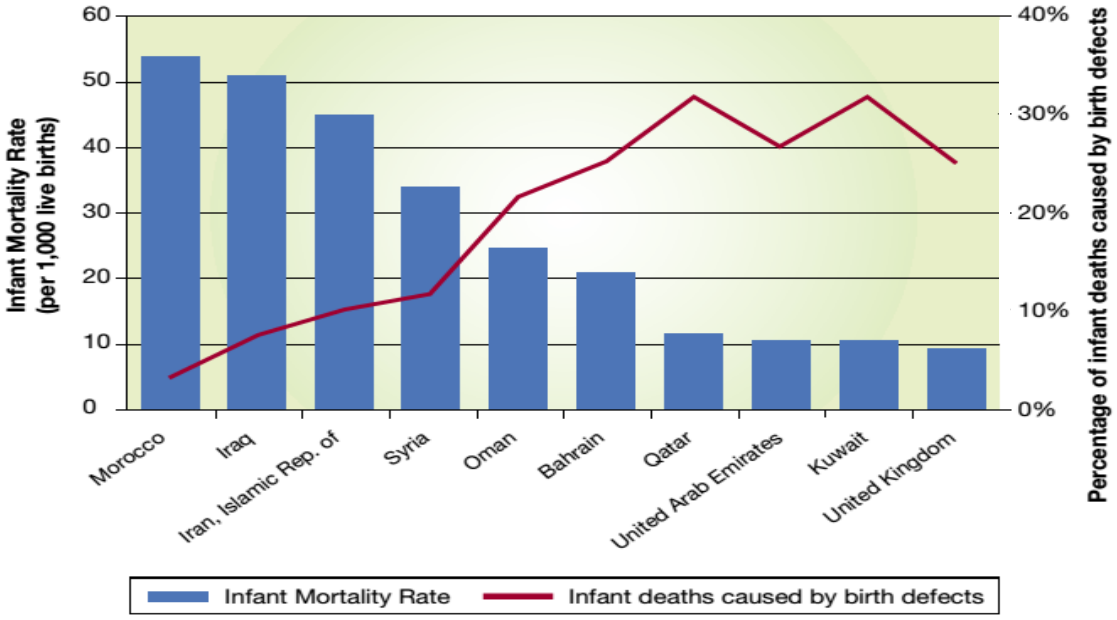
Congenital anomalies are one of the leading causes of pediatric disability and mortality in developed and developing countries. Congenital anomalies have a high societal cost and profoundly affect families. As significant improvements have been seen world-wide in controlling childhood infectious diseases and issues related to poor nutrition, CAs now have a proportionally bigger impact on the health of the world's children (Figure 4) [42, 43].

Worldwide CAs affecting 2-3% of all babies are an important cause of perinatal mortality and childhood morbidity, resulting in approximately 3.2 million birth defect-related disabilities every year [44-46].

CAs are also the leading cause of infant deaths and of intrauterine deaths (stillbirth), resulting in between 8-10,000 deaths each year in the United States. The estimated lifetime costs related to birth defects in the United States was at least $8 billion in 1992 USD for a single year's birth cohort [47-49].

According annual report of birth defects in Canada in 2002, the CAs affected approximately 3% of all newborn babies, accounted for about 12% of pediatric hospital admissions, and remained a leading cause of death among Canadian infants in both the neonatal and postneonatal periods. The mortality rate associated with CAs was 1.9/1000 births in Canada (1995)[50].

Figure 4. Relationship between infant mortality rate and percentage of infant deaths due to birth defect by country



Source: Adapted from WHO, 2006[44]

In Europe, EUROCAT recorded a total prevalence of major congenital anomalies of 23.9 per 1,000 births for 2003–2007. Approximately 2.5% of live births with congenital anomaly die in the first week of life. Perinatal mortality rate associated with congenital anomaly was 0.93 per 1,000 births in 2004 [51].

In Asia, birth defects were associated with an increasing proportion of perinatal deaths in China, and had become one of the major causes of perinatal deaths[52] . The prevalence of CA was 15.4/1000 births and accounted for 7.3 % of infant mortality in China [53]. CA accounted for 14.3 /1000 births and about 25.2% of babies with congenital anomaly died in the perinatal period in South Korea [54].

1.3.3 EMBRYOLOGY OF BIRTH DEFECTS

Since all congenital anomalies are a result of aberrant structural development before birth, basic understanding of normal and abnormal embryogenesis and fetal development is important for prenatal care. Prenatal development can be divided into three time periods (Figure 5):

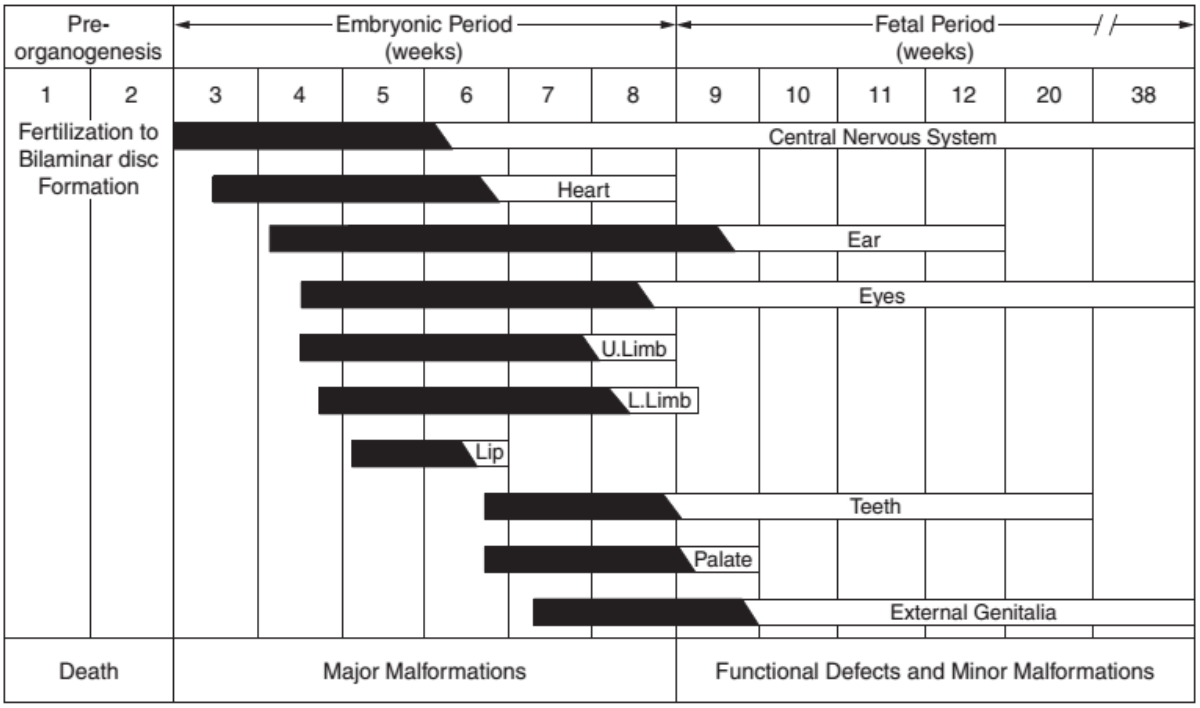
The pre embryonic period extends from the time of fertilization to the end of the second week of gestation. This period is characterized by the presence of pluripotent cells. The presence of these pluripotent cells is also responsible for the "all or none" effect of teratogens during this

period. An environmental insult during this period will either kill the embryo or produce no harm if the embryo survives.

The embryonic stage extends from the beginning of the third week to the end of the eighth week. Because all essential external and internal structures are formed during this period, this is the most critical and vulnerable period of development. The majority of major congenital malformations are a result of alteration in normal development during this stage.

The fetal stage expanding from the ninth week until birth is primarily a period of growth in size and is characterized by rapid body growth and differentiation of tissues and organ systems. During this period, the fetus is less vulnerable to teratogenic effects of various agents but these agents may still interfere with growth and development of organs such as brain and eyes during the fetal period (Figure 5).

Figure 5: Susceptibility to teratogenesis for different organ systems. Solid bar indicates highly sensitive periods



(In: Rimoin DL, Connor JM, Pyeritz RE, eds. Emery and Rimoin's principles and practice of medical genetics Vol I. 3rd ed. New York; Edinburgh: Churchill Livingstone; 1997:383–94.)

1.3.4 ETIOLOGY

Etiology of congenital anomalies is not completely understood despite its quite high prevalence, affecting 2-3% of newborns. A broader knowledge about the causes of birth defects would provide valuable information regarding the outcome and prognosis of

the anomaly, the development and establishment of diagnostic protocols, the design of therapeutic strategies and genetic counseling to the family. The majority of CAs are of unknown origin, which makes prevention problematic. In the multiple factor hypotheses, malformations are determined by the combination of environmental and genetic factors. Gene-environment interactions refer to the circumstance in which certain genes may predispose an individual to a birth defect, but one or more environmental factors are also necessary for the defect to be produced. Their causes are divided into four broad categories and it has been estimated that around 15%-25% are due to recognized genetic conditions (chromosome and single gene causes), 8%-12% are due to environmental factors (maternal-related conditions, drug or chemical exposures), 25%-35% are due to multifactorial inheritance and 30–45% have unknown causes [55-58]. However, Czeizel, et al reported from a study based on data from the first 25 years of the Hungarian Abnormality Registry that the etiology of a congenital malformation was unknown in about 16.8% of the cases, genetic causes in 10.1%, environmental causes in 3.7% and multifactorial causes in about 69.4% [59].

Genetic factors are responsible for a large majority of congenital malformations with identified causes and play an important role in disorders of multifactorial inheritance. Genetic causes of birth defects can occur as a result of one or both parents carrying one or more unfavorable genes or from chromosomal damage in the developing embryo. Genetic causes of birth defects can either be autosomal or sex-linked in nature, recessive or dominant traits, single-gene or multiple-gene disorders, chromosomal defects, or be related to new mutations in the fetus [55]. With better understanding of the human genome and improved techniques in molecular cytogenetic, more and more structural chromosomal abnormalities are being identified as a cause of congenital anomalies previously considered to be of unknown etiology [55].

When it comes to fetal exposure, any exposure that occurs by another way than genes is typically considered as “environmental.” A relatively small proportion of birth defects can be attributed, at least in part, to specific environmental causes such as maternal disease (e.g., rubella) or use of pharmaceuticals (e.g., valproic acid, an anticonvulsant and mood stabilizer). However, the majority of birth defects are considered the result of multiple environmental and/or genetic causes acting together. Environmental agents may play a role by triggering genetic mutations or other chromosomal damage that leads to birth defects. After the thalidomide tragedy in the 1950s, a great deal of emphasis was placed on the

potentially harmful role that drugs can play in the development of CAs. While thalidomide is an extreme example of the potential teratogenicity of a pharmaceutical product, only 1% of CAs with a known cause are attributed to drug therapy. Furthermore, there are only approximately 25 drugs currently in use that are known to have a teratogenic effect[60]. Both the dose and the timing of the exposure are critical to determining whether a particular environmental agent will actually cause birth defects. When examining the potential teratogenicity of an environmental agent, one must keep in mind that for an agent to act as a teratogen, the fetus must have been exposed to at least a threshold dose, during the sensitive period of development for which that particular substance is known to have an effect (Table 3)[55,61].

Table 3: Common Teratogens and Associated Anomalies

Teratogens	Vulnerable Period	Associated Congenital Anomalies
Teratogen Drugs		
Antihypertensive		
ACE inhibitors	13th week-term	Hypocalvaria, renal failure, pulmonary hypoplasia, death
Anticonvulsants		
Phenytoin	18–60 days	Cleft lip/palate, congenital heart defect, hypoplasia of nails.
Valproic acid	18–60 days	Hypertelorism, hyperconvex nails, septooptic dysplasia, cleft lip/palate, limb defects, microcephaly
Retinoids	18–60 days	Central nervous system/ear defects, cleft lip/palate, heart defects, eye anomalies
Androgens	2–24 weeks	Genital tract abnormalities
Infection		
Rubella	First trimester	Cataract, microcephaly, microopthalmia, heart defects
Varicella zoster	8–20 weeks	Microcephaly, limb hypoplasia, cutaneous scars
Maternal Disorders		
Diabetes	First trimester	Neural tube defects, cardiac defects, caudal regression syndrome.
Acid folic deficiency	-	Neural tube defects.
Chemical agent		
Alcohol	First trimester	Microcephaly, maxillary hypoplasia, heart defects
Pesticide	-	Heart Defects, Neural tube defects, Oro facial cleft,, Limb reduction, Hypospadias, Fetal deaths
Dioxine	-	Oro facial cleft, Neural tube defects, Hypospadias

ACE: angiotensin-converting enzyme.Modified from [55,61] (In: Praven Kumar: Dysmorphology. In Congenital malformations, evidence-based evaluation and management. Edited by Kumar P BB. The McGraw-Hill Companies; 2008.; 7.)

1.3.5 NOMENCLATURE AND CLASSIFICATION AND THE CODING OF CONGENITAL ANOMALIES

Congenital anomalies are a group of Rare Diseases for which there is not a single classification of congenital anomalies used throughout the world environmental [62]. Different classifications of congenital anomalies are used in different countries. Congenital anomalies can be classified either based on timing of insult [63, 64], underlying histological changes, or based on its medical, social consequences and involved system [65].

1.3.5.1 Classification based on timing of insult

Malformation: A malformation is a morphologic defect of an organ, part of an organ, or a region of the body due to an intrinsically abnormal developmental process. Since malformations arise during this early stage of development, an affected structure can have a configuration ranging from complete absence to incomplete formation. An example of malformation is neural tube defects.

Disruption: These are congenital anomalies that result from destructive processes that alter a structure after it has normally formed. Disruptions usually affect structures that have previously normally developed and their presence does not imply an intrinsic abnormality of the tissues involved. For example, an amniotic band following amnion rupture may cut across the scalp, face or digits of the fetus, penetrating the skin, soft tissue and bone.

Deformation: This describes a birth defect that results from an aberrant mechanical force distorting normally developing structures. The defect can be an abnormality of form, shape or position of part of the body. Deformations can be reversible after birth depending on the duration and extent of deformation prior to birth.

Both deformations and disruptions affect previously normally developed structures without intrinsic tissue abnormality. These anomalies are unlikely to have a genetic basis, are often not associated with cognitive deficits, and have a low recurrence risk.

1.3.5.2 Classification based on clinical presentation

Single-system defects: These defects constitute the largest group of birth defects that involve only a local region of a single organ system of the body, and represent the largest proportion of birth defects**.** Examples of single system defects are cleft lip/palate and congenital heart defects**.** These anomalies usually have a multifactorial etiology and the recurrence risk is often low.

Multiple-system defects: These involve multiple organ systems and can be further sub-classified based on the relationship between the different anomalies.

Syndrome: This term refers to a constellation of birth defects that consistently occur together and usually have a common specific aetiology. Examples include Down syndrome, Turner syndrome, Apert syndrome and Noonan syndrome.

Association: Association includes clinical entities in which two or more congenital anomalies occur together more often than expected by chance alone and have no well-defined etiology. The link among these anomalies is not as strong and consistent as among anomalies in a syndrome. A common example is the VACTERL association which includes vertebral, anal, cardiac, tracheoesophageal, renal, and limb anomalies. These conditions usually have a low recurrence risk and the prognosis depends on the number of malformations and severity of each underlying defect present in an individual case.

Sequence: The term sequence implies that a single primary anomaly or mechanical factor initiates a series of events that lead to multiple anomalies of the same or separated organ systems and/or body areas. A common example is the Potter sequence in which primary abnormality of renal agenesis leads to oligohydramnios, which in turn results in pulmonary hypoplasia, the characteristic Potter facies, limb deformities, which are due to fetal compression in utero. The recurrence risk is usually low.

Complexes: This is an infrequently used term describing a set of morphologic defects that share a common or adjacent region during embryogenesis. An example is hemifacial microsomia. These defects are also referred to as polytopic field defects.

1.3.5.3 Classification based on medical consequences

Major anomalies: Major malformations are anatomic abnormalities which are severe enough to reduce life expectancy or compromise normal function. About 2–3% of children born with a major anomaly that is evident at birth, such as cleft lip and palate, anophthalmia or radial aplasia. Worldwide approximately 10,000 children are born every day with a major structural anomaly [66].

Minor anomalies: Minor malformations are structural alterations which either require no treatment or can be treated easily and have no permanent consequence on normal life expectancy. Birth defects classified as minor represent distinct departures from normal

development, occurring in 4% or less of the population. Their importance lies in the fact that infants with one or more minor anomalies may also have a major anomaly.

1.3.5.4 Classification based on involved system

This classification is the most frequently used. It consists of congenital anomalies according to the affected body systems. It is by far the easiest classification and it is a precious tool for assessing of congenital anomalies epidemiology.

1.3.5.5 International Classification of Diseases, 10th revision: classification and coding

Classification systems and the coding of birth defects within those systems are central to the surveillance process. At present, the World Health Organization (WHO) and 10 international centers coordinate classification efforts to promote a standardized classification system for organizing coded data for storage, retrieval, and analysis. Using a standardized system, disease information that is collected by various medical professionals can be compared, grouped, and tabulated for statistical purposes. International Classification of Diseases, 10th revision (ICD-10) limits the term to structural malformations and deformations. In the ICD-10, the term "congenital anomalies" was replaced by "congenital malformations, deformations and chromosomal abnormalities" (Q00-Q99) to denote structural malformations and exclude conditions such as "inborn errors of metabolism" (E70-E90). There are several challenges in coding CAs, including the need to distinguish infants with multiple defects and syndromes from those with isolated defects, and the need for strategies for coding suspected defects for which confirmation is not available. Selection of a coding system is central for the use of collected data. In 1979, the British Pediatric Association (BPA) developed a classification of diseases by modifying ICD-9-CM (British). In 1983, staff in centers for disease control and prevention (CDC) birth defects branch modified the BPA coding system and developed a classification system specific to birth defects coding, allowing coding of more detailed descriptions of birth defects and related conditions. However, the modification of the International Classification of Diseases and Related Health Problems (ICD) is the most used system (Table 4).

Birth defects were coded in chapter Q of ICD 10 book containing the following blocks:

Table 4. Classification of birth defect according to ICD 10

N^0	Diagnostic Grouping	ICD-10
1	Congenital malformations of the nervous system	Q00-Q07
2	Congenital malformations of eye, ear, face and neck	Q10-Q18
3	Congenital malformations of the circulatory system	Q20-Q28
4	Congenital malformations of the respiratory system	Q30-Q34
5	Cleft lip and cleft palate	Q35-Q37
6	Other congenital malformations of the digestive system	Q38-Q45
7	Congenital malformations of genital organs	Q50-Q56
8	Congenital malformations of the urinary system	Q60-Q64
9	Congenital malformations and deformations of the musculoskeletal system	Q65-Q79
10	Other congenital malformations	Q80-Q89
11	Chromosomal abnormalities, not elsewhere classified	Q90-Q99

1.3.6 PRENATAL DIAGNOSTIC

The development, advancement, and widespread availability of prenatal screening and diagnostic techniques have made possible the diagnosis of a wide variety of structural and genetic abnormalities prior to delivery. The ability to identify such conditions during the first or second trimester of pregnancy can facilitate alternative approaches for managing affected pregnancies, such as delivery and care of the infant at a tertiary center, undertaking therapeutic interventions during gestation (e.g., fetal surgery), or electively terminating the pregnancy. Prenatal diagnosis has also led to an increased understanding of the natural history of some abnormalities and has allowed to correlate what is observed in the fetus in utero with what is seen in the newborn.

By nature, prenatal diagnosis tends to focus on major malformations and genetic abnormalities that are severe or life threatening. Prenatal diagnosis also allows to detect characteristics such as a limb deficiency that can be identified accurately using available techniques, even when they are nonlethal. However, prenatal diagnostic techniques may not be as sensitive in identifying subtle abnormalities, minor defects, or genetic syndromes that could be diagnosed postnatally [67] .

There are two main groups of methods in prenatal diagnosis: Noninvasive methods including biochemical screening (it requires mother‘s blood sample), ultrasound, and magnetic resonance, and invasive methods including amniocentesis, chorionic villus sampling and cordocentesis (Table 5).

Ultrasound diagnosis is commonly used and provides detailed morphological information. Therefore, the majority of structural anomalies are diagnosed. Special methods like fetal echocardiography may provide additional information. The use of high frequency transvaginal scanning has sometimes anticipated ultrasound screening, performed at 11 – 14 gestational weeks.

Magnetic resonance is relatively new method in prenatal diagnosis and is still quite rare. The image processing must be very quick because the fetus is moving. However, this method is excellent in detection of brain and other soft-tissue anomalies.

Table 5. Summary of invasive prenatal diagnostic tests

	Chorionic villus sampling	**Amniocentesis**	**Cordocentesis**
Purpose	Primarily performed to obtain a fetal karyotype; to diagnose or rule out fetal chromosome problems. Can also be used for DNA testing if indicated.		
Tissue sampled	Tissue destined to become placenta	Amniotic fluid	Fetal blood
Timing	11-13 weeks	Routinely offered >15 weeks	Later in second trimester (usually > 16 weeks)
Risk of miscarriage	1%-2% transabdominal procedure 2%-6% transcervical procedure	0.5%-1.0% for a procedure performed at 15-16 weeks of gestation	3%
Other risk	Risk of limb reduction defects when performed prior to 8 weeks of gestation	2%-3% risk of premature rupture of membranes. Risk of club foot in procedures performed < 12 weeks' gestation	Fetal bradycardia Fetal bleeding
Accuracy of chromosome results	Highly accurate	Highly accurate	Highly accurate
Advantage of the test	Performed early in pregnancy with results available by 14-15 weeks Chorionic villus sampling is preferred for molecular DNA testing	Fluid also tested for alpha-fetoprotein (Neural tube defect screening) Lower risk of procedure-related miscarriage	Reserved for high-risk pregnancies where a rapid diagnosis is required for pregnancy management

Source: Society of Obstetricians and Gynaecologists of Canada, 200[68] DNA: Deoxyribonucleic acid;

Impact of prenatal diagnosis on prevalence of congenital anomalies

The impact of prenatal diagnosis on the birth prevalence of congenital anomalies depends upon several variables, including access to and utilization of prenatal testing, as well as the availability and attitudes towards pregnancy termination following a prenatal diagnosis of an anomaly.

EUROCAT recorded a total prevalence of major congenital anomalies of 23.9 per 1,000 births for 2003-2007. 17.6% of all cases ended with a termination of pregnancy following prenatal diagnosis (TOPFA)[69] . Many recent reports highlighted the dramatic impact of prenatal diagnosis on significant fall in the birth prevalence of children with congenital anomalies. However, this fall varied with the types of congenital anomalies [70-75]. In Europe, Dolk et al reported that the proportion of Down syndrome cases which were prenatally diagnosed and followed by termination of pregnancy in 1995-1999 varied from 0% in Ireland and Malta where termination of pregnancy is illegal, to less than 50% in 14 further regions, and even to 77% in Paris [72]. The Prenatal Diagnosis Committee of ICBDMS has monitored the impact of prenatal diagnosis on the prevalence of Down syndrome since1993. In 1999, 14 programs provided data on 1,757 cases. Among all recorded cases affected with Down syndrome, 53.2% were prenatally diagnosed and electively terminated. The prevalence at birth of Down syndrome decreased over seven years in many programs that showed the highest rates of terminations, suggesting that a high proportion of prenatally diagnosed cases were terminated [76].

A recent international report highlighted the dramatic impact of prenatal diagnosis on the birth prevalence of neural tube defects (Table 6)[77].

Table 6. Proportion of induced terminations (TOP) among total number of neural tube defect cases recorded, by country/registry, 1997-1998

Country/registry	Anencephaly and spina bifida				
	Number of births	Live and still births cases (n)	TOP (n)	Total cases (N)	Proportion of TOP %
Atlanta, USA	88,528	46	32	82	39.0
England and Wales	1,284,096	160	542	702	77.2
Finland	116,911	50	60	110	54.5
France	306,465	35	163	198	82.3
Hungary	198,791	43	67	110	60.9
Israel	39,963	6	1	7	14.3
Italy	305,894	66	105	171	61.4
Northern Netherlands	39,338	19	9	28	32.1
Norway	118,640	51	26	77	33.8

Source: Goujard, 2001[77]; TOP: termination of pregnancies. *.

1.3.7 REGISTRY OF CONGENITAL ANOMALIES

As the main purpose of most registries is to provide information on the prevalence of birth defects, collection of good prevalence data is likely to be expensive and difficult. Depending on logistic opportunities, registries range from those with (assumed) complete coverage of all births of a defined population to hospital-based registries that cover populations that are more vaguely defined (Table 7). Cases of birth defects are generally identified in one of two ways: through ‘active case ascertainment’ (i.e., staff conduct case finding) or through ‘passive case ascertainment’ (i.e. case reports are received by the program). While some surveillance systems use both kinds of ascertainment approaches for case identification; program activities are generally structured around one or the other approach. When comparing prevalence from such different registries, it is important to acknowledge differences – taking into account the way that birth defects are diagnosed and reported, as well as the reliability of numerators of prevalence estimates.

Table 7. Methodological approach for birth defects surveillance

Element	**Option**	
Registry	*Population based*	*Hospital based*
Surveillance	*Active*	*Passive*
Case ascertainment	*Multi-source*	*Single source*
Case definition	*All birth defect*	*Selected birth defect*
Period (age)	*Up to adulthoods*	*Newborn*
Description	*Verbatim*	*Checkbox*
Pregnancy outcome	*All (LB, SB, Abortion)*	*Live birth*
Coding system	*Own*	*ICD, BPA*
Coding process	*Central*	*Local*

LB: live birth, SB: Still birth, BPA: British Paediatric Association. ICD: International Classification of Diseases

Birth defects prevalence is directly related to the method of case identification and type of surveillance approach. Table 8 presents birth defects prevalence based on various surveillance approaches in USA[78].

Table 8. Variations in birth defects prevalence according to surveillance approach

Data Source	**% of babies reported with birth defects**
Birth certificates in 1996	1.5
Newborn hospital discharge data (Florida)	4.3-7.1
Mandatory hospital reporting (New York)	3.4
Linked data sources (North Carolina)	4.7
Active hospital surveillance (Atlanta 1992-1996)	2.6
Physical exam of infants	8.3

Source: Edmonds LD: Birth defect surveillance at the state and local level. Teratology 1997, 56: 5-9[78]

There is currently no unified national monitoring system for birth defects, although many birth defects can be observed shortly after delivery and are recorded on birth certificates. At the present time, there are only two organizations that are in cooperation with Human Genetics Programmes of WHO in doing registry of birth defects. They are International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) which has 42 members representing 38 countries spread across the five continents, and European Registration of Congenital Anomalies and Twins (EUROCAT) which has 43 members in 23 countries [79, 80].

The International Clearing-house for Birth Defects Surveillance and Research, formerly known as International Clearinghouse of Birth Defects Monitoring Systems, consists of 42 registries worldwide that collaborate in monitoring 39 types of birth defects (Table 10). There

are no standard guidelines for the methodology of data collection nor are there consistent definitions for "stillbirth". Some programmes are population based and others are hospital based. The data collections of most of registry from the developed country were obtained from multiple sources (hospital record, laboratories and cytogenetic department report) (Table 9). According report of International Clearinghouse for Birth Defects Monitoring Systems, in 2007 there were only 11 population-based national registries (Australia, Canada, Costa Rica, Czech Republic, England and Wales, Finland, Hungary, Malta, Norway, Spain and Sweden) among 42 participating programmes representing 38 countries spread across the five continents. Most of remaining registry monitoring was population-based regional registries. Some were hospital based registries (Cuba, Mexico, Chile, Iran, Israel, United Arab Emirates, China, Japan and South Africa Birth Defects Surveillance Systems) [81]. In Asia, only four countries (Iran, India, China and Japan) are members of ICBDRS. No one is from South East Asia (Figure 6).

Figure 6. Members of International Clearinghouse of Birth Defects Monitoring Systems

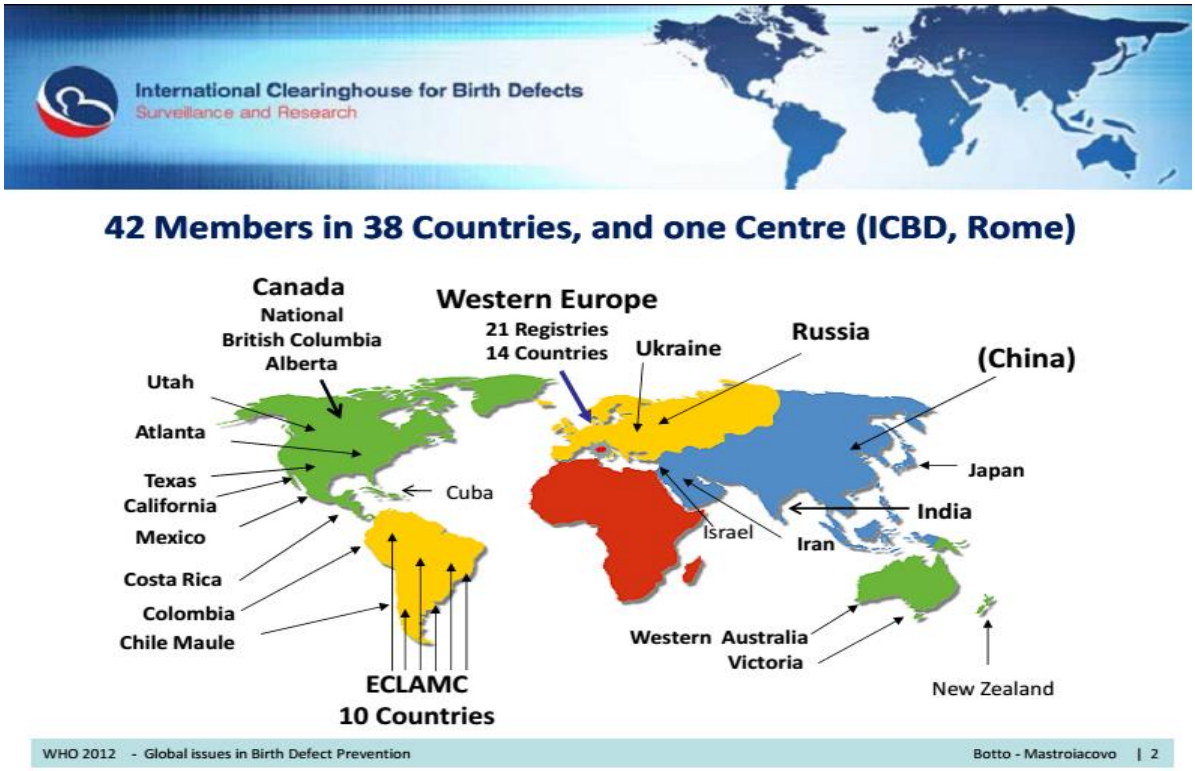


Table 9. Methodological approach for birth defects registry of selected members of ICBDRS

Registry	Canada Alberta	USA Texas	China Beijing	Japan	Costa Rica	Finland	South America	Iran
Type registry	Population-base Regional)	Population -base (Regional)	Population-based (Provincial)	Hospital-based (National)	Population-based (National)	Population-based (National)	Hospital-based (Multi national)	Hospital- Based (Regional)
Time for diagnostic	1 year	1 year	6 weeks	7 days	3 days	1 year	3 days	1 year
TOPFA included	Yes	Yes	No	No	Not permitted	Yes	No	Yes, few malformation
Still births definition	< 20 weeks or <400 g	< 20 weeks	<20 weeks	< 22 weeks	<22 weeks or <500g	<22 weeks or <500g	<500 grs	<20 weeks or <400g
Data source								
Hospital	Yes	Yes	Yes (with ultrasound)	Yes	Yes (with ultra sound)	Yes	Yes	Yes
Pathology	Yes	Yes	Yes	No	No	Yes	No	No
Cytogenetic	Yes	Yes	No	No	Yes	Yes	No	No
Birth certification	Yes	Yes	No	No	No	Yes	No	No
Death certification	Yes	No	No	No	No	Yes	No	

Source: International Clearinghouse for Birth Defects Surveillance and Research. *Annual Report 2009 with data for 2007*, Roma, Italy 2010[81].
*TOPFA :Terminations of pregnancy for fetal anomaly

Table 10. ICBDSR classification of subgroups of anomalies

Anomalies subgroups			
1	Anencephalus and similar	24	Hypospadias
2	Spina Bifida	25	Epispadias
3	Encephalocele	26	Indeterminate sex
4	Microcephaly	27	Renal agenesis
5	Arhinencephaly/holoprosencephaly	28	Cystic kidney
6	Hydrocephalus	29	Bladder exstrophy
7	Anophthalmos	30	Polydactyly, preaxial
8	Micropthalmos	31	Total Limb reduction defects (include unspecified)
9	Unspecified Anophthalmos/Microphthalmos		Transverse
10	Anotia		Preaxial
11	Microtia		Postaxial
12	Unspecified Anotia/Microtia		Intercalary
13	Transposition of great vessels		Mixed
14	Tetralogy of Fallot		Unspecified
15	Hypoplastic left heart	32	Diaphragmatic hernia
16	Coarctation of aorta	33	Omphalocele
17	Choanal atresia	34	Gastroschisis
18	Cleft lip with or without palate	35	Unspecified Omphalocele/Gastroschisis
19	Cleft palate	36	Prune belly sequence
20	Oesophageal atresia/stenosis with or without fistula	37	Trisomy 13
21	Small intestine atresia/stenosis	38	Trisomy 18
22	Anorectal atresia/stenosis	39	Down syndrome
23	Undescended testis		

EUROCAT

EUROCAT is a European network of population-based registries for the epidemiologic surveillance of congenital anomalies. It was started in 1979 and now more than 1.5 million births per year in Europe are surveyed by 43 registries in 23 European countries. EUROCAT Central Registry is currently located at the University of Ulster, Ireland and it houses a standardized central database on cases of congenital anomaly among live births, stillbirths and terminations of pregnancy. This database is updated regularly. EUROCAT registries follow standardized guidelines and employ multiple sources of case ascertainment. They include all infants/still birth (from 20 weeks gestation) with anomalies diagnosed until one year of life. Most of major birth defect types are included. Terminations of pregnancy for fetal anomaly (TOPFA) are also included. The criteria which must be met by registries participating in EUROCAT include the definition of population, data collection and ascertainment, definition and coding of defects, calculation of prevalence rates and confidentiality. In this way, comparisons between prevalence data are possible. The coding system ICD/BPA10 - is the background for the EUROCAT coding (Table 11). Most of major birth defect types are included. Different prenatal screening policies and practices, differences in uptake of prenatal screening and diagnosis due to cultural and organizational factors, and differences in TOPFA laws influence the rate of TOPFA in the population. TOPFA is not encouraged in Poland, and can only be done in case of lethal anomaly. Some countries allow TOPFA at any gestational age (Austria, Belgium, Croatia, England & Wales, France, Germany). Others have an upper gestational age (22-24 weeks) (Finland, Italy, Spain, Sweden Switzerland and Denmark) and yet others have an upper gestational age limit but allow TOPFA for lethal anomalies beyond this limit (Netherlands, Norway, Portugal, Denmark). TOPFA is illegal in Malta and Ireland [51, 69, 80, 82].

Table 11a. EUROCAT definition and coding of the anomalies subgroups

Anomaly	Description of anomaly	ICD10	Comments
All Anomalies	Any case coded within the Q chapter of ICD 10 and other relevant parts of chapters transmitted to EUROCAT	**Q*, D215, D821, D1810, P350, P351, P371**	**Exclude all minor anomalies**
Nervous system		Q00, Q01, Q02, Q03, Q04, Q05, Q06, Q07	
Neural Tube Defects	Neural tube defects inlcude anencephalus, encephalocele, spina bifida and iniencephalus.	Q00, Q01, Q05	
Anencephalus and similar	Total or partial absence of brain tissue and the cranial vault. The face and eyes are present. (incompatible with life)	Q00	
Encephalocele	Cystic expansion of meninges and brain tissue outside the cranium. Covered by normal or atrophic skin.	Q01	exclude if associated with anencephalus
Spina Bifida	Midline defect of the osseous spine usually affecting the posterior arches resulting in a herniation or exposure of the spinal cord and/or meninges.	Q05	exclude if associated with anencephalus, or encephalocele
Hydrocephalus	Dilatation of ventricular system, not due to primary atrophy of the brain, with or without enlargement of the skull.	Q03	exclude hydranencephaly, or association with NTDs
Microcephaly	A reduction in the size of the brain with a skull circumference less than three standard deviations below the mean for sex, age and ethnic origin. Definitions known to vary between clinicians and regions.	Q02	exclude association with NTDs
Arhinencephaly/holoprosencephaly	Absence of the first cranial (olfactory) nerve tract. There is a spectrum of anomalies from a normal brain, except for the first cranial nerve tract, to a single ventricle (holoprosencephaly).	Q041, Q042	
Eye		**Q10-Q15, exclude Q135**	
Anophthalmos/micropthalmos	Anophthalmos: Unilateral or bilateral absence of the eye tissue. Clinical diagnosis; Micropthalmos: Small eye/eyes with smaller than normal axial length. Clinical diagnosis.	Q110, Q111, Q112	
Anophthalmos	Unilateral or bilateral absence of the eye tissue. Clinical diagnosis.	Q110, Q111	
Congenital cataract	Alteration in the transparency of the crystalline lens.	Q120	
Congenital glaucoma	Large ocular globe as a result of increased ocular pressure in fetal life.	Q150	
Ear, face and neck		**Q16, Q178, Q183, QQ187-Q189**	
Anotia	Absent pinna, with or without atresia of ear canal.	Q160	
Urinary		**Q60-64, Q794 exclude Q627, Q633**	
Bilateral renal agenesis including Potter syndrome	Bilateral absence, agenesis, dysplasis or hypoplasia of kidneys including Potter's syndrome. Incompatible with life	Q601, Q606	exclude unilateral Q600.
Renal dysplasia	Maldevelopment of kidney tissue	Q614	
Congenital hydronephrosis	Obstruction of the urinary flow from kidney to bladder. Only if renal pelvis is 10mm or more after birth	Q620	
Bladder exstrophy and/or epispadia	Defect in the closure of the bladder and lower abdominal wall	Q640, Q641	
Posterior urethral valve and/or prune belly	urethral obstruction with dilatation of bladder and hydronephrosis. In severe cases also distended abdomen	Q6420, Q794	
Genital		**Q50-Q52 , Q54-Q56 exclude Q523, Q525**	
Hypospadias	The urethral meatus is abnormally located and is displaced proximally on the ventral surface of the penis	Q54	
Indeterminate sex	Includes true and pseudohermaphroditism male or female	Q56	
Oro-facial clefts		**Q35-Q37**	
Cleft lip with or without palate	Clefting of the upper lip with or without clefting of the maxillary alveolar process and hard and soft palate	Q36-Q37	
Cleft palate	Fissure defect of the soft and/or hard palate(s) or submucous cleft without cleft lip	Q35	

Table 11b. EUROCAT definition and coding of the anomalies subgroups

Anomaly	Description of anomaly	ICD10	Comments
Congenital heart defects		**Q20-Q26**	
Severe congenital heart defects	Severe congenital heart defects have higher perinatal mortality and TOPFA rates. Most livebirths require surgery for survival. It includes: single ventricle, tricuspid atresia, Ebstein's anomaly, hypoplastic left heart, hypoplastic right heart, common arterial truncus, transposition of great vessels, atrioventricular septal defects, tetralogy of fallot, pulmonary valve atresia, aortic valve atresia/stenosis, coarctation of aorta and total anomalous pulmonary venous return.	Q200, Q203-Q204, Q212-Q213, Q220, Q224-Q226,Q230, Q234, Q251, Q262	
Common arterial truncus	Presence of a large single arterial vessel at the base of the heart (from which the aortic arch, pulmonary and coronary arteries originate), always accompanied by a large subvulvar septal defect.	Q200	
Transposition of great vessels	Total separation of circulation with the aorta arising from the right ventricle and the pulmonary artery from the left ventricle.	Q203	
Single ventricle	Only one complete ventricle with an inlet valve and an outlet portion even though the outlet valve is atretic.	Q204	
Ventricular septal defect	Defect in the ventricular septum.	Q210	Exclude unilateral Q600.
Atrial septal defect	Defect in the atrial septum.	Q211	
Atrioventricular septal defect	Central defect of the cardiac septa and a common atrioventricular valve includes primum ASD defects.	Q212	
Tetralogy of Fallot	VSD close to the aortic valves, infundibular and pulmonary valve stenosis and over-riding aorta across the VSD.	Q213	
Tricuspid atresia and stenosis	Obstruction of the tricuspid valve and hypoplasia of the right ventricle.	Q224	
Ebstein's anomaly	Tricuspid valve displaced with large right atrium and small right ventricle.	Q225	
Pulmonary valve stenosis	Obstruction or narrowing of the pulmonary valves which may impair blood flow through the valves.	Q221	
Pulmonary valve atresia	Lack of patency or failure of formation altogether of the pulmonary valve, resulting in obstruction of the blood flow from the right ventricle to the pulmonary artery	Q220	
Aortic valve atresia/stenosis	Occlusion of aortic valve or stenosis of varying degree, often associated with bicuspid valves	Q230	Exclude PDA in preterm/LBW babies (<37 weeks)
Hypoplastic left heart	Hypoplasia of the left ventricle, outflow tract and ascending aorta resulting from an obstructive lesion of the left side of the heart	Q234	
Hypoplastic right heart	Hypoplasia of the right ventricle, always associated with other cardiac malformations	Q226	
Coarctation of aorta	Constriction in the region of aorta where the ductus joins aorta	Q251	
Total anomalous pulm venous return	All four pulmonary veins drain to right atrium or one of the venous tributaries	Q262	
PDA as only CHD in term infants (>=37 weeks)		Q250 Q250	
Respiratory		**Q30-Q34, exclude Q314 & Q320**	
Choanal atresia	Bony or membraneous choanae with no passage from nose to pharynx	Q300	
Cystic adenomatous malf of lung	Cystic structures of the lung, usually unilateral	Q3380	
Skeletal dysplasias		**Q7402, Q77, Q7800, Q782-Q788**	
Craniosynostosis	Premature closure of cranial sutures	Q750	
Congenital constriction bands/amniotic band	Bands in the amniotic fluid that causes constriction of part of the brain, body or limbs, including limb-body-wall complex	Q7980	
Situs inversus	Inverse position of thoracic or abdominal organs or both	Q893	
Conjoined twins	Siamese twins	Q894	
Congenital skin disorders		Q80-Q82	
Abdominal wall defects		**Q792, Q793, Q795**	Exclude association with holoprosencephaly or anencephaly subgroups
Gastroschisis	Protrusion of abdominal contents through an abdominal wall defect lateral to an intact umbilical cord and not covered by a membrane	Q793	
Omphalocele	Herniation of abdominal content through the umbilical ring, the contents being covered by a membrane somethimes ruptured at the time of delivery	Q792	

Table 11c. EUROCAT definition and coding of the anomalies subgroups

Anomaly	Description of anomaly	ICD10	Comments
Digestive system		**Q38-Q39, Q402-Q409, Q41-Q45**	Exclude Q381, Q382, Q3850, Q430, Q4320, Q4381, Q4382
Oesophageal atresia with or without tracheo-oesophageal fistula	Occlusion or narrowing of the oesophagus with or without tracheo-oesophagael fistula	Q390-Q391	
Duodenal atresia or stenosis	Occlusion or narrowing of duodenum	Q410	
Atresia or stenosis of other parts of small intestine	Occlusion or narrowing of other parts of small intestine	Q411-Q418	
Ano-rectal atresia and stenosis	Imperforate anus or absence or narrowing of the communication canal between the rectum and anus with or without fistula to neighbouring organs	Q420-Q423	
Hirschsprung's disease	Absence of the parasympatic ganglion nerve cells (aganglionosis) of the wall of the colon or rectum. May result in cong megacolon	Q431	
Atresia of bile ducts	Congenital absence of the lumen of the extrahepatic bile ducts	Q442	
Annular pancreas	pancreas surrounds the duodenum causing stenosis	Q451	
Diaphragmatic hernia	Defect in the diaphragm with protrusion of abdominal content into the thoracic cavity. Various degree of lung hypoplasia on the affected side	Q790	
Limb		**Q650-Q652, Q658-Q659, Q660, Q681-Q682, Q688, Q69-Q74**	Exclude Q6821
Limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the limbs	Q71-Q73	
Upper limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the upper limb(s)	Q71	
Lower limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the lower limb(s)	Q72	
Complete absence of a limb	Complete absence of a limb	Q710, Q720, Q730	
Club foot - talipes equinovarus	Foot anomaly with equinus of the heel, varus of the hindfoot and adductus of the forefoot	Q660	
Hip dislocation and/or dysplasia	Location of the head of the femur outside its normal position	Q650-Q652, Q6580, Q6581	
Polydactyly	Extra digit or extra toe	Q69	
Syndactyly	Partial or total webbing between 2 or more digits includes minor forms	Q70	
Teratogenic syndromes with malformations		**Q86, P350, P351, P371**	
Fetal alcohol syndrome	Fetal exposure to alcohol during pregnancy with following impact on fetal growth, facial appearence and development	Q860	
Valproate syndrome	Fetal exposure to valproate during pregnancy with impact on fetal growth, facial appearance and development. Often associated with spina bifida	Q8680	
Maternal infections resulting in malformations	Maternal viral infections during pregnancy	P350, P351, P371	
Genetic syndromes + microdeletions		**Q4471, Q6190, Q7484, Q751, Q754, Q7581, Q87, Q936, D821**	Exclude Q8703, Q8704, Q8706, Q8708, Q8716, Q8724, Q8726
Sequences		Q606, Q6410, Q794, Q7980, Q8703, Q8708, Q8724, Q8980	
Chromosomal		**Q90-Q93, Q96-Q99**	Exclude Q936
Down Syndrome	karyotype 47,xx +21 or 47,xy +21 and translocations/mosaicism	Q90	
Patau syndrome/trisomy 13	karyotype 47,xx +13 or 47,xy +13 and translocations/mosaicism	Q914-Q917	
Edwards syndrome/trisomy 18	karyotype 47,xx +18 or 47,xy +18 and translocations/mosaicism	Q910-Q913	
Turner syndrome	karyotype 45,x or structural anomalies of X chromosome	Q96	
Klinefelter syndrome	karyotype 47,xxy or additional x-chromosomes	Q980-Q984	
Anomalies outside normal range			

1.3.8 PREVALENCE OF CONGENITAL ANOMALIES

After long years of debate, the preferred term to describe the frequency of occurrence of birth defects is "prevalence" rather than "incidence". This is in recognition of the high loss rate due to early spontaneous abortions of affected fetuses, so that the "prevalence" represents survival to late pregnancy or birth of the fetus. Counts of early spontaneous abortions (malformed and non-malformed) are generally not available in health data, and diagnosis of congenital anomalies in early spontaneous abortions is very incomplete. With increasing availability of prenatal screening and diagnosis, followed in many countries with the option to terminate an affected pregnancy, terminations of pregnancy for fetal anomaly (TOPFA) have been included in prevalence rates, on the premise that the vast majority wouldn't survived if TOPFA was not performed, and thus they arise from the same population described by the births denominator. This assumption would need to be questioned if the proportion of early TOPFA, with a higher natural spontaneous abortion probability, increases.

Total prevalence of BDs varies greatly from country to country. The frequency depends on the time of observation after birth, the types of malformation included, and the differences in reporting and statistical procedures. This diversity makes difficult the comparison of rates between the different registry programmes. Many studies reported on the prevalence of congenital anomalies in developed countries. Available data on this matter are very rare in developing countries and they are based on hospital births over a period of time rather than on population [80, 83-85].

According to the annual report of birth defect in Canada in 2002, the total birth prevalence of birth defects was 20-30 per 1000 births [50]. In USA the total prevalence was about 30/1000 live births [86]. In Europe, EUROCAT Report 2007 presented a total prevalence (including fetal deaths and terminations of pregnancy for fetal anomaly) of 23.7 per 1,000 births. The live birth prevalence of congenital anomalies was 19.8 per 1,000 live births. The highest total prevalence was recorded in Mainz Germany (56.2/1000 births) and the lowest in Spain and Portugal (10/1000 births) [51]. In Asia, the total prevalence in Singapore was 24 per 1000 births, the birth prevalence(still birth and live birth) of birth defect was 16.85 per 1000 births[87] and live birth prevalence of birth defect was 13.9 per 1000 live births[88]. The birth prevalence of birth defect was 14.3/1000 births in Malaysia [54], 15.4/1000 births in China[89], 12/1000 births in India[83] and 18/1000 in Korea[90]. Song Li et al presented a prevalence of all external birth defects (minor and major birth defect) of 21.75/1000 total births and a

prevalence of all major external birth defects of 7.69/1000 total births in a population - based study in China in 2003 [91] .

The most frequent groups of congenital anomalies were those of heart, musculoskeletal, urinary, chromosomal, and nervous systems (Table 12).

Table 12. Prevalence of congenital anomalies by country.

Anomaly	Eurocat	Malta	Belgium	USA	Australia	China	Taiwan
Nervous system	2.54	1.52	2.45	1.59	2.27	3.09	0.66
Eye	0.35	0.00	0.51	0.86	0.54	-	0.053
Ear, face and neck	0.19	0.77	0.32		0.75	-	-
Congenital heart defects	7.32	12.0	8.36	19.65	15.27	1.71	1.47
Respiratory	0.45	-	-	0.41	1.38		0.07
Oro-facial clefts	1.51	0.77	1.81	1.68	1.74	1.61	1.75
Digestive system	1.66	1.53	1.67	3.18	30.1	0.96	0.63
Urinary	3.21	1.78	5.86	-	6.69	-	0.71
Genital	1.95	3.21	1.84	5.61	5.61	-	0.43
Limb	0.40	4.33	4.15	4.01	3.86		2.05
Skeletal dysplasias	0.86	1.28	2.65	-	12.1	2.06	-
Chromosomal	3.56	2.81	3.38	1.68	6.28	-	0.79

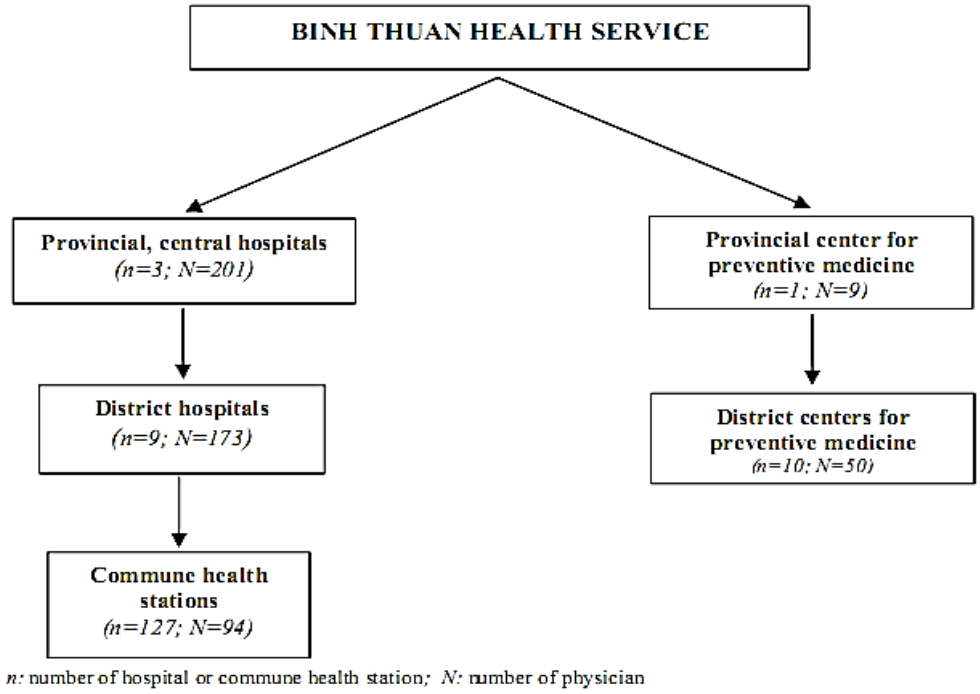
Source from reference [45, 92-97]

1.4 THE PROVINCE OF BINH THUAN

Binh Thuan is a mixed rural province located along the south-central coast of Vietnam, with a population of approximately 1.1 million inhabitants living mainly from agricultural production on an area of 7,992 km^2, divided over 127 administrative communes whereof one is located on an island and 6 are found in mountainous areas. Binh Thuan has more 27 ethnic groups living together, including Kinh, Cham, K'ho, Rai, Chan Ro, Nung, Tay.etc. Kinh ethnic group, with 973, 863 people, account for about 93% of population; it is also the predominant ethnic group of all Vietnamese regions. They have political and economic power and are generally richer than minority groups, with easier access to infrastructure, health services, and education. Minority peoples total nearly 73,137 persons and account for about 7 % of the province's population. The most important ethnic minoritie is Cham, with 29,356 people, accounting for 2.80%, followed by Ra-glai, with 12 541 people, accounting for 1.19%, Chinese, with 11,204 peoples, accounting for 1.07%, and over 24 other ethnic minorities groups, with 20,306 people, accounted for 1.92% of the province's population. Binh Thuan has an organizational health care structure at three levels: three provincial or central health centers with 201 physicians, 10 district health centers with 173 physicians and 127 commune health stations (CHS) with 94 physicians (Figure 7). All CHS provide obstetric and mother- and - child health care, implement prevention programs such as immunization, health promotion but there is less than one physician per CHS and most deliveries are supervised by skilled midwifes who have access to oral and intramuscular drugs and simple small surgical equipment. Delivery forceps and complicated cases are referred to the closest district hospital by an ambulance of district hospital, taxi or more commonly by motorbike.

In Binh Thuan, like in all provinces of Vietnam, the under-5 child mortality rate is collected from routine reports based on the death records at the commune level (A6/YTCS) designed by the Ministry of Health of Vietnam, but the form is very simple and designed more for administrative purpose than for medical purpose. Child death cases are not documented about demographic characteristics (age/gender), socio-economic situation (parents' income, occupation, educational level), urban/rural areas etc.

Figure 7. Structure of Binh Thuan's health care system



n: number of hospital or commune health station; *N:* number of physician

The data on infant mortality are used for provincial statistics and surveys but without specific report on neonatal mortality. Binh Thuan hasn't program of prenatal diagnosis at any level of health care.

The good structure of healthcare at all levels, good access to primary care and a stable population representing the country's major ethnic group, were all suitable conditions for implementing a community-based project to set up a birth defect registry and to study neonatal mortality for the whole population, from the grassroots level to the topmost level of health care in the Province of Binh Thuan.

2 RATIONALE OF OUR STUDY

Neonatal mortality and birth defects have been recognized as a severe public health problem. In developing countries, the neonatal mortality constitutes an important public health problem with both medical and economical implications. Neonatal deaths now account for more than two-thirds of all deaths in the first year of life and for half of all deaths in under-five children. However, in developing countries neonatal mortality have attracted relatively little attention compared to maternal mortality or under-five mortality and in international public health policy and programmes, neonatal deaths still do not receive attention commensurate with their burden [14, 98, 99]. Achieving MDG4 (Millennium Development Goal Nr 4: Reduce child mortality), one of the most important items in the MDGs, will therefore need to include reducing deaths during the neonatal period.

Worldwide, the congenital anomalies continue to be major causes of neonatal and infant mortality follow by low birth weight, infection and asphyxia [14, 20]. The impact of birth defects on the future child, on the child's family and on the community is not restricted to mortality; it also involves the morbidity and disability experienced by those who survive. Available data on this matter are very rare in developing countries and they are based on hospital births over a period of time rather than on population [80, 83-85]. The World Health Organization has indicated the necessity to evaluate the potential burden of congenital anomalies in every country, at whatever stage of development, with a view to introducing preventive measures at the appropriate time.

The Vietnamese government has identified perinatal health and neonatal mortality as priority areas and evidence-based guidelines on reproductive health were launched in 2003 for improving newborn care and survival [31].

There are currently no data on birth defects available at the population level in Vietnam. Vietnam hasn’t had any organization in charge of doing registry or surveillance of birth defects. In Vietnam, the under-five mortality rate has dropped considerably over the last 30 years (55/1,000 to 30/1,000), while neonatal mortality remained basically unchanged in the range of 15/1,000 during the time period 1970–2000 [32]. There have been few studies on neonatal mortality in communities in Vietnam and no data on NMR in communities of Southern Vietnam have been published yet.

Vietnam has good policies to provide equitable healthcare for people, and Vietnam has a good structure of primary health care; these are two suitable conditions for implementing a population-based program study for neonatal mortality and congenital anomalies.

Reliable data on congenital anomalies and neonatal mortality in the resource-limited setting of Vietnam provide accurate informations on the burden of congenital anomalies and neonatal mortality. Such data can be useful to identify and prioritise interventions, especially low-cost interventions that improve perinatal care and outcomes in this population. Such data also provide evidence for maternal health program and policy development.

3 OBJECTIVES AND RESEARCH QUESTIONS

The purpose of this project was to determine whether or not any disparities exist in the prevalence of congenital anomalies between the regions of the Province of Binh Thuan or between the Province of Binh Thuan and other registries in the world, and to establish a network of all health professionals performing a physical examination of newborns for detecting congenital anomalies. Our study aim was also to determine the prevalence of neonatal mortality and their determinants in the Province of Binh Thuan. Although in the Province of Binh Thuan, all CHS have skilled midwives and all hospitals have an obstetric department, there is a lack of pediatrician and of modern material devices such as ultrasound in many district hospitals. We therefore restricted our project to external congenital anomalies.

This thesis has addressed the following questions:

1. What is prevalence of external congenital anomalies in the Province of Binh Thuan?
2. Are there any differences in prevalence of external congenital anomalies between districts of the Province of Binh Thuan?
3. Is the prevalence of babies with external congenital anomalies in the Province of Binh Thuan significantly different from other registries?
4. What factors are associated with external congenital anomalies in the Province of Binh Thuan?
5. Is the detection rate of external congenital anomalies at hospital level different from that at the commune health station level?
6. What is the rate of neonatal mortality in the Province of Binh Thuan?
7. What are the leading causes of neonatal deaths in the Province of Binh Thuan ?
8. Are there factors associated with neonatal deaths in the Province of Binh Thuan?
9. What is the prevalence of heart murmurs in infants born in the Province of Binh Thuan ?
10. Is the infant growth curve in the Provicne of Binh Thuan different from WHO standards?

4 METHODS

A 2-months training of 452 health professionals giving delivery cares in 127 Commune Health Stations (CHS) and in 12 provincial or district hospitals (DH) was setup in 2006. After a successful 6-months pilot study, a one-year registry of EBDs was established in 2008, and subsequently a whole registry in 2010.

Data were collected by examining the newborns and interviewing the mothers. All live births of women who resided in the province were physically examined to detect EBDs within 24 hrs after birth in all DH obstetric departments and in all CHS. All deaths occurring within first month of live were registered at all health facilities in whole the Province of Binh Thuan.

The CAs screening in infant ≤ 9 months was integrated into the vaccination and child malnutrition control program at all CHS in the district of La Gi in the Province of Binh Thuan. All live births born between 1November 2009 and 30 October 2010 in the Lagi district were examined for detecting heart murmur and other CAs can be detected by simple examinations, whenever they come to CHS for vaccination or for status nutrition verification, according to current immunization and malnutrition control program schedule at 3^{th}, 6^{th} and 9^{th} month of life.

Techniques of examination were primarily systematically observing, palpating and measuring the length, the weight, and the head circumferences of the newborn. Results of the examinations of each newborn were then noted in the predesigned forms, along with information on characteristics of mother and child that were collected by direct interview of the mother. In case of suspecting EBDs, a detailed clinical description of the EBD was collected and a photo of EBD was taken by a trained local health professional.

Interviewers were medical doctors, assistant physicians or midwives who give delivery care to pregnant women or who give direct examination to newborns at any level of the health facilities. Notification forms were filled when the mother was interviewed, when the newborn was examined and also at the time of infant examination.

The methods of measurements used were based on the recommendation of the WHO[100]. Birth-weight measurements were obtained at delivery using a scale that was accurate to 10 grams. Infants were measured fully unclothed and in the supine position. Recumbent length was measured with a baby board (UNICEF) and recorded to the nearest 0.1cm. A nonflexible

plastic tape was used for measuring head circumference and the result was also recorded to the nearest 0.1 cm. Absolute poverty legal certificates or poverty legal certificates, housing type, and personal income per month were used to classify maternal economic status.

Early Neonatal Mortality Rate (ENMR) was defined as number of deaths during the first completed six days of life per 1,000 life births. Late Neonatal Mortality Rate (LNMR) was defined as number of deaths between 7 and 27 days per 1,000 live births. Neonatal deaths were defined as neonates who were born alive but died within 28 days after birth. The Neonatal Mortality Rate (NMR) was calculated per 1,000 live births.

EBDs were coded using the International Classification of Diseases system-10, Clinical Modification (ICD10-CM) and common EBDs were pictured in an atlas along with a brief description of the defect. A final review of diagnoses including review of photographs and written describing EBDS was done by Pr. Yves Gillerot who is a Belgian expert clinical geneticist. In case of disagreement between the written descriptions, photographs and the coding, all records of newborn with EBDs were reviewed again and discussed with local pediatrics physicians. The team decided the most likely diagnosis as a group.

A newborn with multiple external defects was counted as one case unit, with regard to analysis of characteristics of birth defect cases. A newborn can have more than one defect. Each defect was counted as one unit when specific analyses for that particular defect or for system defect were performed. As a result, numerically adding up the number of defects would exceed the number of cases with defects.

The cause of deaths which was based on the patient profile provided by facilities health was reviewed by a local expert pediatric physician. The cause of a neonatal death was also assigned according to the event that caused the death, as follows: preterm or low birth weight, birth asphyxia or hypoxia, infection, congenital abnormality, other, and unknown.

Data collection of external congenital anomalies at birth was performed by means of a structured form which contained the three following parts: The first part contains demographic profile of the mother, medical and obstetric history, and complications in present pregnancy and labor. The second part pertains to neonatal characters including Apgar score, gestational age, birth weight, head circumference, length, sex, history of birth defects in siblings.The third part was about diagnosed congenital anomalies with checklist.

The data of neonatal deaths was filled in the notification form contained the following for all neonatal deaths: place of death, mother's name, address, sex of baby, date of death, date of birth, place of birth, and cause of death. These data were later cross-checked with data collected by the birth defect registry that covered all live births to a mother residing in the province. The data on mother's demographic profile, mother's obstetric characteristics, and neonatal characteristics including sex, gestational age, and birth weight were extracted from the birth defect registry to be linked with neonatal deaths. All local health participants received a Manual guide of CA detection which has following contents: 1.How to examine newborns to detect congenital anomalies; 2. How to measure the anthropometrics parameters. 3. How to fill in the form correctly; 4 Atlas with the picture of common external congenital anomalies along with a brief description of defect.

Alongside Manual guide of CA, the participant had also a Manual of Data Management which has four major contents concerning steps from checking and editing notification forms to making a data file and sending it to Binh Thuan Health Service by the time regulation. There were also minor contents concerning the preset codes of health facilities, administrative- geographic units, and ethnic groups. This manual is for data processors and used with a Microsoft Excel designed sheet which was ready for entering the data.

All of the forms in paper version were checked and edited by local trained data processor, so that missing or invalids can't be missed. Then, data were entered with Microsoft Excel designed sheet and than sent monthly to trained data processors from Binh Thuan Health Service who checked all the notification forms, data files and pictures for their quantities and appropriateness before transferring to the central processor unit at University of Medicine Pham Ngoc Thach who checked all the notification forms, data files and pictures for their quantities and appropriateness before processing and analyzing the data with STATA.

Statistical analyses were performed using STATA statistical software. We used Poisson model to compute 95% confidence intervals on mortality and on ratios for assessing risk factors related to neonatal death.

The study was approved by the Binh Thuan Provincial Health Service and the Pham Ngoc Thach University Ethical Review Committee, Hochiminh City, Vietnam. All mothers provided written informed consent for themselves and their baby prior to enrolment in the study, and consent to photograph was obtained from the parents of an affected newborn. Informed consent was obtained from all participants.

5 RESULTS

5.1 EXTERNAL CONGENITAL ANOMALIES AT BIRTH

Article: External birth defects in Southern Vietnam: a population-based study at the grassroots level of health care in Binh Thuan province

Authors: *Truong Hoang, Dung The Nguyen, Phuong Van Ngoc Nguyen, Dong A Tran, Yves Gillerot, Raymond Reding and Annie Robert.*

Journal: BMC Pediatrics 2013, 13:67

SUMMARY:

Background: There currently exists no data on birth defects from population-based studies in Vietnam. Our study's aim was to assess external birth defect (EBD) prevalence among live newborns in Binh Thuan Province in Vietnam with the help of health workers at all levels of the health system.

Methods: A 2-month training session for 452 health professionals (HP) practicing delivery care in 127 Commune Health Stations (CHS) and in 12 provincial or district hospitals (DH) was setup in 2006. After a successful 6-month pilot study, a one-year registry of EBDs was established in 2008. All live newborns were screened for EBDs within 24 hours after birth in all DH obstetric departments and in all CHSs. Trained local HPs collected information by filling out a predesigned form and by photographing the affected newborn. EBDs were coded using the International Classification of Diseases system-10, Clinical Modification. The study was repeated in 2010.

Results: Throughout 2010, out of a total of 13,954 newborns, 84 cases with one or more EBDs were reported, representing an overall prevalence rate of 60.2 per 10,000 live births. The most common groups of EBDs were limbs (27.2/10,000), orofacial clefts (20.1/10,000) and the central nervous system (7.9/10,000).

Conclusions: This first population-based study in Vietnam, which required coordination efforts at the local level, provides baseline prevalences of external birth defects. Data on EBDs from this study in southern Vietnam may be useful for setting up a regional population-based registry of birth defects in Vietnam.

Keywords: Birth defect, External birth defect, Population-based study, Southern of Vietnam, Live births, ICD-10, Limbs defect, Orofacial clefts.

BMC Pediatrics

RESEARCH ARTICLE Open Access

External birth defects in southern Vietnam: a population-based study at the grassroots level of health care in Binh Thuan province

Truong Hoang[1,4*], Dung The Nguyen[1], Phuong Van Ngoc Nguyen[1,4], Dong A Tran[1], Yves Gillerot[2], Raymond Reding[3] and Annie Robert[4]

Abstract

Background: There currently exists no data on birth defects from population-based studies in Vietnam. Our study's aim was to assess external birth defect (EBD) prevalence among live newborns in Binh Thuan Province in Vietnam with the help of health workers at all levels of the health system.

Methods: A 2-month training session for 452 health professionals (HP) practicing delivery care in 127 Commune Health Stations (CHS) and in 12 provincial or district hospitals (DH) was setup in 2006. After a successful 6-month pilot study, a one-year registry of EBDs was established in 2008. All live newborns were screened for EBDs within 24 hours after birth in all DH obstetric departments and in all CHSs. Trained local HPs collected information by filling out a predesigned form and by photographing the affected newborn. EBDs were coded using the International Classification of Diseases system-10, Clinical Modification. The study was repeated in 2010.

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Background

The toll of birth defects worldwide has been recognized as a severe public health problem. Birth defects, affecting 2-3% of all infants, are a major cause of perinatal mortality and childhood morbidity in both developed and developing countries [1–5].

Many studies have reported the prevalence of congenital anomalies in developed countries. Available data on this matter is very rare, however, in developing countries. Moreover, the few studies available are based on hospital births over a period of time rather than on a population [1,6–8].

At the present time, there are only two organizations in cooperation with the WHOs Human Genetics Programme in order to establish a registry of birth defects. These organizations are: the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), which has 46 members representing 31 countries spread across the five continents [9], and the European Registration of Congenital Anomalies and Twins (EUROCAT), which has 43 members in 23 countries [10].

EUROCAT registries follow standardized guidelines and use multiple-source case ascertainment methods. They include all infants, including still births (from 20 weeks

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gestation), with anomalies diagnosed within the first year of life. Most major birth defect types are included. Termination of pregnancy for foetal anomaly (TOPFA) is also included. The criteria that must be met by registries participating in EUROCAT include a definition of the population, data collection and ascertainment, definition and coding of defects, calculation of prevalence rates, and confidentiality [8].

There is currently no data on birth defects available at the population level in Vietnam. The country is lacking an organization that is responsible for the registry or surveillance of birth defects. However, Vietnam has strong policies that seek to provide equitable healthcare for its people, as well as a good primary healthcare structure. EBD surveillance is therefore possible.

Binh Thuan is a rural province located along the south-eastern coast of Vietnam, with a population of approximately 1.1 million on an area of 7,992 km^2, divided over 127 administrative communes. The population is over 90% Kinh ethnicity, which is the predominant ethnic group in Vietnam. As presented in Figure 1, Binh Thuan has an organizational health care structure at three levels: provincial or central health centers, district health centers and commune health stations (CHS).

All CHSs provide obstetric and mother-and -child healthcare, and implement prevention programs such as immunization and health promotion. However, there is less than one physician per CHS and most deliveries are supervised by midwives. Binh Thuan does not have a program for prenatal diagnosis at any level of healthcare. The good structure of healthcare at all levels, good access to primary care and a stable population representing the country's major ethnic group were all suitable conditions for implementing a population-based program for a birth defect registry within a population from the grassroots level to the topmost level of health care in Binh Thuan province.

Our study's aim was to assess EBD prevalence among live newborns in Binh Thuan Province in Vietnam with the help of health workers at all levels of the health system.

Methods

A 2-month training session for 452 HP practicing delivery care in 127 Commune Health Stations (CHS) and in 12 provincial or district hospitals (DH) was setup in 2006. After a successful 6-months pilot study, a one-year registry of EBDs was established in 2008. After a few modifications in the setup, we conducted a whole registry in 2010.

In order to be included in this study, (1) the mother had to reside in the province, (2) the mother had to sign a consent form for enrolment in the study, (3) gestational age had to be at least 22 weeks, and (4) the baby had to be alive at birth.

All live births were physically examined to detect EBDs within 24 hours after birth in all DH obstetric departments and in all CHSs. When an EBD was suspected, a detailed clinical description of the EBD was collected and a photo of EBD was taken by a trained local health professional.

Trained local HPs collected information by filling out a predesigned form and by photographing the affected newborn. An external birth defects atlas and a manual for detecting EBDs in newborns were provided to each HP during training.

Data collection was performed by means of a structured form which contained three parts. The first part inquired on the mother's demographic profile, on medical and

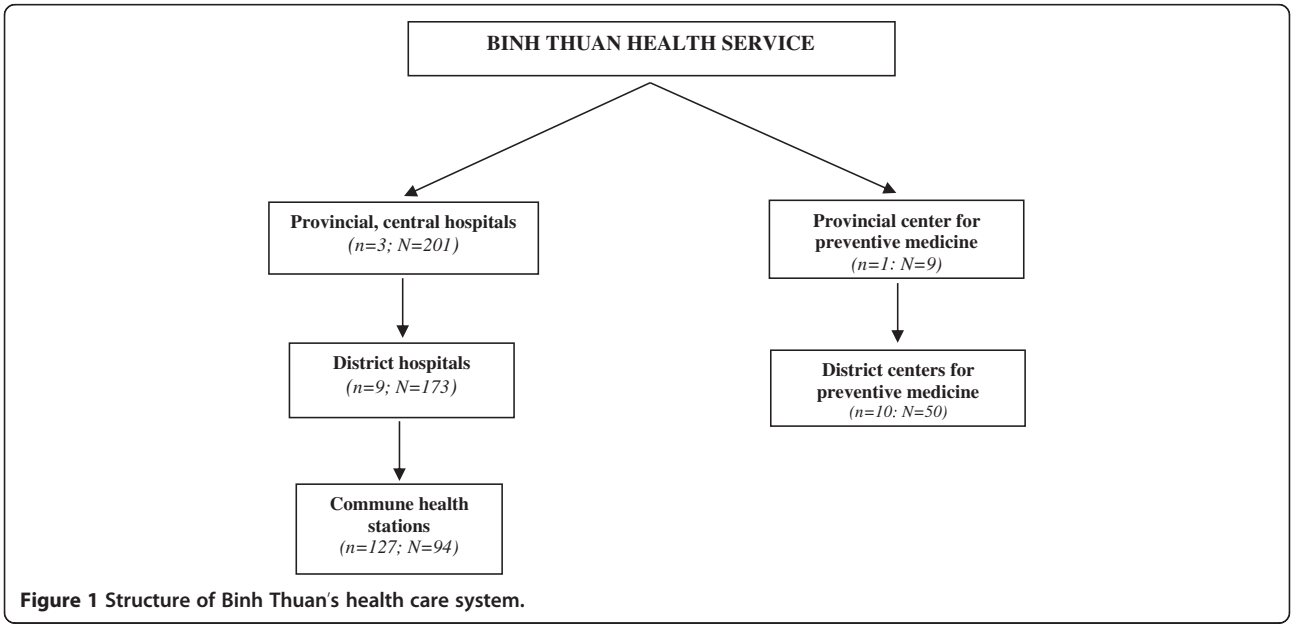

Figure 1 Structure of Binh Thuan's health care system.

obstetric history, as well as on complications during the present pregnancy and labour. The second part pertained to neonatal characteristics, including sex, the Apgar score, gestational age, birth weight, head circumference, length, and history of birth defects in siblings. Finally, the third part was composed of a checklist for diagnosed congenital anomalies.

Birth-weight measurements were obtained at delivery using a scale (Testut, Paris, France) that was accurate to 10 grams. Infants were fully unclothed and in the supine position. Recumbent length was measured with a baby board (UNICEF) and recorded to the nearest 0.1cm. A non-flexible plastic tape was used for measuring head circumference of the newborns and the result was also recorded to the nearest 0.1 cm. The two latter measurements were obtained within 24 hours after delivery. The methods of measurements used were based on the recommendation of the WHO [11]. Absolute poverty certificates or poverty certificates, housing type, and personal income per month were used to classify maternal economic status.

EBDs were coded using the International Classification of Diseases system-10, Clinical Modification (ICD10-CM) [12] and common EBDs were pictured in an atlas along with a brief description of the defect.

Instructions for photographing and describing EBDs are contained in the manual. The manual also describes the technique for screening for EBDs in newborns during the physical exam.

All data (collection forms and photos of EBD cases) on live births were rechecked and entered into a Microsoft Excel sheet by a local trained data processor (a local health professional) before sending monthly data to a processing center at the Provincial Health Service.

All photographs with a written description of an EBD were reviewed and classified by one of the authors (Y.G) who is a Belgian expert in clinical genetics. In case of disagreement between the expert's diagnosis and the local coding, the photograph and the written description were reviewed and discussed with local paediatric physicians. The team decided the most likely diagnosis as a group.

Statistical analyses were performed using the STATA statistical software.

Total prevalence was calculated by dividing the numerator (EBDs) by the relevant denominator (total live births) for the same period of time at the same place.

A newborn with multiple external defects was counted as one case unit for analysing birth defect case characteristics. When a newborn had more than one defect, each defect was counted as one unit when specific analyses for that particular defect or for system defect were performed. As a result, numerically adding up the number of defects could exceed the number of cases with defects.

The birth defect registry project was approved by the Binh Thuan Provincial Health Service and the Pham Ngoc Thach University Ethical Review Committee, Hochiminh City, Vietnam. All mothers provided written informed consent for themselves and for their baby prior to enrolment in the study, and consent to photograph was obtained from the parents of an affected newborn.

Results

Maternal socio-demographic characteristics

In 2010, a total of 13,954 newborns were registered, corresponding to a birth rate of 12.7 per one thousand people. The number of mothers was 13,877 because there were 71 pairs of twins (5.12 / 1,000 mothers) and 3 triple births (0.17 / 1,000 mothers). A caesarean section was performed for 17% of the deliveries.

Mean maternal delivery age was 26.3 ± 5.5 years (mean ± SD) with a range of 13–50 years (Figure 2).

1.8% of mothers were aged over 40 years. 1,171 mothers (8.4%) were younger than 20 years, including 16 mothers who were 13 to 15 years.

Regarding maternal gravidity, gravidity 2–3 accounted for about half of mothers. Primigravida accounted for

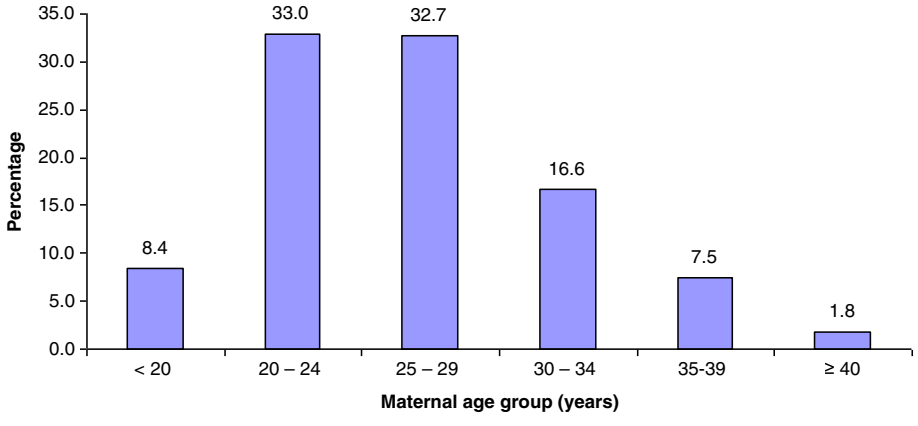

Figure 2 Histogram of maternal ages at delivery.

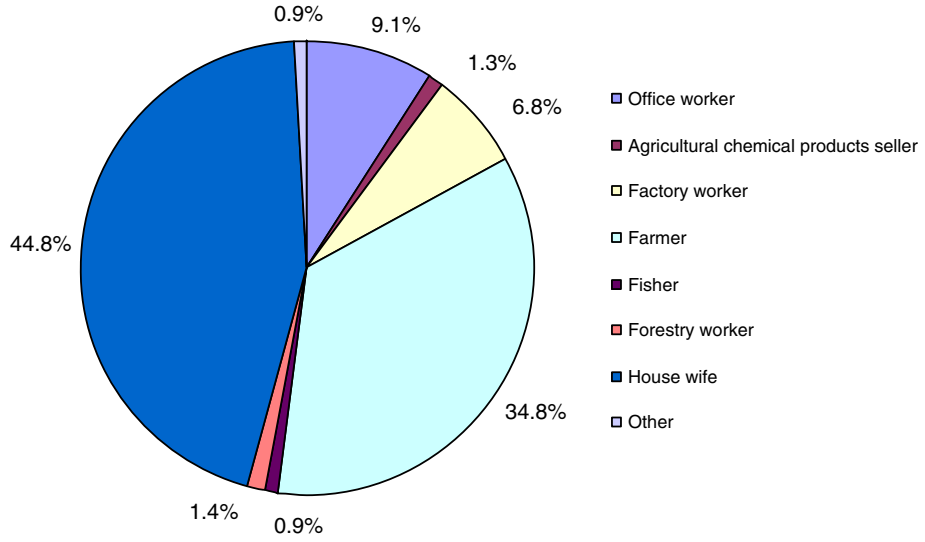

Figure 3 Distribution of mother's occupations.

about a third (33.8%) of mothers and gravidity was 4 or more in 13.0%.

Figure 3 shows the distribution of professional activity of the mothers. Housewife and farmer accounted for over 80% of the mothers' occupations.

Half of the mothers had a secondary school or higher education degree, and 3.4% of mothers were illiterate (Figure 4).

There were about 2% of mothers living in absolute poverty, 7% of mothers living in poverty, and over 90% of mothers living in a better economic status.

Over 92% of mothers were from the Kinh ethnic group, and 70% of mothers lived in rural areas. Previous miscarriage was reported by 5% of mothers. Four babies were born from a mother in a consanguineous marriage (2.9/10,000 live births).

Neonatal characteristics

There were 7,209 boys and 6,743 girls (sex ratio = 1.07). Two newborns had an indeterminate sex. The mean birth weight was 3,116 ± 432 g (mean ± SD) with a range of 400–5,300 g. Low birth weight accounted for 5% all live births. The mean gestational age for live births was 39.4 ± 1.6 weeks. About 8.2% of live births were premature. The mean birth length was 49.9 ± 2.3 cm (mean ± SD) with a range of 22–60 cm. The mean head circumference at birth was 32.6 ± 1.9 cm (mean ± SD) with a range of 16–60 cm for all live births. An Apgar score below 7 was observed in 6.4% of live births.

External birth defect characteristics

There were 84 cases with one or more EBDs, representing an overall prevalence rate of 6.02 per 1,000 live births. In

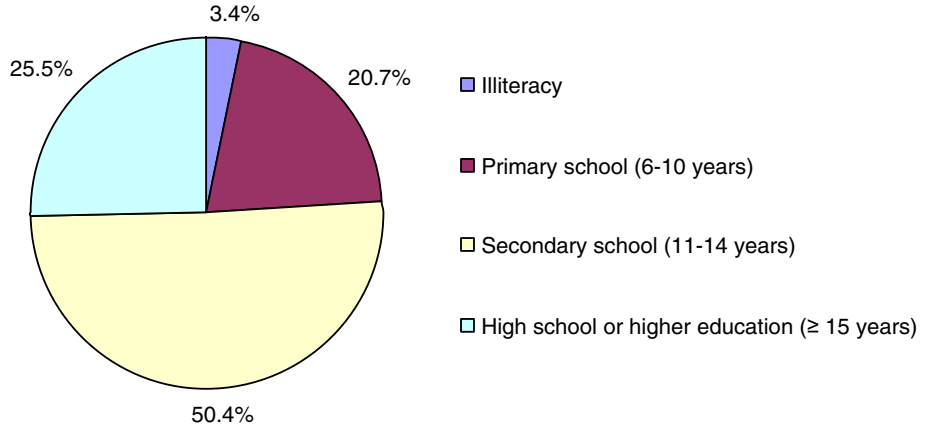

Figure 4 Distribution of maternal education level.

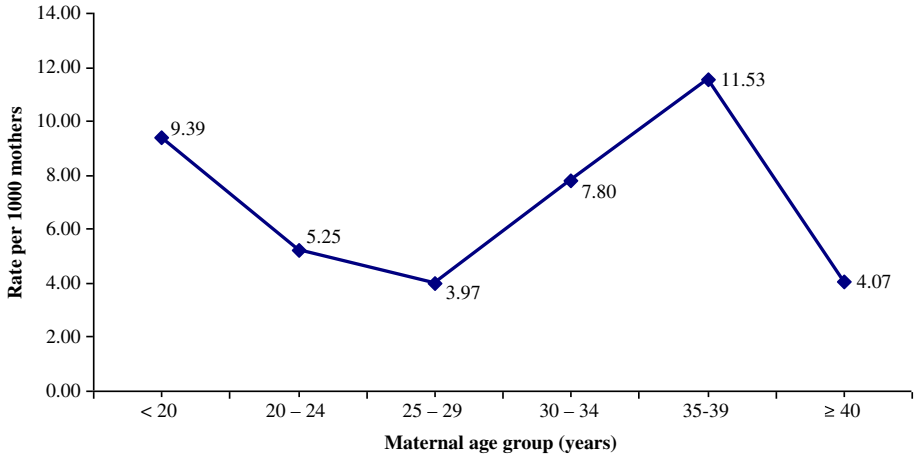

Figure 5 Distribution of the prevalence of external birth defect by maternal age at delivery.

terms of sex distribution, 47.6% of the birth defect cases were boys (n=40), and 50.0% were girls (n=42).2.4% had ambiguous genitalia (n=2).

For mothers giving birth to a baby with external birth defects, the mean maternal delivery age was 27.0 ± 6.2 years (mean ± SD), with a range of 17–40 years.

The under 20 age group (9.39/1,000 mothers) and the 35–39 year age group (11.53/1,000) showed a 2.37 (95% CI: 1.09 - 4.95) and 2.91 (95% CI: 1.37 - 5.98) fold higher prevalence of overall external birth defects when compared to the 25–29 year age group (3.97/1,000), respectively (Figure 5).

External birth defects among women with primigravida and gravida 4 or more were 2.3 (95% CI: 1.43 - 3.70) and 2.2 (95% CI: 1.17 - 4.08) times higher than in women with gravida 2 or 3, respectively.

Regarding the maternal education level, the prevalence of EBDs was highest in the illiteracy group, and similar in other groups. Table 1 shows that the prevalence of EBDs decreased with increasing maternal economic status (trend test p-value = 0.03).

The prevalence ratio (PR) of EBDs between literate mothers and illiterate mothers was 2.81 (95% CI: 1.02 - 5.76).

Table 1 Relationship between prevalence of external birth defects and selected maternal characteristics

Maternal characteristics	External birth defects n = 84 (%)	Prevalence/ 1,000 mothers	PR[¥]	95% CI
Gravidity				*p= 0.06**
1	41 (*44.8*)	8.75	2.31	1.43 – 3.75
2 -3	28 (*33.3*)	3.79	1	-
≥ 4	15 (*17.9*)	8.29	2.18	1.15 – 4.04
Education level				*p= 0.78**
Illiteracy	7 (*8.3*)	15.05	2.42	1.06 – 5.49
Primary school (6-10 years)	14 (*16.7*)	4.87	0.78	0.41 – 1.51
Secondary school (11–14 years)	41 (*48.8*)	5.86	0.94	0.57 – 1.60
High school or higher education (≥ 15 years)	22 (*26.2*)	6.22	1	-
Economic status				*p= 0.03**
Very poor	3 (*3.6*)	13.82	3.50	0.71 – 17.44
Poor	9 (*10.7*)	9.33	2.36	0.58 – 9.69
Well	70 (*83.3*)	5.74	1.46	0.43 – 5.39
Well-to-do	2 (*2.4*)	3.94	1	-
Occupation of mother				*p = 0.39**
Farmer and agricultural chemical product sellers	35 (*31.6*)	5,003	1.37	0.82 – 1.95
Other	49 (*63.9*)	8,874	1	-

* *Trend test p-value*; [¥] PR: Prevalence ratio.

The EBD prevalence was higher in mothers with a history of miscarriage (9.40/1,000 live births vs. 6.37/1,000 live births for mothers without a previous miscarriage), in mothers who had a caesarean section (7.37/1,000 vs. 5.8/1,000 for mothers who delivered vaginally), in Kinh mothers (6.29/1,000 vs. 4.09/1,000 for other ethnicities), and in rural resident mothers (6.26/1,000 vs. 5.67/1,000 for urban resident mothers). These differences, however, were not significant between groups (Table 2).

The mean birth weight was 2,802 ± 593 g (mean ± SD) with a range of 1,000-4,300 g for babies presenting external birth defects. External birth defects were 4.75 times (95% CI: 2.81 - 8.03) more frequent among live births with low birth weight than among live births who weighed more than 2,500 g.

The mean gestational age for live births was 38.2 ± 3.5 weeks (mean ± SD) for babies with external birth defects. Babies born at less than 37 weeks of gestation were 2.09 times (95% CI: 1.17 - 3.27) more likely to have an external birth defect than babies born at 37 weeks or more.

EBDs were 4.89 times (95% CI: 2.95 – 7.87) more frequent among newborns with an Apgar score under 7 points at five minutes than among newborns with an Apgar score of 7 or more.

The mean birth length was 48.2 ± 4.2 cm (mean ± SD) with a range of 33–60 cm. The mean head circumference at birth was 31.4 ± 5.7 cm (mean ± SD) with a range of 16–60 cm for babies with external birth defects. There were no external birth defects in newborns from mothers in a consanguineous marriage (Table 3).

Regarding level of health care, about one in seven (15.2%) infants was born outside of a hospital (Figure 6).

The most commonly encountered group of anomalies were limbs, which accounted for 27.2/10,000 live births, followed by orofacial clefts (20.1/10,000) and the central nervous system (7.9/10,000). Prevalence at birth for selected external birth defects is shown in Table 4 together with prevalences reported by full member EUROCAT registries, Belgium and Taiwan.

The prevalence of EBDs in Binh Thuan province was close to Taiwan data and not far from EUROCAT or Belgian data for most external birth defects. No cases of spinabifida were detected in our study.

Table 2 Relationship between prevalence of external birth defects and selected live births characteristics

Live births characteristics	External birth defects n = 84 (%)	Prevalence 1,000 live births	PR	95% CI	P value
Birth weight					
< 2500g	17 (*20.2*)	23.55	4.75	2.81 – 8.03	<0.001
≥ 2500g	67 (*79.8*)	5.06	1	-	
Gestational age					
< 37 weeks	13 (*15.5*)	11.61	2.09	1.17 – 3.27	0.012
≥ 37 weeks	71 (*84.5*)	5.57	1	-	
AFGAR score at 5 minutes					
< 7	21 (*25.0*)	23.60	4.89	2.95 – 7.87	<0.001
≥ 7	63 (*75.0*)	4.82	1	-	

Table 3 Distribution of external birth defects across level of health care

Level of health care	All live births	Overall external birth defects	
	N = 13,954 (%)	n = 84 (%)	Per 1,000 live births
Central hospital	9,026 (64.7)	58 (69.0)	6.43
District hospital	2,803 (20.1)	16 (19.1)	5.71
Commune health station	2,125 (15.2)	10 (11.9)	4.71

Discussion

The prevalence of birth defects can be influenced by many factors including case definition, TOPFA, the time of observation after birth, population study methods, case ascertainment methods and reporting and statistical procedures used [13–16].

Termination of pregnancy is legal up to 22 weeks in Vietnam, but reporting of pregnancy termination is not required. However, prenatal diagnosis does not exist in our study's population. We therefore believe that the reason for termination of pregnancy in Binh Thuan is rarely an external birth defect. Consequently, TOPFA most likely does not have an influence the prevalence of the birth defects.

We found that the prevalence of EBDs across the age distribution tended to be a U-shaped curve; prevalence dropped substantially for women over 40 years of age and only marginally for other age groups. For non-chromosomal defects, the U-shaped pattern of prevalence across maternal age has been documented by many authors [7,15,17].

In this study, the relationship between maternal education and an EBD did not necessarily mean that maternal education itself was a risk factor for EBDs. Educational qualification most probably determines socio-economic level and/or occupation and prenatal care behavior. It is therefore conceivable that education might affect the occurrence of EBDs indirectly [18].

Most reported associations between occupational exposures and adverse reproductive outcomes in epidemiological studies are equivocal and often controversial [19]. Significant association of occupational pesticide exposure and all birth defects were reported by Nurminen, et al. from a study in Finland [20], and by Restrepo et al. in Colombia [21]. Our findings show that the prevalence of EBDs was not significantly different between women involved in agricultural activities and/or working as an agricultural

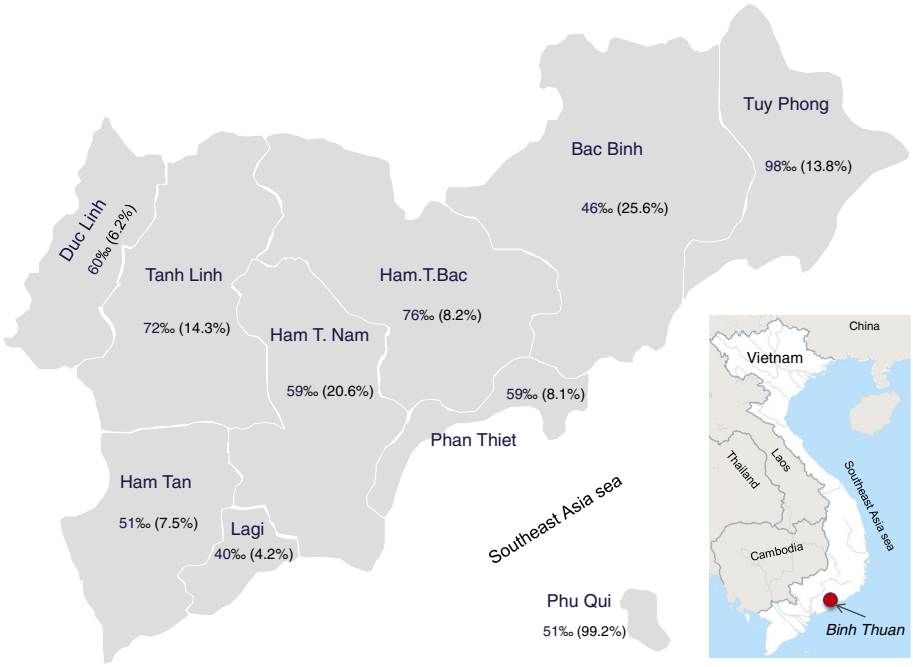

Figure 6 Birth defect distribution (‰) and proportion of babies born in commune health station (%) within each district.

chemical products seller and mothers involved in another occupation.

Our results show an increased prevalence of external birth defects occurring among mothers with either primigravida or gravida over 4.

According to Swain et al., infants born to gravida 4 or more mothers have higher rate of birth defects when compared to mothers of lower gravidity [22]. Tan et al. reported that the prevalence of birth defect increased with birth order [23].

The relationship between the mother's age at delivery and gravidity may be one possible explanation for the high rate of EBDs at both extremes of maternal gravidity in the present study.

This study demonstrates that birth defects are significantly associated with preterm birth and low birth weight. Although preterm and low birth weight infants are more likely to have birth defects, the effect of birth defects on preterm birth and low birth weight has been difficult to study because of multiple confounding risk factors [24,25].

Many studies have documented male preponderance in birth defects [26,27]. However, in the present study, a very slight female preponderance was found (42 females versus 40 males).

As expected, the overall prevalence of EBDs in our study (6.02 per 1000 live births) was lower than the EUROCAT (25.53/1000) and Belgian (23.11/1000) registries [11] because the present study reported only EBDs detected within 24 hours after birth. Our finding was similar to the prevalence rate in Taiwan, which is 7.3/1000 births. In Taiwan, EBDs were detected within a few days after birth [26].

When considering the type of external birth defect, limb defects, nervous system defects, orofacial clefts and external genital system defects are by far among the most common birth defects worldwide [28–31]. In the present study, limb defects, orofacial clefts and central nervous system defects were the three most common groups.

In our study, the most common limb defects were clubfoot, polydactyly and limb reduction, respectively.

Club foot is the common type of limb defect. Prevalence varies widely in among recent international reports. According to data from EUROCAT, the prevalence of clubfoot was reported to be 10.31/10,000 total births for all members, 11.21/10,000 in Belgium and varied from low (3.22 per 10,000) to high (18.00 per 10,000) in Ukraine and Saxony-Anhalt (Germany), respectively [10]. In recent studies in the United States, Parker et al. reviewed data from the 10 population-based birth defect surveillance programs (6,139 cases of clubfoot) to better estimate the prevalence of clubfoot and found the overall prevalence of clubfoot to be 19.2 per 10,000 live births [32]. Boo et al. reported an incidence of clubfoot in Malaysia at 45 per 10,000 live births [33]. In our study's group, club foot was the second most common EBD and the prevalence of 12.18/10,000 live births fell within the range reported for other registries.

Polydactyly is a major group. It is a defect that is easily detectable after birth and is an isolated finding in 85% -

Table 4 Prevalence of selected birth defects (per 10,000 live births) in Vietnam in comparison to the prevalences reported by full member EUROCAT registries, Belgium and Taiwan

Congenital anomalies subgroups	Vietnam	Full member EUROCAT[+]	Belgium[+]	Taiwan[*]
Nervous system				
Neural Tube Defects				
Anencephalus and similar	3.58	3.50	3.16	1.07
Encephalocele	0.72	1.11	1.42	0.37
Spinabifida	0	4.74	4.89	0.58
Hydrocephaly	1.43	5.31	5.52	3.55
Microcephaly	2.15	2.37	1.74	0.58
Arhinencephaly/ holoprosencephaly	0	0.85	1.26	nr
Ear				
Anotia	0.72	0.34	0.47	nr
Microtia	2.15	nr	nr	nr
Respiratory				
Choanal atresia	0.72	0.79	0.95	0.21
Orofacial clefts				
Cleft lip with or without palate	14.33	8.63	12.00	12.80
Cleft palate	5.37	5.59	3.59	4.67
Abdominal wall defects				
Gastroschisis	1.43	2.82	1.89	1.20
External genital system				
Hypospadias	0.72	17.51	10.58	3.35
Indeterminate sex	1.43	0.59	0.63	0.99
Limb				
Limb reduction	4.30	5.05	5.05	3.22
Club foot	12.18	10.31	11.21	4.42
Polydactyly	6.45	8.69	6.79	7.97
Syndactyly	2.87	5.23	6.95	4.34
Other limb defects	1.43	nr	nr	nr

[+] EUROCAT http://www.eurocat-network.eu/accessprevalencedata/prevalencetables. Date access 03/11/2013; * Data from reference 13; nr: none reported.

88% of cases [34]. Our polydactyly prevalence of 6.45/10,000 live births was comparable to other European prevalence rates of 6.79/10,000 for Belgium, 6.80/ 10,000 for Paris, and 6.6/10,000 for Portugal respectively [10]. The prevalence of this birth defect is much higher in China (22.4/10, 000) [34] and in Alberta, Canada (18.84/10,000) [9]. Prevalence of polydactyly was reported to be lower in Barcelona, Spain (3.06/10,000) [10] and in Lombardy, Italy (5.82/10,000) [27].

Limb reduction is one of the most common types of limb defects and accounts for 3.2 to 7.06 per 10,000 births in the literature [10,26,27]. This very visible birth defect is symbolic because it launched the development of congenital anomalies surveillance activities worldwide after the thalidomide tragedy in the early 1960s. Limb reduction prevalence was found to be 4.3/10,000 live births among our newborns.

Orofacial clefts are among the most common of all major birth defects. Orofacial clefts are usually obviously visible immediately after birth.

Cleft lip with or without palate involved 20 out of 13,954 live births (14.33 per 10,000 live births), which is similar to the prevalence in Northern Ireland (14.70 per 10,000 live births) [10,27,35], lower than in Pakistan (19.10 per 10,000) [36] but higher than in full member EUROCAT registries (8.63 per 10, 000) [10], in Norway (10.9 per 10,000) [37], China (18.9 per 10,000) [38] and Korea (10.3 per 10,000) [39].

According the international perinatal database report on typical oral clefts, the prevalence of cleft lip with or without cleft palate from 54 registries in 30 countries over at least 1 complete year during the period 2000 to 2005 was 9.92 per 10,000 births, which was lower than our finding [40].

Isolated cleft palate is very difficult to detect prenatally due to shadowing artefacts from amniotic bands or other overlying structures.

The prevalence of 5.37 per 10,000 live births for cleft palate in this study was comparable to those observed in the full member EUROCAT registry (5.59 per 10,000) [10] and in Lombardy, Italy (5.82/10,000) [27]. Our figure was slightly higher than those reported in Taiwan (4.67 per 10, 000) [41], and in Belgium (3.59 per 10,000) [10], but lower than those reported in Wessex, United Kingdom (10.0/10 000) and in Ireland (7.21/10,000) [9].

Neural tube defects can be categorized as either anencephalus or similar (lack of closure in the head region) or spinabifida (lack of closure below the head). The two major categories of neural tube defects occur in approximately equal frequencies at birth [13,42].

Our data revealed that the prevalence for anencephalus or similar was 3.58 per 10,000 live births. This figure is comparable to that of the full member EUROCAT registry (3.50/10,000) and Belgium (3.16/10,000) [10]. In contrast with the relatively high frequencies of anencephaly, we did not observe any spinabifida in the present study or in the pilot study in 2008 with 16,593 births. The explanation for the absence of spinabifida cases in our study is complex. It may be due in part to the small sample size, the diagnostic technique used, and/or genetic factors.

As expected, the prevalence of hydrocephaly in our study (1.43/10,000 live births) was low compared to the full member EUROCAT registry (5.31/10,000), Belgium (5.52/10,000) and other registries [10,26,27,29,39]. Hydrocephaly is a malformation that is easier to diagnose by prenatal ultrasound scanning. It is not often obvious at

birth and is usually detected after birth by an increasing head circumference that crosses percentiles on the growth chart. We therefore believe that hydrocephaly was underdiagnosed in our study.

Hypospadias is considered the most common congenital malformation in the genitourinary system. Usually hypospadias is detected at birth by a detailed examination of the newborn or by abnormal flow of urine during urination. Experienced clinical personnel are required to detect hypospadias. In our study, newborns were examined within 24 hour after birth by a local health provider with limited expertise in hypospadias recognition. Thus the prevalence of hypospadias was low (0.72/10,000 live births) compared to other registries [10,27,29,39].

The prevalence of external birth defects was not different between commune health stations and hospitals demonstrating health workers' abilities in detecting EBDs at commune health stations in Binh Thuan province.

Internal organ defects are not visible during a physical exam or they are often asymptomatic, particularly during the first 24 hours of life. In this study, since the examinations were executed by simple measurements and observations of the newborn, birth defects of internal organs (e.g. digestive system heart and circulatory system, internal urogenital system and certain domains of the central nervous system) were undetected.

Conclusions

This first population-based study in Vietnam which required coordination efforts at the local level provides baseline prevalence of external birth defects. External birth defects can be diagnosed at birth; because our study was able to diagnose the majority of external birth defects occurring in Binh Thuan, the current data can be compared to the prevalence data of other registries.

Data on EBDs from this study in southern Vietnam may be useful in setting up a regional population-based registry of birth defects in Vietnam.

Abbreviations

CHS: Commune health stations; DH: Provincial or District Hospitals; EBDs: External Birth Defects; EUROCAT: European Registration of Congenital Anomalies and Twins; HP: Health Professionals; ICD10-CM: International Classification of Diseases System-10, Clinical Modification; ICBDSR: International Clearinghouse for Birth Defects Surveillance and Research; TOPFA: Termination of Pregnancy For Foetal Anomaly.

Competing interests

None of the authors of the above manuscripts has declared any conflict of interest statement.

Authors' contributions

TH participated in the design, carried out the study, performed the statistical analyses and drafted the manuscript. RR, TDA and YG provided advice in the design of the study and the analytical strategy and contributed to the manuscript revision. NNVP helped in the data analysis and report. AR and DNT are head of the project; they provided advice on the structure, the data analysis and presentation, and supervised the manuscript redaction. No author has any financial or private interest in this research project. There is no organization sponsoring this research which is granted by the Commission Universitaire pour le Développement (www.cud.be), which is a public funding from the Belgian government. The corresponding author has full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors read and approved the final manuscript.

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5.1.1 ADDITIONAL RESULTS OF EXTERNAL CONGENITAL ANOMALIES STUDY

A total of 192 cases with one or more EBDs were registered among 29,056 newborns, accounted a for overall prevalence rate of 6.6 per 1,000 live births. The sex distribution of the birth defect cases was 51.6% male (n=99), 46.9% female (n=90) and 1.6 % with ambiguous genitalia (n=3). Mean maternal delivery age was 26.5 ± 3.5 years (mean ± SD) with a range of 13-50 years for all live births and 28.1 ± 4.7 years with a range of 17-40 years for mothers giving birth to a child with external birth defects. Prevalence of EBDs across the age distribution tended to be a U-shaped curve, because the prevalence dropped substantially for women more than 40 years of age and only marginally for other age groups (Figure 8).

Figure 8. Distribution of the prevalence of external birth defect by maternal delivery age

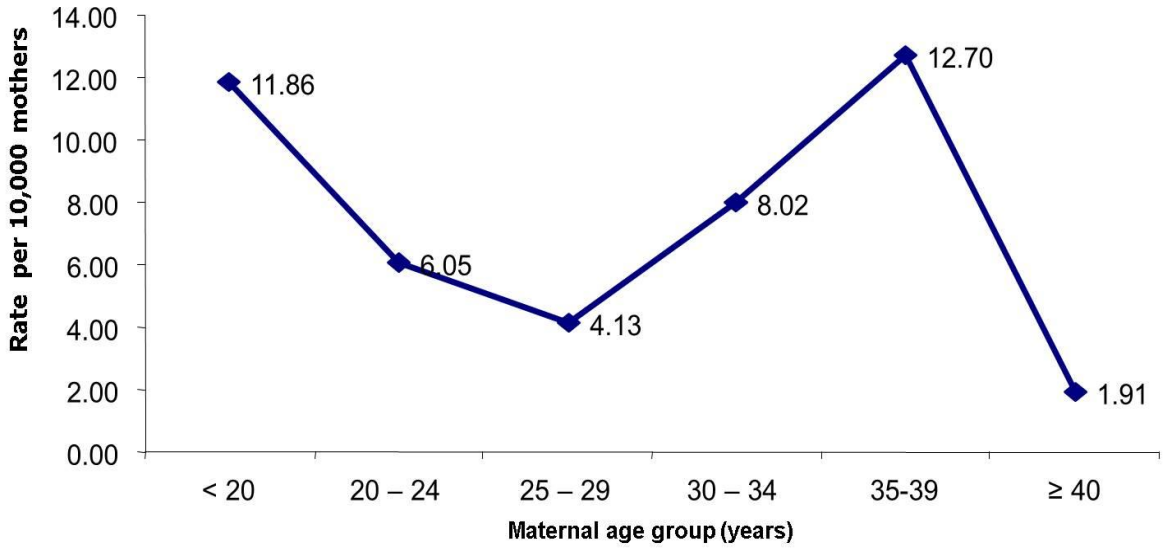
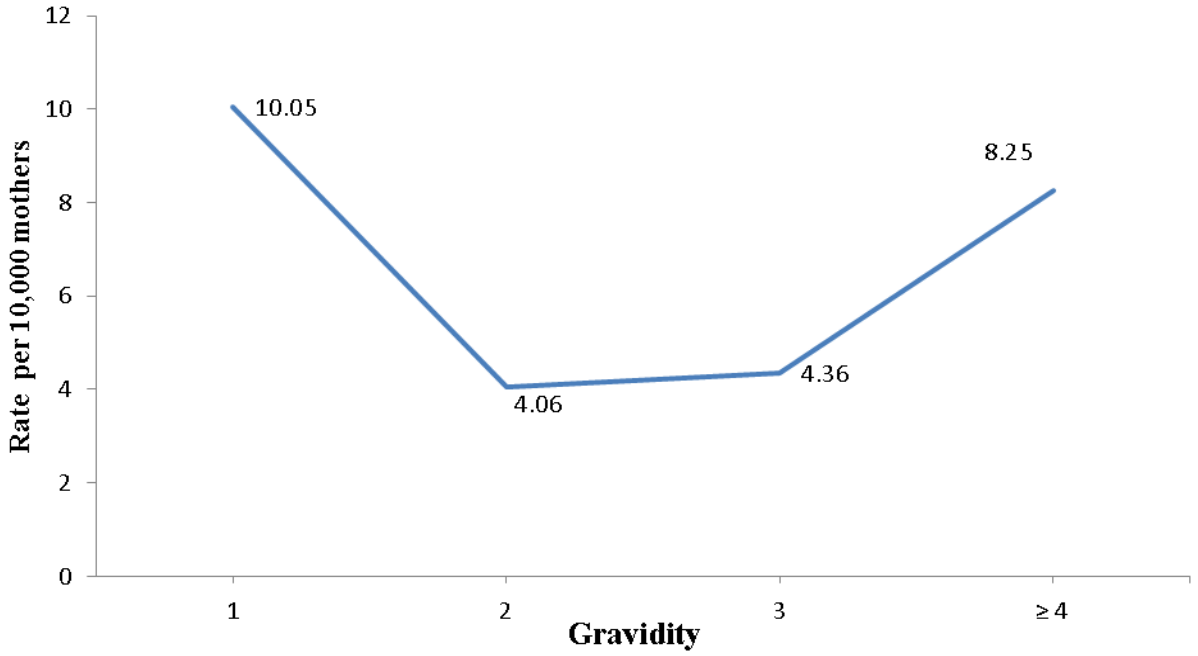


Figure 9. Distribution of the prevalence of external birth defect by gravidity



The Figure 9 shows that higher prevalence of birth defects tended to occur among either the mother with primagravida, or the mother with gravida 4 or more.

Table 13. Prevalence of external birth defects according to birth weight and gestational age

	All live births	**Overall external birth defects**	
	N = 29,056 n *(%)*	n = 192 n *(%)*	Per 1,000 live births
Birth weight			
< 2500g	1,349 (4.6)	39 (20.3)	29.8
≥ 2500g	27,707 (95.4)	153 (79.7)	5.6
Gestational age			
< 37 weeks	3,284 (11.3)	35 (18.3)	10.7
37 – 42 weeks	24,999 (86.0)	155 (80.7)	6.2
> 42 weeks	773 (2.7)	2 (1.0)	2.6

Regarding the characteristics of newborns, the prevalence of EBDs was the highest in premature group and in newborn having a low birth weight (Table 13).

Table 14. Prevalence of selected birth defects (per 10,000 live births) in Vietnam as compared with the prevalence reported in full member EUROCAT registries, Belgium and Taiwan

Congenital anomalies subgroups	Vietnam	Full member EUROCAT[+]	Belgium[+]	Taiwan[*]
Nervous system				
Neural Tube Defects				
Anencephalus and similar	3.1	3.50	3.16	1.07
Encephalocele	0.3	1.11	1.42	0.37
Spinabifida	0	4.74	4.89	0.58
Hydrocephaly	1.0	5.31	5.52	3.55
Microcephaly	2.4	2.37	1.74	0.58
Arhinencephaly/holoprosencephaly	0.3.	0.85	1.26	nr
Ear				
Anotia	0.3	0.34	0.47	nr
Microtia	1.4	nr	nr	nr
Respiratory				
Choanal atresia	0.7	0.79	0.95	0.21
Orofacial clefts				
Cleft lip with or without palate	17.2	8.63	12.00	12.80
Cleft palate	6.2	5.59	3.59	4.67
Abdominal wall defects				
Gastroschisis	1.0	2.82	1.89	1.20
Anorectal	1.7			
External genital system				
Hypospadias	1.0	17.51	10.58	3.35
Indeterminate sex	1.7	0.59	0.63	0.99
Limb				
Limb reduction	4.8	5.05	5.05	3.22
Club foot	13.4	10.31	11.21	4.42
Polydactyly	6.5	8.69	6.79	7.97
Syndactyly	4.1	5.23	6.95	4.34

[+] *EUROCAT 2011 http://www.eurocatnetwork.eu/ACCESSPREVALENCEDATA/Prevalence Tables. Date access 05/18/2012*; * *Data from reference* [94]; nr: *none reported*

The prevalence of EBDs in Binh Thuan province was close to Taiwan data and not far from EUROCAT or Belgium data for most external birth defects. We didn't observe any spinabifida, in the present study with 29,056 live births (Table 14).

5.1.2 SPINA BIFIDA: ADDITIONAL DISCUSSION

Our prevalence of anencephalus or similar was 3.1 per 10,000 live births, closed to that in full member Eurocat registry (3.50/10,000) and in Belgium (3.16/10,000). In contrast with the relatively high frequencies of anencephaly, no cases of spinabifida were detected in our study with 29,056 live births as in the pilot study in 2006 with 16,325 live births.

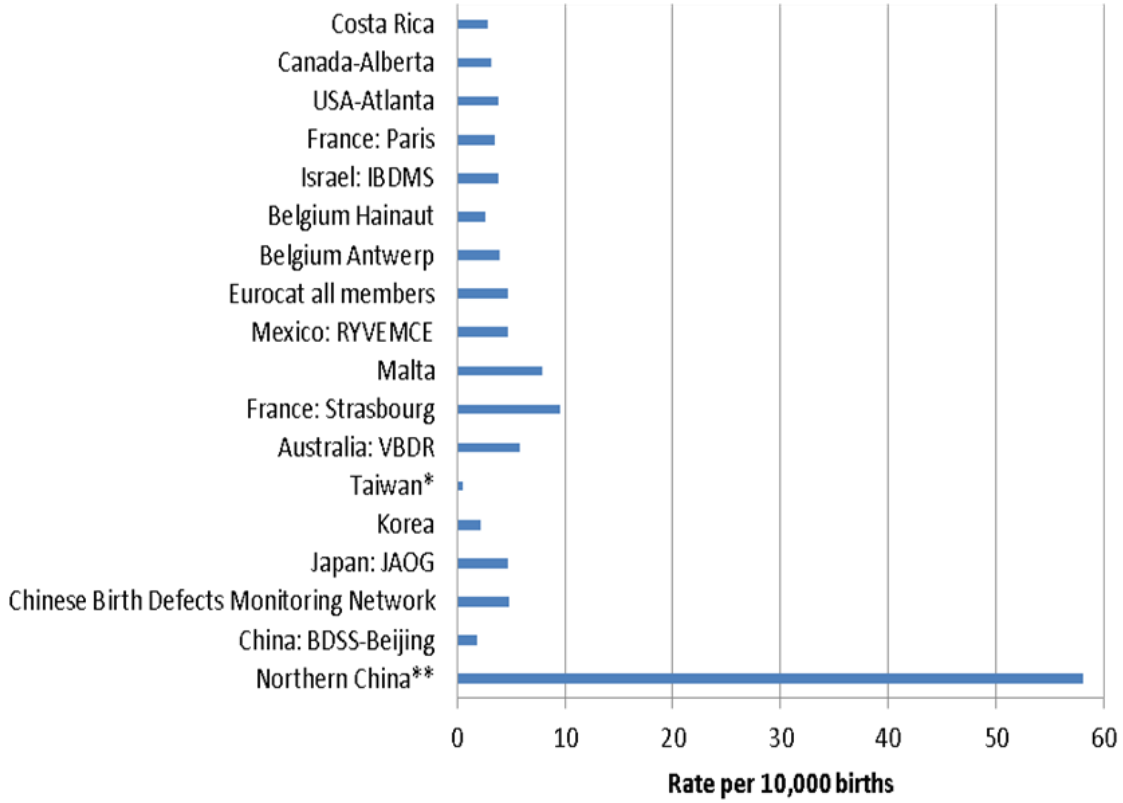
Spina bifida is the collective term used to describe a group of multiple, complex congenital abnormalities and anomalies of the neural tube known as myelodysplasias. Etiology of neural tube defect (NTD) is unclear. Most of the non-syndromic NTD are of multifactorial origin. No Mendelian pattern of inheritance has been reported. Association with single gene defects, enhanced recurrence risk among siblings, and a higher frequency in twins than in singletons indicate the presence of a strong genetic contribution to the etiology of NTD. Recent in vitro and in vivo studies have highlighted the molecular mechanisms of neurulation in vertebrates but the morphologic development of human neural tube is poorly understood. The UK and Hungarian studies showed that periconceptional supplementation of women with folate reduces significantly both the first occurrence and recurrence of NTD in the offspring. This led to mandatory periconceptional folate supplementation in a number of countries. Encouraged by these results of clinical studies numerous laboratory investigations focused on the genes involved in the folat, vitamin B12 and homocysteine metabolism during neural tube development. Up to now, no clinical or experimental study has provided unequivocal evidence for a definitive role for any of these genes in the causation of NTD suggesting that a multitude of genes, growth factors and receptors interact in controlling neural tube development by yet unknown mechanisms [101].

Neural tube defects can be categorized as either anencephalus or similar (lack of closure in the region of the head) or spina bifida (lack of closure below the head).The two major categories of neural tube defects occur in approximately equal frequencies at birth [102].

NTDs rank among the commonest categories of birth defects, alongside with congenital heart anomalies and genitourinary defects. Globally, the total annual number of affected births was estimated at 323,900, and variations in prevalence have been reported, ranging from 0.5 to 58.1 per 10,000 births in specific geographical locations (Figure 10). Higher frequencies occur in miscarriage material.

Major geographic, socioeconomic, and racial differences in the incidence of the defects and variations in birth prevalence have been documented over time. In general, the highest incidence of neural tube defects in the world is thought to occur in Northern Chinese where the prevalence of spina bifida is 58.1 per 10,000 births [103]and in Northern Ireland and South Wales where the incidence of anencephaly is 6.7 per 10,000 and the incidence of spina bifida is 4.1 per 10,000 births. In North America, the incidence generally decreases from east to west and in any given area, is highest among Hispanics, lowest in blacks and Asians, and intermediate in non-Hispanic Caucasians[104].

Figure 10. International variations in the prevalence of spina bifida

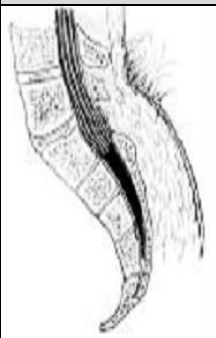


Source: *[103],**[105]Except as noted, data for all areas are those published by the International Center for Birth Defects and the European Registration of Congenital Anomalies.

Figure 10 presents the international variations in the prevalence of spina bifida in which Taiwan reported the lowest prevalence of spina bifida of 0.58/10,000 births. This result was lower than other registry because of terminations of pregnancy not reported in this study.

Details descriptions of spinabifida were presented in Table15.

Table15. Types of spinabifida

	SPINA BIFIDA OCCULTA	MENINGOCELE	MYELOMENINGOCELE	MYELOCELE
Anatomy				
Definition	Failure of the posterior element of vertebrae	The protruding sac contains meninges and spinal fluid	The protruding sac contains spinal cord and spinal fluid	Cystic cavity in front of the anterior wall of the spinal cord
Posterior element of spine	Failure of fusion	Failure of fusion	Failure of fusion	Failure of fusion
Meninges herniate and form a cystic sac	No cystic sac formation	Cystic sac formation present	Cystic sac formation present	Cystic cavity is in front of the anterior wall of the spinal cord
Content of cystic sac	No cystic sac formation	Spinal fluid meninges	Spinal fluid meninges. Spinal cord	
Associated findings	A frequent sings in 50% of children is the presence of: pigmented nevus, angioma, dimple or dermal sinus overlying skin	With or without intact skin at site of sac Incomplete skin coverage leads to leakage of CFS	Arnold Chiari malformation which is complicated by hydrocephalus in over 90% of the cases – with or without intact skin at site of sac	-
Clinical symptoms	No neurologic deficit Rarely associated with sacral lipoma	In absence of other underlying of malformation, neurologic signs are normal. Meningocele occurs in ≤ 10% of cases of spina bifida cystica	Motor paralysis Sensor deficits Neurologic bowel and bladder	
Spinal cord level involved	Most common level is L 5-S1	75% of these lesions affect the lumbar and lumbosacral segments. (the remainder are located at sacral or thoracic area but very rare at cervical level)	75% of these lesions affect the lumbar and lumbosacral segments. (the remainder are located at sacral or thoracic area but very rare at cervical level)	75% of these lesions affect the lumbar and lumbosacral segments. (the remainder are located at sacral or thoracic area but very rare at cervical level)
Prevalence	Normal variant in approximately 5-10% of the population	Meningocele occurs in ≤ 10% of cases of spina bifida cystica	Myelomeningocele affect an overwhelming majority of group with spinabifida cystica	

In Vietnam, no data on spina bifida have been published yet. There was only a local rapport of Health Service of Hochiminh City in 2010 showing that the spinabifida was the lowest rate among all congenital anomalies. There were 23 cases of spinabifida observed, among 11,790 cases of anomalies congenital detected in all hospitals of the city, accounted for 0.2 % of all congenital anomalies (Table 16) [106].

Table 16. Number of cases of congenital anomalies detected in the hospitals in Hochiminh city compared with data of Belgium

Congenital anomalies	Hochiminh		Belgium*	
	Children <15 years	Percent	Infant	Percent
Spina bifida	23	0.2	17	1.2
Other congenital anomalies of the nervous system	164	1.4	128	8.7
Congenital anomalies of the circulatory system	3,792	32.2	399	27.1
Cleft lip and cleft palate	1,265	10.7	98	6.6
Small intestine atresia/stenosis	78	0.7	11	0.7
Other congenital anomalies of the digestive system	1,870	15.9	100	6.8
Undescended testicle	719	6.1	-	-
Other congenital anomalies of urino-genital organs	1,737	14.7	234	15.9
Congenital deformities of hip	147	1.2	18	1.2
Congenital deformities of feet	176	1.5	94	6.4
Others congenital anomalies of the musculoskeletal system	834	7.1	138	9.4
Others congenital anomalies	948	8.0		0.0
Chromosomal abnormalities	37	0.3	254	17.2
All congenital anomalies	**11,790**	**100.0**	**1,474**	**100.0**

* Data from EUROCAT(http://www.eurocat-network.eu/default.aspx)

It remains difficult to explain why there was no case of spinabifida in the present study. The small number of cases of birth defect, genetic factor or diagnostic technique used can contribute to this result.

The diagnosis of a myelomeningocele or meningocele is readily made either on a prenatal ultra-sound or at birth when the lesion is noted on the newborn's back. Therefore the risk for missing cases of spina bifida by clinical examination was low. As prenatal diagnosis does not exist in our population study, termination of pregnancy would seldom be for defects and would have not influence the spina bifida prevalence.

NTDs can be caused by environmental (folate-dependent malformation) and genetic factor. But in this study, we had a relatively high frequency of anencephaly but no case of spinabifida. Therefore, the absence of spinabifida would not be caused by environmental factors.

As neural tube abnormalities affect the entire length of the spine and central nervous system, most individuals with myelodysplasias have associated brain abnormalities. This often results in hydrocephalus affecting almost all persons with spina bifida. May be the low number of cases of hydrocephalus in our study is in line with no case of spinabifida.

Still birth could not be registered in the present study because of the fetal edema after birth and a socio-cultural problem with fetal death. The Vietnamese culture does not permit to examine a death fetus for detecting the congenital anomalies. Unregistered still birth may be an explication of the absence of spina bifida in our study.

Because of anencephaly and spinabifida are not controlled by the same gene, genetic factor may be one explication for this problem.

5.2 NEONATAL MORTALITY

Article: Determinants and causes of neonatal mortality: A prospective population-based study in rural Southern of Vietnam

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Journal: BMC Pediatrics (under review).

SUMMARY:

Background: Although neonatal mortality (NM) remains a public health problem in Vietnam there is no published data on NM from communities in Southern of the country.

The study aimed at accessing NM, identifying its causes and its determinants in the Province of Binh Thuan located in the North of Southern Vietnam.

Methods: We prospectively registered all infants born in all health facilities of Binh Thuan in the whole year 2010 (N = 13,954 live births).

Results: NM was 7.4 per 1,000 live births, the very early neonatal mortality was 4.2 per 1,000 live births, and the early neonatal mortality was 6.2 per 1,000 live births. Low birth weight/ pre-maturity (33.3%), birth asphyxia (22.5 %), neonatal infection (21.6 %), and congenital malformation (15.7 %) were the major causes of neonatal death. NM was higher in illiterate mothers, ethnic minority mothers, mothers living in rural area, primigravida, and mothers aged <20. Using multivariate Poisson regression model, illiterate mothers (ratio of NM =3.73; 95% CI: 1.81 – 7.68), teenage (under age 20) mothers (1.87; 1.05 – 3.38), mother living in rural area (1.68; 1.09 – 3.23), primigravida (2.26, 1.50 – 3.42), low birth weight (11.41; 7.20 – 18.06), prematurity (2.99; 1.87 – 4.79) were associated with significant increased risk of neonatal death.

Conclusions: The programmes of health awareness should target mothers and babies at high risk, especially illiterate mothers, teenage mothers, ethnic minority mothers, and antenatal care to reduce neonatal mortality in this region. Data on neonatal mortality from our study may be useful in prioritizing intervention programmes aiming at achieving the objectives of fourth Millennium Development Goal in Vietnam.

Key words: *neonatal mortality, prospective population - based study, Southern of Vietnam, maternal education, teenage mothers.*

Background

About 3.8 million deaths occur every year in babies younger than 28 days of which almost all (99%) occur in developing countries and constitute an important public health problem with both medical and economical implications [14, 107]. In developed countries, neonates are now a major focus of child health, both for mortality and morbidity reduction. However, in developing countries neonatal mortality has attracted relatively little attention compared to maternal mortality or under-five mortality, in international public health policies and programmes, neonatal deaths still do not receive attention commensurate with their burden [14, 98, 99].

In September 2000, 189 member countries of the United Nations committed themselves to eight goals towards universal development and poverty eradication. These goals were called Millenium Development Goals (MDGs). The fourth goal (MDG4), one of the most important items in the MDGs, was to reduce infant and child mortality by two thirds between1990-2015 [98].

Neonatal deaths now account for more than two thirds of all deaths in the first year of life and for half of all deaths in under-five children. Two thirds of the world's neonatal deaths occur in just 10 countries, mostly in Asia, and the annual neonatal mortality has remained unchanged in the past decades [14, 99, 108]. Achieving MDG4 will therefore need to include a reduction in deaths during the neonatal period.

The Vietnamese government has identified perinatal health and neonatal mortality as priority areas and evidence-based guidelines on reproductive health were launched in 2003 for improving newborn care and survival [31]. Vietnam is also committed to the MDGs. Viet Nam has already achieved the targets for both under-five mortality and infant mortality, with both these rates being halved between 1990 and 2006. The under-five mortality rate has dropped considerably over the last 30 years (55/1,000 to 30/1,000), while neonatal mortality remained basically unchanged in the range of 15/1,000 during the time period 1970–2000 [32]. Knowledge about the neonatal mortality rate (NMR) and its determinants and causes should contribute to plan interventions aiming at reducing neonatal mortality with available resource, in order to achieve MDG4.

There have been few studies on neonatal mortality in communities in Vietnam. Officially, the NMR in Vietnam was 12/1,000 live births in 2004 [33]. Graner et al reported a NMR of 11.6/1,000 live births over the period 1999-2005 in a rural population in Northern Vietnam [34]. A recent study in the province of Quang Ninh of Northern Vietnam reported a NMR of 16 /1,000 live births over the period 2008-2010

[35]. No data on NMR in communities of Southern Vietnam have been published yet.

Binh Thuan is a mixed rural province located along the south-central coast of Vietnam, with a population of approximately 1.1 million inhabitants living mainly from agricultural production on an area of 7,992 km2, divided over 127 administrative communes whereof one is located on an island and 6 are found in mountainous areas. Binh Thuan has more 27 ethnic groups living together, including Kinh, Cham, Ra-glai , Chinese, K'ho, Rai, Chan Ro, Nung, Tay and other small groups. Kinh ethnic group, with 973, 863 people, account for about 93% of population; it is also the predominant ethnic group of all Vietnamese regions. Kinh have political and economic power and are generally richer than minority (non-Kinh) groups, with an easier access to infrastructure, health services, and education. Ethnic minorities represent about 73,137 persons or 7 % of the province's population. The most important ethnic minority is Cham, accounting for 2.80% of the province's population, followed by Ra-glai (1.19%), Chinese (1.07%), and over 24 other ethnic minorities groups (1.92%). Binh Thuan has an organizational health care structure at three levels: three provincial or central health centers with 201 physicians, 10 district health centers with 173 physicians and 127 commune health stations (CHS) with 94 physicians. All CHSs provide primary health care including antenatal care and delivery. Most deliveries at all CHS are supervised by skilled midwifes who have access to oral and intramuscular drugs and simple small surgical equipment. Complicated cases are referred to the closest district hospital by an ambulance of district hospital, taxi or more commonly by motorbike.

In Binh Thuan, like in all provinces of Vietnam, the under-5 child mortality rate is collected from routine reports based on the death records at the commune level (A6/YTCS) designed by the Ministry of Health of Vietnam, but the form is very simple and more designed for administrative purpose than for medical purpose. Child death cases are not documented about demographic characteristics (age/gender), socio-economic situation (parents' income, occupation, educational level), urban/rural areas. The data on infant mortality are used for provincial statistics and surveys but without specific report on neonatal mortality. However, the good structure of healthcare at all levels, the good access to primary care and a stable population representing the country's major ethnic group, were all suitable conditions for implementing a community-based study to identify causes and potential determinants of neonatal death in the Province of Binh Thuan.

Methods

The present study is part of a population - based registry study of external birth defect in the Province of Binh Thuan which was recently published [109]. In this study, all infants born in 2010 to mothers resident in Binh Thuan who delivered after 22 weeks of gestation in one of the 139 health facilities were registered.

The present study included all deaths occurring in the first month of life of these infants born to residents in the year 2010. Predesigned forms on women and babies' profile were provided to health facilities to be filled out by a trained local heath professional at CHS level or a trained local physician at hospital. This form contained the following data for all neonatal deaths: place of death, mother's name, address, sex of baby, date of death, date of birth, place of birth, and cause of death. These data were later cross-checked with data collected by the birth defect registry that covered all live births to a mother residing in the province. The data on mother's demographic profile, mother's obstetric characteristics, and neonatal characteristics including sex, gestational age, and birth weight were extracted from the birth defect registry to be linked with neonatal deaths.

In addition, the cause of a neonatal death was also assigned according to the event that caused the death, as follows: preterm or low birth weight, birth asphyxia or hypoxia, infection, congenital abnormality, other, and unknown.

The cause of death provided by health facilities was reviewed by a local expert pediatric physician. In case of disagreement in the allocation of cause of death, the profile of patient was reviewed and discussed with three local pediatric physicians. The team decided as a group what the most likely diagnosis was.

All data on neonatal deaths were rechecked and entered into a Microsoft Excel sheet by a local trained data processor (a local health professional) before sending data to a processing center at the Provincial Health Service, on a monthly base.

Very early neonatal mortality rate was defined as number of deaths during the first 24 hours of life per 1,000 live births. Early Neonatal Mortality Rate (ENMR) was defined as death during the first completed six days of life per 1,000 life births. Late Neonatal Mortality Rate (LNMR) was defined as deaths between 7 and 27 days per 1,000 live births. Neonatal deaths were defined as alive neonates who died<28 days after birth. The Neonatal Mortality Rate (NMR) was calculated per 1,000 live births.

Statistical analyses were performed using STATA statistical software. We used Poisson model to compute 95% confidence intervals on mortality and on ratios for

assessing risk factors related to neonatal death.

The study was approved by the Binh Thuan Provincial Health Service and the Pham Ngoc Thach University Ethical Review Committee, Hochiminh City, Vietnam. Before entering in the study, all mothers were informed about the study and were asked for written consent. Informed consent was obtained from all participants.

Results

In 2010, a total of 13,954 newborns were registered, corresponding to a birth rate of 12.7 per one thousand people. There were 7,209 boys and 6,743 girls (sex ratio = 1.07). Two newborns had an indeterminate sex. The number of mothers was 13,877 because there were 71 twins (5.12 / 1,000 mothers), 3 triple births (0.17 / 1,000 mothers) and 13,803 singleton births.

Two Kinh mothers aged 26 and 31 who lived in rural area died due to postpartum hemorrhage at the same district hospital, corresponding to a maternal mortality ratio of 14.3/ 100,000 live births.

Among the 71pairs of twins, 12 pairs were of opposite gender, and 59 were of the same gender. The sex ratio was 1.15 (76/66). The mean birth weight was 2,673 ± 509 g (mean ± SD) with a range of 1,900-3,600g. The low birth weight (<2,500 g) accounted for 38.8% (55/142) of twins and the very low birth weight (<1,500 g) accounted for 4.9% (7/142) of twins. The mean gestational age was 38.3 ± 2.3 weeks (mean ± SD) with a range of 32.0 - 43.0 weeks. About 33.8% of twins (48/142) were born prematurely, and 32.4% of the twins (46/142) were born by caesarean section. The mean maternal delivery age was 28.0 ± 4.9 years (mean ± SD) with a range of 19-40 years, primigravida accounted for a third (35.2%) and the gravidity was 4 or more for 9.8% of mothers. About 5% of mothers were from the non-Kinh ethnic group, 46.5% of mothers lived in urban areas, and 4 .2 % of mothers lived in poverty. About 90% of mothers had a secondary school or higher education degree and 1.4 % of mothers were illiterate. There were no neonatal deaths among the 71 pairs of twins.

All three sets of same gender triple births died within 24 hours after delivery including 6 boys and 3 girls. All of them were premature with range 23-35 weeks and had a very low birth weight with range of 600 – 1,300g at birth. These triples born from mother aged 30, 32 and 40 years, and gravidity was 2, 1 and 4, respectively.

Among 13,803 live singleton births registered, 7,127 were boys resulted in sex ratio of 1.07 (7,127 /6,674). The mean birth weight was 3,120 ± 430 g (mean ± SD) with a range of 400-5,300 g for all live singleton births. About 5% had a low birth weight, 0.62% had a very low birth weight at birth and 2.6% weighted above or equal 4,000 g at

birth. The mean gestational age was 39.4 ± 1.6 weeks (mean ± SD) with a range of 23.0 - 50.5 weeks for all singleton births, and 8.0 % of live births were premature.

Regarding the 13,803 mothers with singletons, maternal delivery age was 26.3 ± 5.5 years (mean ± SD) with a range from 13 to 50 years. There were 1,180 *(8.6%)* mothers who gave birth <20 years, including 16 mothers who were 13 to 15 years, and 1.7% of mothers were aged over 40 years. The primigravida accounted for a third (35.2%) of mothers and the gravidity ≥ 4 for 9.8% of mothers. About a quarter of the mothers didn't finish secondary school degree, including 3.4 % of illiterate mothers. There were 1.6 % of mothers living with a National Certificate of absolute poverty and 7.0 % of mothers living with a National Certificate of poverty. About 10% of mothers were from the ethnic minority group, and 69.3% of mothers lived in rural areas. There were 2,125/13,803 (14.7%) of mothers who delivered in a CHS.

Among the 13,803 live singleton births there were 102 neonatal deaths in the year 2010, corresponding to a NMR of 7.4 per 1,000 live births (95% CI: 6.0–9.0 / 1,000). 52.0% were boys and 48.0% were girls, resulting in a NMR for boys at 7.4/1000 (95% CI: 5.7 – 9.7/1,000) and for girls at 7.3/1,000 (95% CI: 5.6 – 9.7/1,000), and a sex ratio of 1.08 for all neonatal deaths.

Of the 102 neonatal deaths, 58 (56.9%) died within 24 h of delivery, representing a very early mortality rate of 4.2 per 1,000 live births (95% CI: 3.2–5.4 / 1,000), and another 27 deaths had occurred within the first week, representing a proportion of early neonatal deaths of 83.3% (85/102), and an ENMR of 6.2 per 1000 live births (95% CI: 5.0 - 7.6/1,000) (Figure 11).

Causes of death are reported in Table 17. Low birth weight and prematurity was the leading cause of death, followed by births asphyxia or hypoxia, and most of these deaths occurred within 24h of birth.

Figure 11. Age of neonatal death cases during the year 2010 in Binh Thuan province, Vietnam

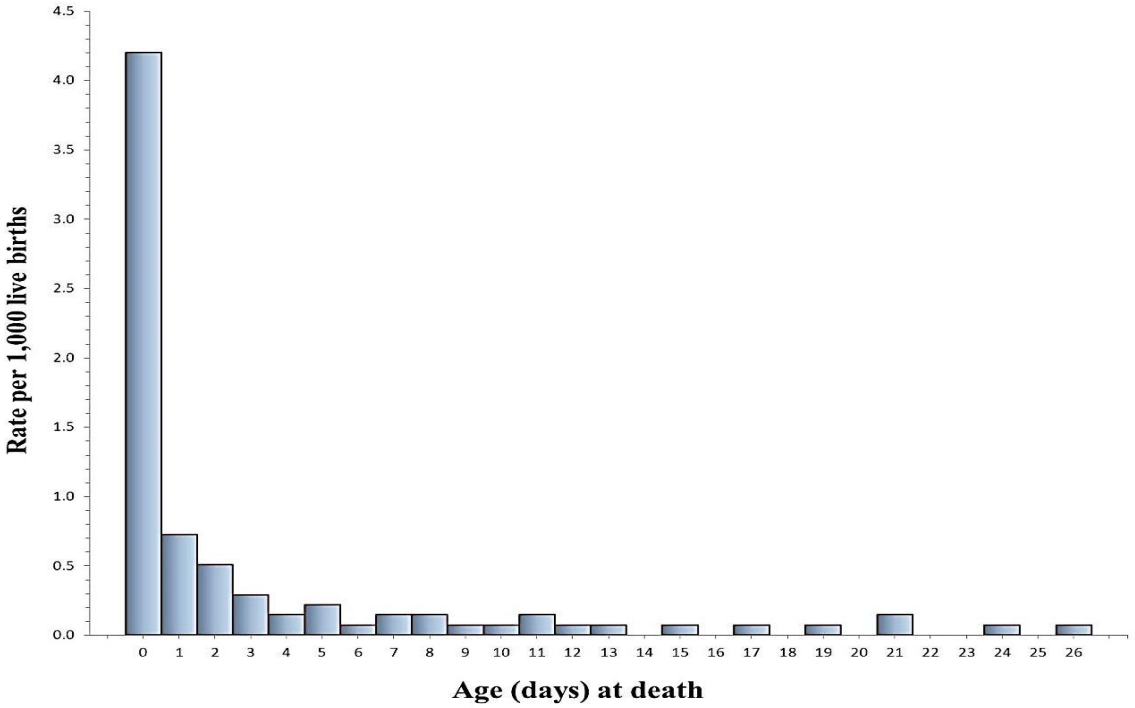

Table17. Causes of neonatal death during the year 2010 in the Province of Binh Thuan , Vietnam according to time of death

Causes of death	**< 24h (n=58)**		**Day 1-6 (n=27)**		**Day 7-27 (n=17)**		**Total (N=102)**	
	n	***%***	**n**	***%***	**n**	***%***	**N**	***%***
Low birth weight / pre-maturity	25	*43.1*	7	*25.9*	2	*11.8*	**34**	***33.3***
Birth asphyxia or hypoxia	20	*34.5*	3	*11.1*	0	*0.0*	**23**	***22.5***
Neonatal infection	0	*0.0*	10	*37.0*	12	*70.6*	**22**	***21.6***
Congenital anomalies	11	*19.0*	3	*11.1*	2	*11.8*	**16**	***15.7***
Others							**4**	***3.9***
Prolonged labour	1	*1.7*	0	*0.0*	0	*0.0*	-	-
Neonatal jaundice	0	*0.0*	2	*7.4*	0	*0.0*	-	-
Accident vehicle	0	*0.0*	0	*0.0*	1	*5.9*	-	-
Unknown	1	*1.7*	2	*7.4*	0	*0.0*	**3**	***2.9***

Infection was the main cause of deaths over the late neonatal period, while prematurity/ low birth weight and congenital anomalies continued to contribute to deaths.

Early, late and overall neonatal mortality rates according to maternal and neonatal characteristics are presented in Table 18, and ratios are illustrated on Figure 12.

Not surprisingly, a low birth weight and prematurity were associated with a very high death rate. Although only15% of mothers delivered in a commune health station, it was reassuring and encouraging to register a similar death rate between hospital and CHS deliveries, with 3 deaths (3.0%) in CHS: one case of anencephaly and two cases of low birth weight /premature.

Figure 12. Neonatal mortality ratios by selected maternal –neonatal characteristics in the Province of Binh Thuan

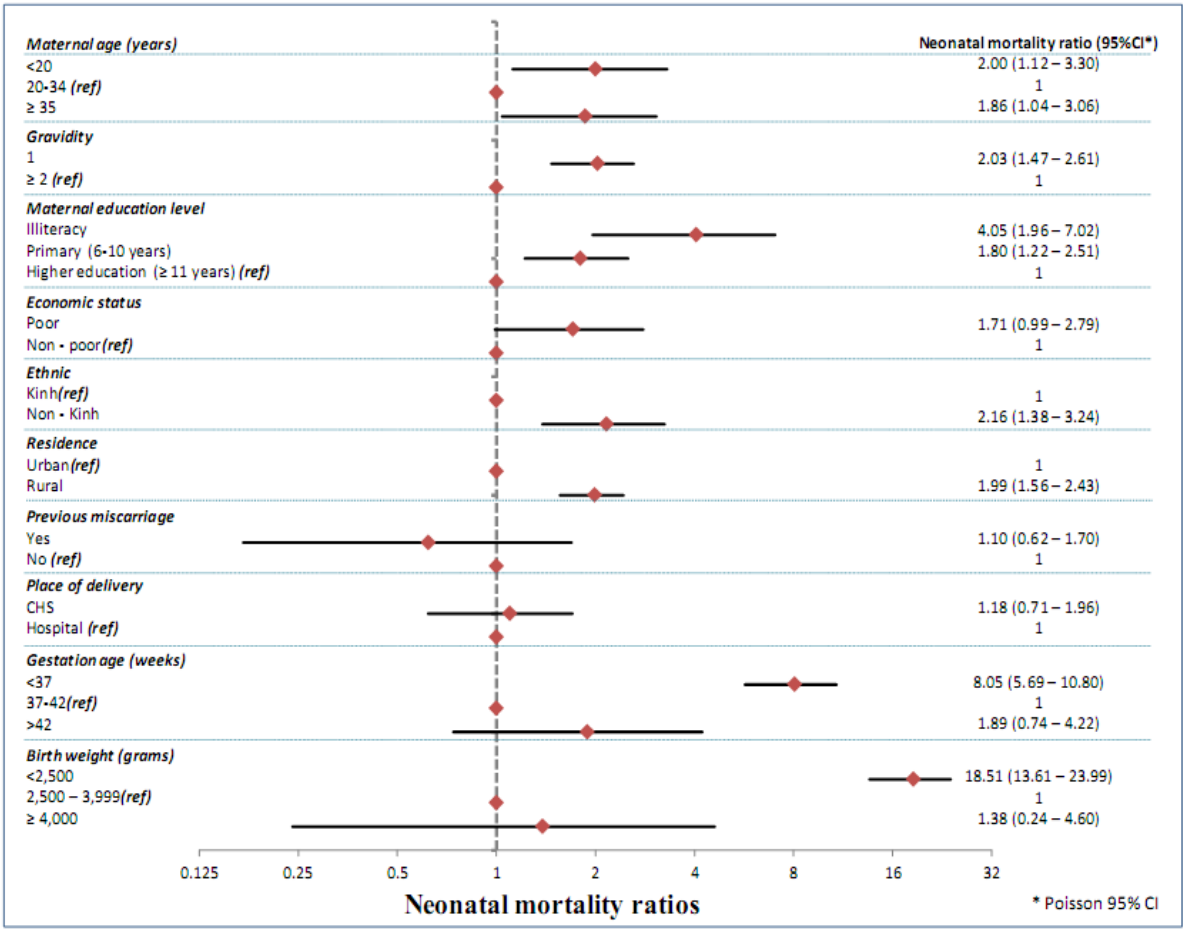

Table 18. Maternal-neonatal characteristics of neonatal deaths in the Province of Binh Thuan during the year 2010.

Variables	Neonatal deaths								
	Living singleton		Day 0-6 (n=85)		Day 7-27 (n=17)		Total (n=102)		
	N=13,803 *(%)*		n	*(/ 1000)*	n	*(/ 1000)*	n	*(/ 1000)**	95%CI [¥]
Maternal age (years)									
<20	1,180	*(8.5)*	10	*(8.5)*	5	*(4.3)*	15	*(12.7)*	7.1 – 20.9
20-34	11,349	*(82.3)*	63	*(5.6)*	9	*(0.8)*	72	*(6.3)*	4.9 – 7.9
≥ 35	1,274	*(9.2)*	12	*(9.4)*	3	*(2.4)*	15	*(11.8)*	6.6 – 19.4
Gravidity									
1	4,682	*(33.9)*	41	*(8.8)*	9	*(1.9)*	50	*(10.7)*	8.1 – 14.3
≥ 1	9,121	*(66.1)*	44	*(4.8)*	8	*(0.9)*	52	*(5.7)*	4.1 – 7.1
Education level									
Illiteracy	466	*(3.4)*	9	*(19.3)*	2	*(4.4)*	11	*(23.6)*	11.4 – 40.9
Primary (6-10 years)	2,860	*(20.7)*	25	*(8.7)*	5	*(1.8)*	30	*(10.5)*	7.1 – 14.6
Secondary or Higher education (≥ 11 years)	10,477	*(75.9)*	51	*(4.9)*	10	*(1.0)*	61	*(5.8)*	4.5 – 7.4
Economic status									
Poor	1,178	*(8.5)*	12	*(10.2)*	2	*(1.7)*	14	*(11.9)*	6.9 – 19.5
Non-poor	12,625	*(91.5)*	73	*(5.8)*	15	*(1.2)*	88	*(7.0)*	5.6 – 8.5
Ethnic									
Kinh	12,402	*(89.9)*	69	*(5.6)*	13	*(1.0)*	82	*(6.6)*	5.24 – 8.00
Non-Kinh	1,401	*(10.1)*	16	*(11.4)*	4	*(2.9)*	20	*(14.3)*	9.1 – 21.4
Residence									
Urban	4,227	*(30.6)*	18	*(4.3)*	3	*(0.7)*	21	*(5.0)*	2.7 – 6.4
Rural	9,576	*(69.4)*	67	*(7.0)*	14	*(1.5)*	81	*(8.5)*	6.9 – 10.9
Previous miscarriage									
Yes	636	*(4.6)*	3	*(4.7)*	0	*(0.0)*	3	*(4.7)*	1.3 – 12.7
No	13,167	*(95.4)*	82	*(6.2)*	17	*(1.3)*	99	*(7.5)*	6.1 – 9.1
Place of delivery									
Hospital	11,678	*(84.6)*	73	*(6.2)*	11	*(0.9)*	84	*(7.2)*	5.7 – 8.9
Commune health station	2,125	*(15.4)*	12	*(5.6)*	6	*(2.9)*	18	*(8.5)*	4.5 – 12.4
Gestation age (weeks)									
< 37 weeks	1,103	*(8.0)*	37	*(33.5)*	4	*(3.7)*	41	*(37.2)*	26.3 – 49.9
37 – 42 weeks	12,126	*(87.9)*	44	*(3.6)*	12	*(1.0)*	56	*(4.6)*	3.4 – 5.9
> 42 weeks	574	*(4.1)*	4	*(7.0)*	1	*(1.7)*	5	*(8.7)*	3.4 – 19.5
Birth weight (gram)									
< 2500	663	*(4.8)*	45	*(67.9)*	4	*(6.5)*	49	*(73.9)*	54.3 – 95.8
2,500-3,999	12,776	*(92.6)*	38	*(3.0)*	12	*(0.9)*	50	*(3.9)*	2.9 – 5.3
≥ 4000	364	*(2.6)*	2	*(5.5)*	1	*(2.8)*	3	*(8.3)*	1.0 – 18.4

*: Neonatal mortality rate [¥] IC 95% : Poisson 95% CI

Table 19. Poisson regression analysis for factors associated with neonatal mortality

Variables	RR	95%CI	P value
Maternal age (years)			
<20	1.87	1.05 – 3.38	0.03
20-34	1	-	-
≥ 35	1.5	0.83 – 2.64	0.19
Gravidity			
1	2.26	1.50 – 3.42	<0.01
≥ 1	1	-	-
Maternal education level			
Illiteracy	3.73	1.81 – 7.68	<0.01
Primary (6-10 years)	1.53	0.96 – 2.45	0.07
Higher education (≥ 11 years)	1	-	-
Ethnic			
Kinh	1	-	-
Non-Kinh	1.62	0.95 – 2.89	0.08
Residence			
Urban	1	-	-
Rural	1.68	1.09 – 3.23	0.02
Gestation age (weeks)			
< 37 weeks	2.99	1.87 – 4.79	<0.01
≥ 37 weeks		-	-
Birth weight (gram)			
< 2,500	11.41	7.20 – 18.06	<0.01
≥ 2,500	1	-	-

Table 19 shown that maternal age <20 or ≥ 35, and gravidity 1 were associated with a significantly higher neonatal mortality. However, neonatal mortality was also significantly higher in poor people, in ethnic minorities, in rural inhabitants, and there was a significantly increase in neonatal mortality as the education level of the mother decrease; among illiterate mothers, the NMR as 4.05 times higher than among mothers with a secondary education level or higher. Using multivariate Poisson regression analysis revealed that there was a significant increased risk of neonatal death among babies with low birth weight ($p<0.001$), premature babies ($p < 0.01$), babies of illiterate mothers ($p < 0.01$), babies of teenage (under age 20) mothers ($p<0.03$), babies of primigravida mothers ($p < 0.01$), and among babies from a mother living in rural area ($p < 0.02$).

Illiteracy was associated with a higher neonatal mortality, independently with low birth weight and prematurity. Among

illiterate mothers, there was 5.6 % of low birth weight and 9.8 % of prematurity, and among literate mothers, these proportions were 4.8 % (p = 0.42) and 7.9 % (p = 0.13), respectively. Teenage mother was also an independent predictor of neonatal mortality because it was not correlated with low birth weight or with prematurity. Low birth weight was 5.5% in teenage mothers and 4.7% (p=0.23) in mothers aged >20 and prematurity was 8.9% in teenage mother and 7.9% (p=0.25) in mother aged >20.

Ethnicity was not an independent predictor of neonatal mortality because of its relationship with illiteracy and with low birth weight. Illiteracy was quite higher among non Kinh mothers than in Kinh mothers (10.9% vs 2.5%, p < 0.001). Among non Kinh mothers, 6.5% had a low birth weight baby, compared with 4.6% among Kinh mothers (p<0.001).

Ethnicity, mode of delivery, place of delivery, previous miscarriage, and maternal economic status were no more associated with neonatal mortality in the multivariate regression model.

Discussion

Neonatal mortality

Officially, the NMR in Vietnam was 12/1,000 in 2004 [33]. A neonatal mortality rate of 16 ⁄ 1,000 from NeoKIP community-based trial in the Province of Quang Ninh of Northern Vietnam over the period 2008-2010 was reported by Nga, NT et al [35]. Dinh P Hoa et al also reported a neonatal mortality rate of 16 ⁄ 1,000 live births over the period 1986-2000 in Bavi district, Northern Vietnam [32]. NMR was reported as 11.6/1,000 live births over the period 1999-2005 in a rural population in Northern Vietnam [34]. In our population, the NMR was 7.4/1,000 live births.

The lower NMR in the Province of Binh Thuan may have been due to the collected data that didn't cover the neonatal deaths occurring outside of health facilities. Reports from developing countries have shown improvements in perinatal and neonatal outcomes with increased coverage by health services and skilled birth attendants [110]. The relative high level of health care coverage with skilled birth attendance available at the all level of care and easy transportation for referrals in the Province of Binh Thuan may also contribute to a lower neonatal mortality rate compared with studies in other provinces of Northern Vietnam.

Comparing with other studies in developing countries [14, 108], the findings of our study revealed a very high proportion of early neonatal deaths (83.3%) but comparable to 80.6% reported by Nga,NT et al in Quang Ninh province of Northern Vietnam [35].

Causes of neonatal deaths

With a NMR of 7.4⁄1000, causes of neonatal deaths in our study differed somewhat from

the WHO-derived global estimates [14, 111]. Congenital anomalies accounted for a proportion of 15.7% of neonatal deaths in Binh Thuan, which was higher than to the global average of 7-8% [14, 35, 111], and also higher than the 7% reported in the Province of Quanh Ninh in Northern of Vietnam [35]. Prematurity/low birth weight, which accounted for 28% of the neonatal deaths in the global average [111], and for 37.8% in Quang Ninh province[10], was 33.3% in our study, not far from published studies. Birth asphyxia accounted for a similar proportion (22.5%) of neonatal deaths in Binh Thuan compared to the global average of 23% [111]. Birth asphyxia was reported to be higher proportion (33.2%) in the Province of Quang Ninh of Northern Vietnam [35].

In the presented study, the high proportion of early neonatal death and the high proportion of deaths due to birth asphyxia and premature/ low birth weight show that newborn care is still a problem especially for newborns under 7 days of age. Infection was the cause of death in 21.6% of the neonatal deaths in our study, which is much lower than the global average of over one third of the neonatal deaths [14]. It is also higher than the 13% reported in recent study conducted in the Province of Quang Ninh of Northern Vietnam [35]. Our findings that infections is an important contributor to neonatal deaths that occur in late neonatal period which is consistent with reports on the causes of neonatal death in developing countries [112]and also with other report from Vietnam [35]. This result highlights the importance of monitoring delivery and hospital-acquired infection and it highlights also the need for improving perinatal management and care of newborns at health facilities.

Determinants of neonatal deaths

Preterm birth is well recognized as a major determinant of mortality during the perinatal period and a key to understanding the etiology of both fetal and neonatal deaths [113]. As expected, the preterm birth was strongly associated with neonatal deaths in our study. It is consistent with a prospective cohort study performed in Tunisia [114]. The influence of prematurity on increasing risk of neonatal deaths was also evidenced by Imtiaz Jehan et al in a population-based cohort study in Pakistan [115]. Mercer A et al also reported prematurity as the main risk factor of neonatal death among singleton babies in rural areas of Bangladesh [116].

Birth weight is also well recognized factor associated with neonatal mortality. The association between birth weight and mortality is one of the most studied topics in neonatal and perinatal epidemiology [117]. The weight-specific mortality curve has an inverse J-pattern, with highest value for the smallest infants [117]. It is obvious from Figure 12 that low birth weight was the most important factor associated with neonatal

mortality, as reported by several neonatal studies [110, 118, 119].

The male-to-female ratio in neonatal mortality in developing countries is estimated at 1.3[120]. Neonatal mortality was higher in males than in females, a biologically expected difference [121], that we also found in our study with a sex ratio of 1.08.

Most neonatal deaths occurred at hospital (97%) and about 85% of mothers delivered at hospital because of a relatively easy access to higher level of care and early transfer of severe cases from CHS to closest hospital in the Province of Binh Thuan.

Maternal age was found to be significantly associated with neonatal mortality with increased at extremes of age (maternal age <20 or ≥ 35 years). Such findings was consistent with published data from a study in Nepal showing that infants born to mothers aged 12 to 15 years were at a higher risk of neonatal mortality than those born to women aged 20 to 24 years [122]. In a retrospective cohort study of 3,886,364 nulliparous pregnant women aged <25 years who give birth to a singleton between 1995 and 2000 in The United States, Chen X.K et al indicated that teenage pregnancy was associated with increased risks of neonatal mortality [123].

An important covariate of neonatal mortality was found to be the education of mother. Mother's education seems to be directly related with the health of an infant. The mother's education influences her choices and skills in health care practices. An educated mother usually provides better care of infant than a mother without education or with a lower level of education [124]. Our findings showed that the neonatal deaths had inverse relation to mother's education. Illiterate mothers had a significantly increased neonatal mortality. This result was in line with other studies that shown higher risk of neonatal mortality in mother with lower level of education [125-127]. By contrast, a study in Nepal reported that maternal education was predictor of mortality only for infants who died in the post-neonatal period, but not in the neonatal period [128].

Several studies worldwide indicated that ethnicity was a major risk factor for neonatal death [129, 130]. Despite recent efforts to improve socioeconomic status in remote areas, ethnic minority groups remain the poorest and most isolated people in Vietnam [131]. A study in Bavi district, a rural district in the Red River Delta region of Northern Vietnam, reported that neonatal mortality rates were significantly higher among ethnic minorities, and that the gap between them and the majority group was increasing [32]. In our study, the minority ethnic was significantly associated with increased neonatal mortality in univariate analysis. However, this variable was loose importance in favour of maternal ethnic when

multivariate analysis was conducted subsequently. The univariate ethnic effect on neonatal mortality can be attributed to illiteracy and low birth weight rather than to any genetic effect.

Our findings showed significantly higher risk of neonatal mortality in rural group than in urban group. Such findings in the Province of Binh Thuan could be explained by the socioeconomic inequalities between the groups; mothers living in rural areas generally have a less favorable health care outcome than their urban counterparts. Our result was in line with others studies showing profound socio-economic disparities between rural and urban populations, in terms of neonatal death [132].

Our findings show that several factors influence the NMR, which need to be addressed if neonatal survival is to be improved. The most obvious editable factors are mother's education and teenage mothers. This evidence suggests that improving maternal education and preventing teenage pregnancy may be two key factors for improving neonatal survival in the Province of Binh Thuan.

Conclusions

In present study, the primary causes of neonatal mortality was consistent with WHO reports on the causes of neonatal in developing countries which can be prevented if proper care is given in a timely manner.

The programs of health awareness should target mothers and babies at high risk, especially programs focusing on illiterate mothers, teenage mothers, ethnic minority mothers and programs aiming to improving antenatal care to reduce low birth weight and prematurity, and also to reduce neonatal mortality in this region.

Data on neonatal mortality from this study in Southern Vietnam may be useful in prioritizing the intervention programmes for achieving the objectives of MGD, especially for MDG 4 in Vietnam.

List of abbreviations

CHS: Commune health stations

ENMR: Early Neonatal Mortality Rate

MDGs: Millennium Development Goals

MDG4: Fourth Millennium Development Goal

NM: Neonatal Mortality

NMR: Neonatal Mortality Rate

Competing interests

None of the authors of the above manuscripts has declared any conflict of interest statement.

Authors' contributions

TH participated in the design, carried out the study, performed the statistical analyses and drafted the manuscript. AR provided advice in the design of the study and the analytical strategy and contributed to the manuscript

revision. NNVP, DLNN helped in the data analysis and report. AR and DNT are head of the project; they provided advice on the structure, the data analysis and presentation, and supervised the manuscript redaction. All authors read and approved the final manuscript. No author has any financial or private interest in this research project.

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5.3 FOLLOW UP OF INFANT DURING 9 MONTHS OF LIFE

Title: Frequency of heart murmurs and the normal anthropometric measurements for infant under 9 months in Lagi district of the Province of Binh Thuan, Vietnam.

Authors: *Truong Hoang, Dung The Nguyen, Phuong Van Ngoc Nguyen, Dong A Tran, Yves Gillerot, Raymond Reding and Annie Robert*.

Journal: ready to sumbit to BMC Pediatrics

SUMMARY:

Background

Detection of a murmur on routine examination may be a clue to the presence of heart disease and overs the possibility of early, presymptomatic diagnosis. Our study aims were to access prevalence of heart murmur and other birth defect occurring later after birth that can be detected by simple clinical examination, and to evaluate a physical growth curve of infant under 9 months of age in Lagi district of the Province of Binh Thuan, Vietnam.

Method

The heart murmurs screening in infant ≤ 9 months was integrated into the vaccination and child malnutrition control program at the all CHS in Lagi district. The babies were examined whenever they come to CHS for vaccination or for status nutrition verification according to current immunization and malnutrition control program schedule at 3^{th}, 6^{th} and 9^{th} month of life.

Results

Three cases with heart murmur were detected at 9 months of age representing 2.3 per 1,000 (3/1247) live births. Weight for age and height for age was higher in the boys than girls. The physical growth curves for Lagi's boys and the girls were close to WHO standard curves for height, weight, head circumference and BMI.

Conclusion

The lack of experience of health professionals from local health stations in cardiac examination of infants were possible the main causes of the low prevalence of heart murmurs in current study. The physical growths of infants were in line with WHO standards until the age of 9 months in both sexes.

Introduction

The many birth defects of internal organs (eg digestive system, heart and circulatory system, internal urogenital system and central nervous system) have been undetected by simple routine neonatal examination due to their invisible signs during the first 24 hours of life. Congenital heart diseases are the most common group of congenital malformations. The difficulties in detecting heart disease at neonatal examination are well known. The neonatal examination takes place at a time of rapid change in the cardiovascular system as part of its adaptation to extra uterine life. These changes may produce murmurs which can be mistaken for heart disease [133, 134]. The prevalence of structural congenital heart disease is estimated to be around 1% of all live births. Up to six in every 1,000 live born babies have a cardiovascular malformation which presents in infancy, but is asymptomatic at birth [135]. Routine neonatal examination fails to detect more than half of babies with heart disease; examination at 6 weeks misses one third. Despite recent developments in interventional and surgical techniques, heart disease in children continues to be an important cause of morbidity and mortality [136, 137]. Murmur may be created by abnormal flow patterns in the heart and vessels resulting from congenital heart abnormalities. Approximately one percent of newborns have a heart murmur, and 31 to 86 percent of these infants have structural heart disease [136, 138, 139], including asymptomatic newborns. The early detection of a murmur in infant should prompt early referral to a pediatric cardiologist for diagnosis or appropriate reassurance.

We conducted a study to access prevalence of heart murmur and other birth defects occurring later after birth that can be detected by simple clinical examination, and to evaluate a physical growth curve of infant under 9 months of age in the district of Lagi, in the Province of Binh Thuan, Vietnam.

Methods

Lagi is district of Northern of the Province of Binh Thuan with an area of 182.2 km² and a population of 105,727 as of 2011 (650hab/km²) of which the majority of peoples 87,122 (82.4%) live in rural areas. Lagi is near Hochiminh city (the largest and richest city of Vietnam) borders with South East Asia Sea in South. Lagi port is one of the largest ports in Binh Thuan province and region. The economic growth rate rose to 11.6% in 2011. Income per person was 1.171 USD/person. Lagi is second richest district in the Province of Binh Thuan, followed by Phan Thiet city. Lagi has very good health structure, and good transport structure. Lagi has 9 CHS and one district hospital. In 2006,

100% CHS have a doctor and 100% of CHS has midwives.

The study comprised all live births born between 1November 2009 and 30 October 2010 in the Lagi district. The CA screening in infant ≤ 9 months was integrated into the vaccination and child malnutrition control program at the all CHS in Lagi district. The babies were examined whenever they come to CHS for vaccination or for status nutrition verification according to current immunization and malnutrition control program schedule at 3^{th}, 6^{th} and 9^{th} month of life. Routine examination including primarily systematically observing, palpating, measuring length, weight, head, circumferences, and heart examination for detecting heart murmur of the babies was undertaken by trained health professionals at CHS. Trained local health professionals collected information in predesigned forms. A common external birth defects atlas and a guideline manual for detecting heart murmur in infant were provided to each participant during one month of the training.

Statistical analyses were performed using the STATA statistical software. The deviations from the WHO standard curves were evaluated for statistical significance using the infant specific means of relative deviations from the standards. The statistical description of weight and length growth has two objectives, the estimation of mean and variation of attained weight and length as functions of infant age and the corresponding growth velocity also as a function of infant age. This study was approved by the Ethical Review Committee of the Binh Thuan Provincial Health Service and of Pham Ngoc Thach University, Hochiminh city Vietnam. All mothers provided written informed consent for themselves and their baby prior to enrolment in the study.

Results

There 1,663 newborn from mothers living in Lagi were registered in the external birth defect study. There were 1,392 infants present for first screening of heart murmurs at the age of 3 months in the follow up study. Among these infants, 64 cases lost follow up at 6 month and 54 cases lost of follow up at 9 month.

Among remaining 1,247 infants, there were 641 boys and 606 girls (sex ratio = 1.06). The mean birth weight was 3,115 ± 410 g (mean ± SD) with a range of 1,800-4,900g. The low birth weight (<2,500 g) accounted for 4.3% (53/1,247). The mean gestational age was 38.3 ± 2.3 weeks (mean ± SD) with a range of 32.0 - 43.0 weeks. About 16.3% of babies (204/1,247) were born prematurely, and 14.7% of babies (184/1,247) were born by caesarean section.

Mean maternal delivery age was 26.6 ± 5.7 years (mean ± SD) with a range of 15-46

years. Primigravida accounted for 42.3% (532/1,247) and the gravidity was 4 or more for 6.1% (76/1,247) of mothers. About 92% of mothers had a secondary school or higher education degree and 1.2% of mothers were illiterate. About 1.3% of mothers were from non-Kinh ethnic group, and 4 .2 % (53/1,247) of mothers lived in poverty.

Three cases with heart murmur were detected at 9 months of age representing 2.3 per 1,000 (3/1247) live births. Among these three cases, one had a cleft plate. All of them were boys were born at term between 40 and 41 weeks and had a normal birth weight between 2800 and 3000g at birth. These babie's mother aged 25, 18 and 33 years, and gravidity was 1, 1 and 2, respectively. All mothers of theses babies delivered at a CHS, had a secondary school or higher education degree, and none living in poverty.

Growth study was conducted with the full term newborn. A total 1067 infants born full term were measured at 3, 6, and 9 months of age for weight (kg), length (cm) and head circumference (cm). The boys were 550 (51.5%) while the girls were 517 (48.5 %) given a sex ratio (boys/girls) of 1.06. Boys had a higher weight, length for age than girls. The mean and standard deviation of the length/height according to gender and age together with WHO standards are shown in Figure 13 and Table 20.

Figure 13. Estimated mean curves of height (length) for age by sex compared with WHO standards

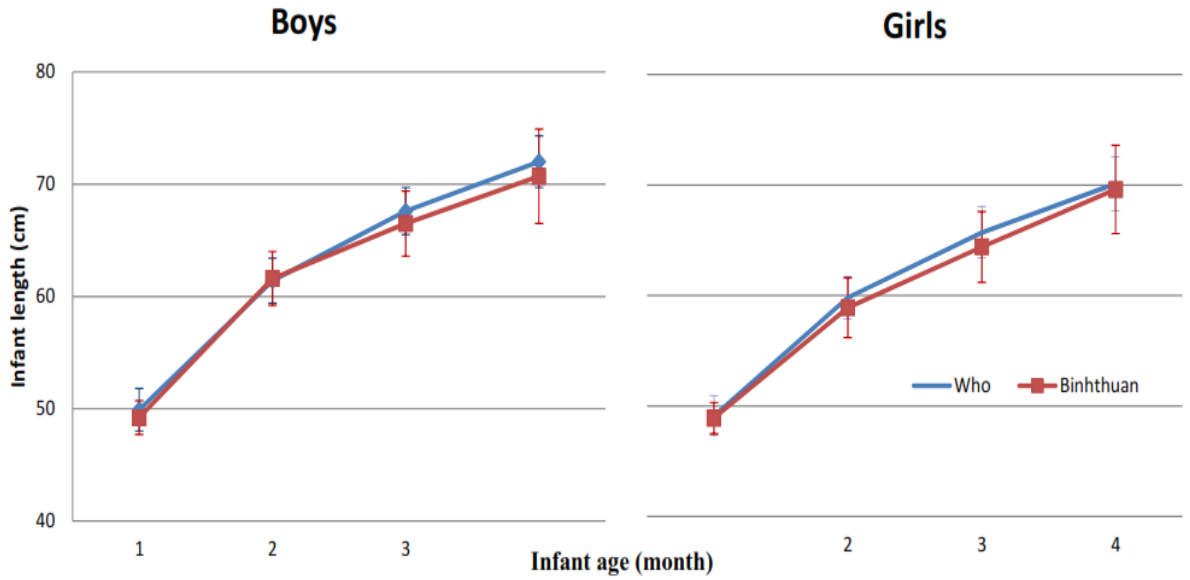


Table 20. Comparison of height (cm) for age and sex in the Lagi district with WHO standards

Age (month)	Boys				Girls			
	Binh Thuan		WHO		Binh Thuan		WHO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	49.2	1.5	49.9	1.9	48.9	1.4	49.1	1.8
3	61.6	2.4	61.4	2.0	58.9	2.7	59.8	1.9
6	66.5	2.9	67.6	2.1	64.4	3.2	65.7	2.3
9	70.7	4.2	72.0	2.3	69.6	4.0	70.1	2.4

The curves for height in Lagi district were close to WHO growth curves in boys. Girls in Lagi district had a slightly lower height growth curve than WHO reference, but without a statistically significant difference.

Data on weight of infant related to age and sex can be seen in Table 21 and Figure 14 show growth curve for weight by sex, in the first 9 months of life compared with WHO standard curves. Figure 15 and Table 22 shown that growth curve for Lagi's boys and the girls were closed to WHO standards for the head circumference. As seen in Figure 16 and Table 23, BMI indices were slightly higher than WHO BMI references at 3 and 6 months of age for both sexes, but this difference was not significant.

Figure 14. Estimated mean curves of weight for age by sex in Lagi district, together with WHO standards.

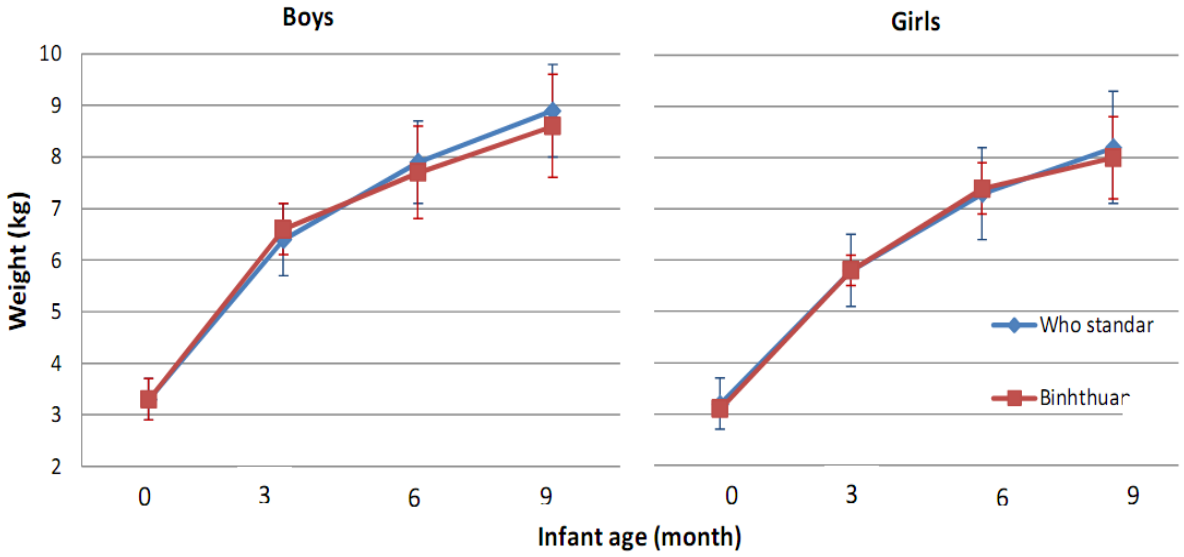


Table 21. Comparison of weight (kg) for age and sex in Lagi district with WHO standards

Age (month)	Boys				Girls			
	Binh Thuan		WHO		Binh Thuan		WHO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	3.3	0.4	3.3	0.4	3.1	0.3	3.2	0.5
3	6.6	0.5	6.4	0.7	5.8	0.5	5.8	0.7
6	7.7	0.9	7.9	0.8	7.4	0.8	7.3	0.9
9	8.6	1	8.9	0.9	8.0	1.5	8.2	1.1

Table 22. Comparison of head circumference in Lagi district with WHO standards by age and sex

Age (month)	Boys				Girls			
	Binh Thuan		WHO		Binh Thuan		WHO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	33.57	1.8	34.5	1.3	33.6	1.9	33.9	1.2
3	39.8	2.4	40.5	1.2	39.8	2.6	39.5	1.3
6	43	1.8	43.3	1.3	41.5	1.9	42.2	1.3
9	44.6	2.0	45	1.3	43.1	2.0	43.8	1.4

Figure 15. Estimated mean curves of head circumference for age by sex in Lagi district, together with WHO standards.

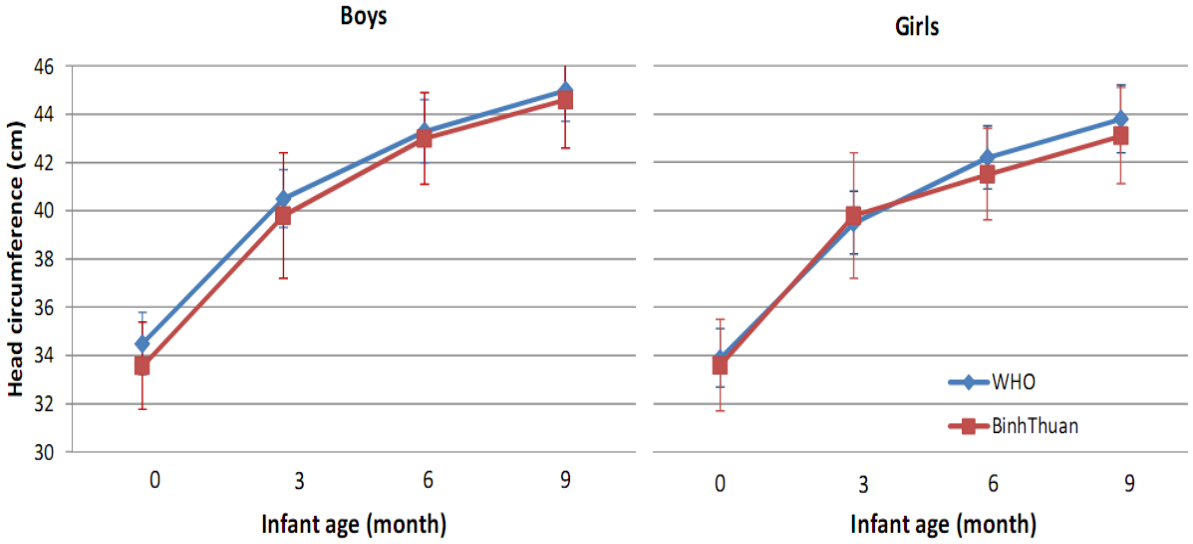
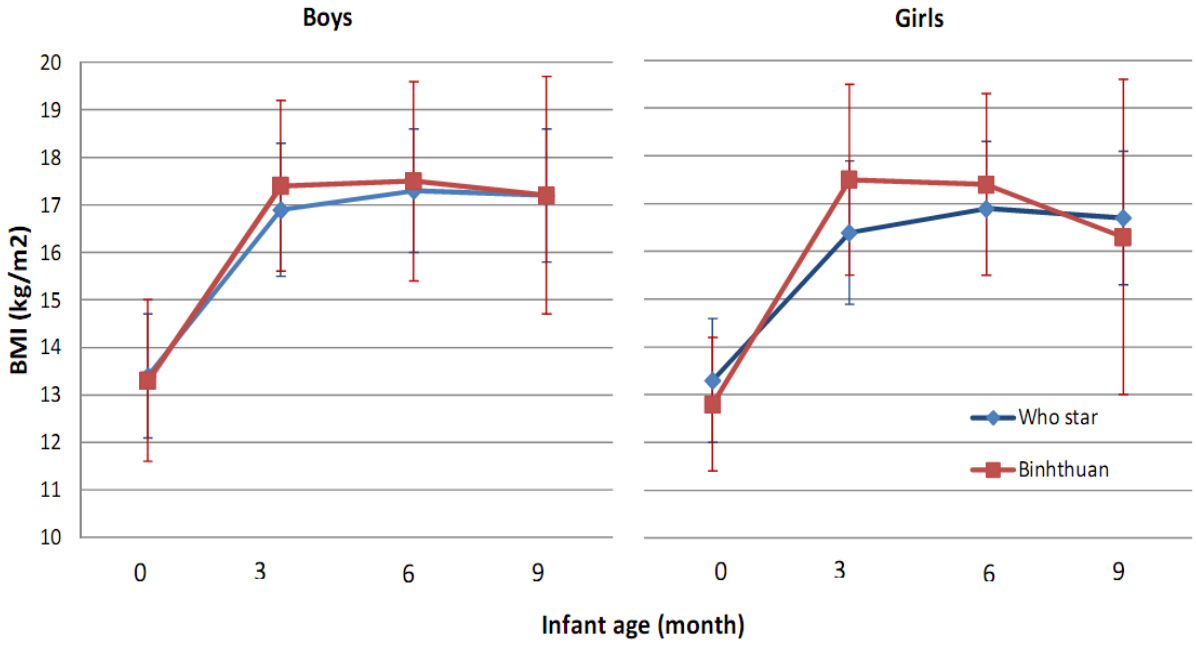


Table 23. Comparison of BMI in Lagi district with WHO standards by age and sex

Age (month)	Boys				Girls			
	Binh Thuan		WHO		Binh Thuan		WHO	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	13.3	1.7	13.4	1.3	12.8	1.4	13.3	1.3
3	17.4	1.8	16.9	1.4	17.5	2.0	16.4	1.5
6	17.5	2.1	17.3	1.3	17.4	1.9	16.9	1.4
9	17.2	2.5	17.2	1.4	16.3	3.3	16.7	1.4

Figure 16. Estimated mean curves of BMI for age by sex in Lagi district together with WHO standards.



Discussion

Although congenital heart disease are present at birth, there are often no signs and most babies are asymptomatic. Detection of a murmur on routine examination may be a clue to the presence of heart disease and allows an early presymptomatic diagnosis. Therefore, auscultation should be part of routine clinical examination of a child and is recommended in Health for All Children [140]. Functional murmurs are rare in young infants, and the presence of a cardiac murmur should be regarded as a conclusive sign of a congenital malformation of the heart, regardless of the quality of the murmur. Identification and treatment of heart disease before development of

symptoms is associated with an improved outcome. Early referral of all asymptomatic babies with murmurs is recommended.

There were many studies of incidence of heart murmurs in neonates, but few studies in infants. Mary et al reported an incidence of murmurs at birth of 17 per 1,000 newborns, 3.9 per 1000 at the age of 6 months, and 71 per 1000 at the age of 12 months [141]. In this study, author reports that when a murmur is first heard at 6 months and persists until 12 months, the chance that there is a congenital heart disease is 1:7 and when a murmur is first heard at 12 months, the chance falls to 1:50. In the study of Gregory et al reported that heart murmurs were heard in 47 of 5,395 babies at six to eight weeks of age, accounting for 0.9 percent of all babies [142]. In the present study, only 3 cases had heart murmurs, accounting for 0.23 per 1,000 infants at the age of 9 months. Our result was very low compared with these of two previous studies. A first reason of a low prevalence of murmurs in our study may be the fact that infants were investigated by a non pediatric cardiologist heath professional. A second reason may be due to missing data. It is common in Vietnam that women go back to their home district for living a few time with their mother after delivering, especially if there is a problem with the baby. In our study, 271 babies were absent at first examination at 3th months of life. Of whom may some newborns have cardiac congenital anomalies.

In our follow-up, we also assessed the physical growth of infant. In general, the physical growth rate of a child is rapid the first eight months of life and thereafter decreases with age until the adolescence growth spurt. Impaired stature growth in early life is associated with poor functional outcomes later in life and these children don't usually catch up in growth. The World Health Organization (WHO) Working Group on Infant Growth recommends anthropometric assessments of infants in order to assess nutritional adequacy and the impact of illness. Based on child growth in multiple studies, the WHO developed growth standards to determine whether physiological needs for growth and development are met during important childhood periods[27]. The last standards of WHO were published in 2006. The standards intend to show how healthy, breastfed children living under favorable conditions should grow in all populations, regardless of time and place. There are several indicators of infant and child growth and size. Each indicator has its weaknesses and strengths, and there is not a single one that is ideal during a long period of growth, as the correlation between height and weight varies [143].

A low weight for age is an important risk factor for death often due to diarrhea, malaria, measles and pneumonia [144]. Using the 2006 WHO standards better highlights the proportion of infants at an elevated risk than previous standards. Our study shows that the curve of weight by age was in infant from Lagi district in Vietnam similar to the WHO standard curve for both sexes. Our height for age, head circumference for age and BMI for age curves were also closed to WHO reference standards. In the current study, differences in height and weight between boys and girls were also comparable to previous studies in Vietnam [145, 146].

A recent study in Vietnam reported that urban boys and girls had curves of height and weight above the WHO standards but rural children curves of weight and for length were below WHO standards. This study indicated that genetic factors could not explain deviations in weight growth at a population level in Vietnamese infants [147]. Vaktskjold et al reported that infant in Central Vietnam had lower height for age, weight for age and BMI for age in late infancy than the WHO standard population, but only in rural areas; the was no difference for infants living in urban areas. In our study conducted in a rural area, the physical growth during the first 9 months of life was close to WHO standards.

Some unavoidable differences in the study designs, data collection and administrative procedures might explain that we don't find the same results as Vaktskjold. Our smaller sample size might be seen as a limitation but the good training of involved health workers has minimized potential biases.

Conclusions

From this study conducted in a rural area of the Province of Binh Thuan, we can conclude that physical growths of infants are in line with WHO standards until the age of 9 months in both sexes.

However, the very low prevalence of heart murmurs found in this setting is of limited value, due to the lack of experience of health professionals from local health stations in cardiac examination of infants. Developing such competency at the local health station level would reduce infant morbidity and mortality due to cardiac congenital anomalies in rural areas of Vietnam.

List of abbreviations

BMI: Body mass index

CHS: Commune health stations

WHO: World Health Organization

Competing interests

None of the authors of the above manuscripts has declared any conflict of interest statement.

Authors' contributions

TH participated in the design, carried out the study, performed the statistical analyses and drafted the manuscript. AR provided advice in the design of the study and the analytical strategy and contributed to the manuscript revision. NNVP helped in the data analysis and report. AR and DNT are head of the project; they provided advice on the structure, the data analysis and presentation, and supervised the manuscript redaction. All authors read and approved the final manuscript. No author has any financial or private interest in this research project.

There is no organization sponsoring this research which is granted by the Commission Universitaire pour le Développement (www.cud.be), which is a public funding from the Belgian government.

The corresponding author has full access to all the data in the study and had final responsibility for the decision to submit for publication.

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The study was supported by a grant from the Commission Universitaire pour le Développement (CUD) program, Belgium (www.cud.be). We are very grateful to A. T.D, Ti N.V, Nhon N.V, Hong L.V and their colleagues at Binh Thuan province for their help and support on data collection.

6 GENERAL DISCUSSION

Achieving MDG4, one of the most important items in the MDGs, need to include reducing deaths during the neonatal period. The Vietnamese government has identified perinatal health and neonatal mortality as priority areas and evidence-based guidelines on reproductive health were launched in 2003 for improving newborn care and survival [31]. The impact of birth defects on the future child, on the child's family and on the community is not restricted to mortality. Because of the particular impact of congenital malformations on public health, the World Health Organization has indicated the necessity to evaluate the potential burden of congenital anomalies in every country, at whatever stage of development, with a view to introducing preventive measures at the appropriate time [148]. The general goal of this project was to improve the mother and infant health by focusing on birth defect prevalence and neonatal mortality in the Province of Binh Thuan.

The first part of this work shows that the prevalence of external birth defects in the Province of Binh Thuan generally fell within the range reported for EUROCAT, Belgium data or other registries [45, 51, 54, 87, 90, 94] for most external birth defects, except with spinabifida. Contrasting with the relatively high frequency of anencephaly, no case of spinabifida was detected in our study. Several explanations can be proposed to explain the absence of spinabifida that is rare but very visible at birth; The small number of birth defect, the non registry of still births, genetic factors or diagnostic technique used may contribute to such a result. Our results also showed that limb defects, orofacial clefts and nervous central system defects were the three most common groups of congenital anomalies. The higher prevalence of EBDs tended to occur among either the mother with primagravida or the mother with gravida 4 or more. Maternal age was also found to be associated with EBDs with increased EBD prevalence at extremes maternal age either <20 or ≥ 35 years. These results were in line with to that in the literature [85, 87, 94, 149, 150]. Prevalence of external birth defects was not different between commune health stations and hospitals, showing a good capacity of health workers from commune health stations to detect EBDs. In addition, the orofacial clefts and limb defects prevalence showed that the risk of underreporting was very low, because the prevalence of these two common of external birth defects were close to other registries such results demonstrate the quality of a birth defect registry.

Since examinations were performed with basic technologies, birth defects of internal organs, especially circulatory system, have not undetected because not visible or asymptomatic

particularly during the first 24 hours of life. The follow-up study of these babies was set up to detect heart murmurs and other birth defects appearing after birth, during the first 9 months of life. This follow-up study showed that the prevalence of heart murmurs detected by simple routine clinical examination at the level of CHS was 2.3 per 1,000 (3/1247) live births in the Province of Binh Thuan. This result was very low when compared with those of others studies.

Such low prevalence of heart murmurs in our study may be explained by a lack of experience of CHS worker in cardiac examination o infants. The follow-up study also showed estimated physical growth curves of babies under 9 months close to WHO standard curves for height, weight, head circumference and BMI.

This work also addressed the important topic of neonatal mortality in South of Vietnam. In our population, the neonatal mortality rate was 7.4/1,000 live births which was lower than other studies in North of Vietnam reporting neonatal mortality rate between 11 and 16 per 1,000 live births. Our collection of data didn't cover the neonatal deaths occurring outside of health facilities of the Province of Binh Thuan. The relative high level of health care coverage with skilled birth attendance that are available in cities such as Hochiminh city and the easy transportation for referrals outside of the Province of Binh Thuan may have contributed to the lower neonatal mortality rate observed in the Province of Binh Thuan, as compared with studies in other provinces of Northern Vietnam. Nevertheless, the primary causes of neonatal mortality in the Province of Binh Thuan are consistent with the WHO reports on the causes of neonatal deaths in developing countries [112]. Infection was the important contributor (76%) to neonatal deaths that occur in late neonatal period (between 7 and 27 days of life), while prematurity, low birth weight and congenital anomalies contribute to deaths during the whole first month of life. The educational level of mother probably impact on the socio-economic level and on prenatal care behavior. The mother's education influences her choices and skills in health care practices and is directly related to the health of infants. Our findings showed that the neonatal death was inversely related to mother's education level; Neonatal mortality was higher for illiterate mothers. Maternal age was also found significantly associated with neonatal mortality which was increased in teenage mothers (age <20). Such findings are consistent with several published studies [125-127]. The neonatal mortality was also significantly higher among ethnic minorities (non-Kinh) in the Province of Binh Thuan as in another study in Northern Vietnam [32]. Despite recent efforts to improve socioeconomic status in remote areas, ethnic minority groups remain the poorest and

the most isolated people in Vietnam [131]. Mothers living in rural areas generally have less favorable health care outcomes than their urban counterparts. The socioeconomic inequalities between communities can contribute to a higher risk of neonatal mortality in rural areas than in urban areas in the Province of Binh Thuan.

The major strength of this study is the use of population-based registries, allowing a large sample size, but requiring also a lot of efforts to collect at the local data related to all births to mothers resident in whole province. Data derived from population-based data are less liable to bias than hospital-based data. Up to date, there is no ideal model in congenital anomaly surveillance. In the resource-limited setting of the Province of Binh Thuan, this current study provided a data collection protocol which allows the detection of external birth defects by persons with limited medical training at the local level using a very simple material.

Some limitation of this work should be mentioned. Live births with congenital anomalies are not always diagnosed at birth or in the early neonatal period. The birth defect of internal organs, particularly cardiac anomalies which are the most common group of congenital anomalies have been undetected in this project due to their invisible signs during the first 24 hours of life. The limited experience of local health professional for heart examination of infants probably explained the small prevalence of murmurs we found. Although the Province of Binh Thuan had a good structure of health care from grassroots level to central level, unregistered neonatal deaths occurring outside of health facilities was also a limitation of this project. Another limitation of our follow-up study was that many babies were not present for vaccination at the age of 3 months. The most probable reason is that it is common in Vietnam that women go back to their home district for living a few time with their mother after delivering and they bring their babies to the closest commune health station for vaccination because of the vaccination is free anytime and anywhere for any infant under 12 months in Vietnam.

7 CONCLUSIONS AND PERSPECTIVES

Despite some limitations, our study provides basic information on the magnitude and spectrum of public health problems caused by neonatal mortality and different types of external congenital anomalies diagnosed at birth in the Province of Binh Thuan.

At present there is no active birth defect register or surveillance programmes in Vietnam. The population-based registry study is the first study which identified a suitable approach for the recognition and reporting of external birth defects by health professional using the simple materials at the grassroots level of health care, and provided essential baseline data of external birth defects to establish a population-based registry of birth defects in Vietnam. The results from the project underline the pressing need to improve the prenatal screening of birth defects in remote areas of Vietnam.

What is the relevance of the current findings to action for reducing neonatal mortality? Clearly, this study provided neonatal mortality rates by detailed cause of death for neonates living in the Province of Binh Thuan. The identification of mothers and babies at a high risk with adequate data collection is the first step toward developing robust interventions and a policy response. Besides the developing of strategies to reach the poorest sections of the population and the ethnic minority groups, the current evidence proposes to enhance maternal education and to prevent teenager pregnancy as two keys factor for improving neonatal survival in the Province of Binh Thuan.

The current evidences also call for training health professionals from commune health stations to cardiac examination of infants.

Future studies including interventional programmes are required to test the impact of these previous proposes. The surprising absence of spinabifida in the population of Binh Thuan is also raises up a question requiring further investigation: Why is the spinabifida case rate so low in the Province of Binh Thuan?

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9 ANNEX: ATLAS AND NOTIFICATION FORMS

ATLAS OF BIRTH DEFECTS

LIST OF COMMON EXTERNAL BIRTH DEFECT

SYSTEM	ICD code
Nervous system	
Neural Tube Defects:	
Anencephalus and similar	Q00
Encephalocele	Q01
Spina Bifida	Q05
Hydrocephaly	Q03
Microcephaly	Q02
Arhinencephaly / holoprosencephaly	Q04.1/Q04.2
Eye	
Anophthalmos	Q11.0
Microphthalmos	Q11.1
Cataract	Q12.0
Ear	
Microtia	Q17.2
Anotia	Q16.0
Respiratory	
Choanal atresia	Q30.0
Orofacial clefts	
Cleft lip with /without cleft palate	Q36/Q37
Cleft palate	Q35
Digestive system	
Oesophageal atresia and stenosis	Q39
Ano-rectal atresia and stenosis	Q42
Abdominal wall defects	
Gastroschisis	Q79.3
Omphalocele	Q79.2
Urinary	
Bladder extrophy	Q641
Genital	
Hypospadias	Q54
Indeterminate sex	Q56
Limb	
Upper limb reduction	Q71
Complete absence of upper limb	Q71.0
Absence of upper arm and forearm with hand present	Q71.1
Absence of both forearm and hand	Q71.2
Absence of hand and fingers	Q71.3
Longitudinal reduction defect/shortening of arm	Q71.4
Fewer 5 fingers	Q71.8
Lower limb reduction	Q72
Complete absence of lower limb	Q72.0
Absence of thigh and lower leg with foot present	Q72.1
Absence of both lower leg and foot	Q72.2
Absence of foot and toe	Q72.3
Longitudinal reduction defect/shortening of leg	Q72.4
Split foot	Q72.7
Club foot - talipes equinovarus	Q66.0
Polydactyly	Q69
Syndactyly	Q70
Darwfism	Q77.4
Other malformations	
Arthrogryposis multiplex congenita	Q74
Congenital constriction band/ amniotic band	Q79.8
Conjoined twins	Q89.4
Disorders of skin	Q80-Q82

All live born babies should be examined systematically for birth defect by physicians or nurse using the check list and atlas manual. Any newborn or infant suspected of having a birth defect will be taken a photo. In those cases where a photograph is not or difficult to obtained, the detailed written clinical description of birth defect will be made. All birth defects with photo or written description will be review by a geneticist for final diagnostic.

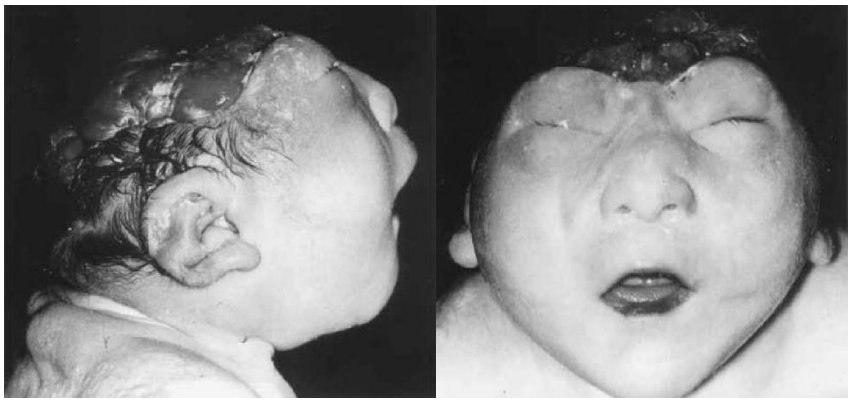
Infant who risk for birth defects:

1. Infants who weigh less than 2,500 grams or are < 36 weeks gestational age
2. Fetal and neonatal deaths
3. Infants with a history of asphyxia at birth (Apgar score at 5 minutes less than 7)
4. Infants admitted to neonatal intensive care or special care nurseries
5. Multiple births
6. Infants with respiratory distress
7. Infants with heart murmurs

I.NERVOUS SYSTEM

1. ANENCEPHALUS *(ICD10:Q00)*

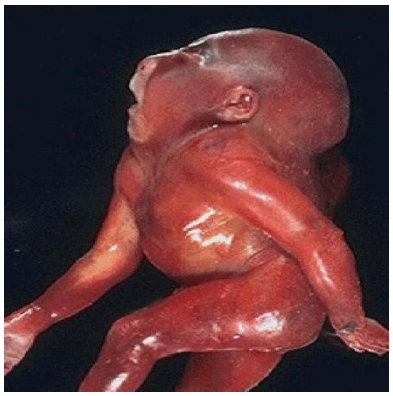
Description: Total or partial absence of brain tissue and the cranial vault. The face and eyes are present.



Note: Incompatible with life, die within the first 48 hours of life. *Associated malformation*: Anotia, cardiac defect, cleft lip and plate.

2. INIENCEPHALY *(ICD10:Q00)*

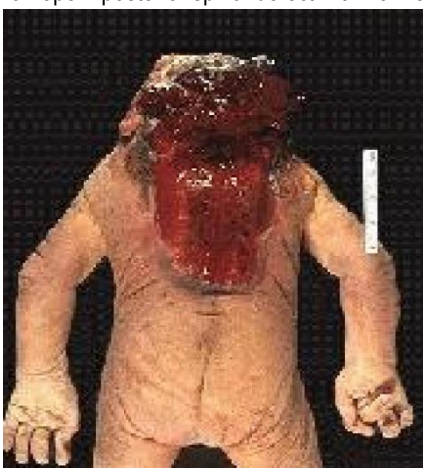
Description: a type of anencephaly, that combines extreme retroflexion (backward bending) of the head with severe defects of the spine.



Note: Diagnosis can be made immediately after birth because the head is so severely retroflexed that the face looks upward. Incompatible with life, die within the first 48 hours of life. *Associated malformation:* Anotia, cardiac defect, cleft lip and plate.

3. CRANIONRACHISCHISIS *(ICD10:Q00)*

Description: Anencephaly continuous with an open posterior spinal defect with no meninges covering the neural tissue.



Note: Incompatible with life, die within the first 48 hours of life. *Associated malformation:* Anotia, cardiac defect, cleft lip and plate.

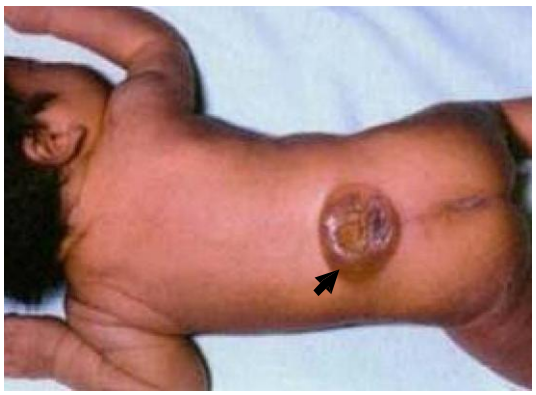
4. ENCEPHALOCELE *(ICD10:Q01)*

Description: Cystic expansion of meninges and brain tissue outside the cranium covered by normal or atrophic skin.

Note: 75% of encephaloceles are in the occipital region. *Associated malformations:* Facial clefts, Ophthalmia/microphthalmia, Cardiac defects, Limb reduction defects, Polydactyl.

5. SPINA BIFIDA *(ICD10:Q05)*

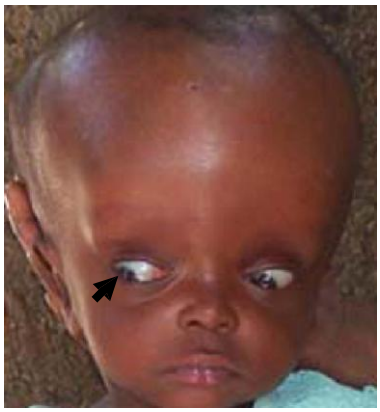
Description: Midline defect of the osseous spine usually affecting the posterior arches resulting in a herniation or exposure of the spinal cord and/or meninges.

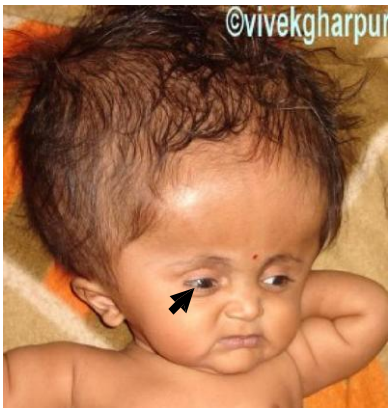


Note: 90% of cases of open spina bifida are myelomeningoceles. 70% of myelomeningoceles are in the lumbar or lumbosacral region. *Associated malformation:* Hydrocephalus, Cardiac defects, Anal atresia, Abdominal wall defects, Facial clefts, Anophthalmia/ Microphthalmia, Limb reduction defects.

6. HYDROCEPHALY *(ICD10:Q03)*

Description: Dilatation of ventricular system, not due to primary atrophy of the brain, with or without enlargement of the skull.

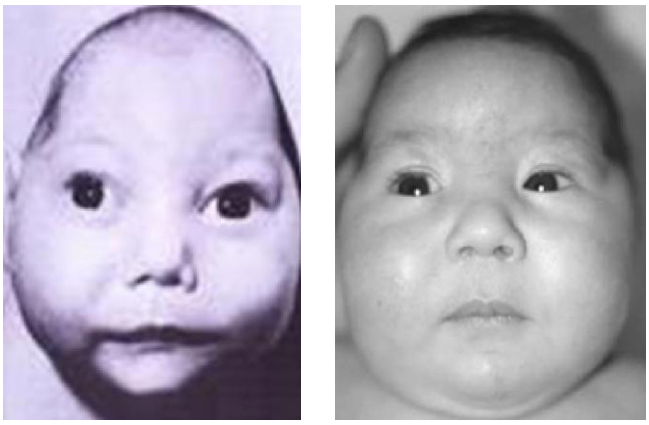




Note: Hydrocephalus is characterized by an increasing head circumference that crosses percentiles on the growth chart. The fontanels may be tense or bulging with widened cranial sutures. Neurologic findings such as loss of upward gaze (the "setting sun sign). *Associated malformation*: Neural Tube Defects

7. MICROCEPHALY *(ICD10:Q02)*

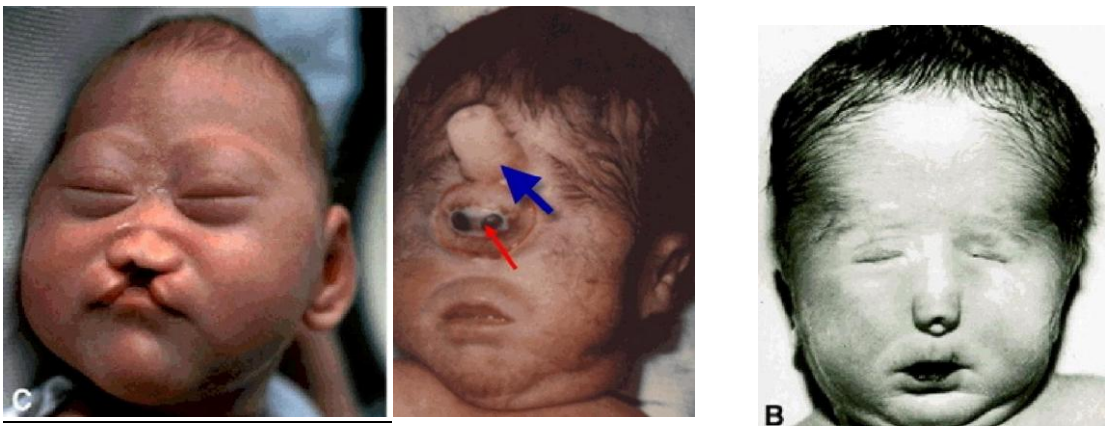
Description: A cranial vault that is smaller than normal for aged.



Note: Microcephalus may be defined variously as head circumference 5th standard deviations below the mean for age. Serial head circumference measurements are more meaningful than a single determination, particularly when the abnormality is minimal. Microcephalus itself is not a primary malformation, but a sign that the brain is small. It has a wide variety of causes. It is a component of a number of genetic syndromes.

8. HOLOPROSENCEPHALY *(ICD10:Q04)*

Description: The developing forebrain fails to divide into two separate hemi spheres and ventricles.



Note: Holoprosencephaly is accompanied by the characteristic pattern of facial anomalies in about 80% of affected individuals: Hypotelorism, one median eye, various degrees of abnormal nasal development (single nostril…) and occasional median CL .Holoprosencephaly can be isolated or can be part of trisomy 13 or occasionally other syndromes.

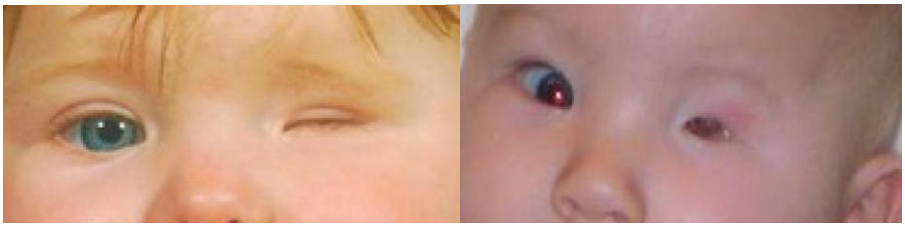
II. EYE

1. ANOPHTHALMOS / MICROPHTHALMOS *(ICD10:Q11)*

Description:

Anophtalmia: Unilateral or bilateral absence of the eye tissue.

Microphthalmos: Small eye/eyes with smaller than normal axial length.

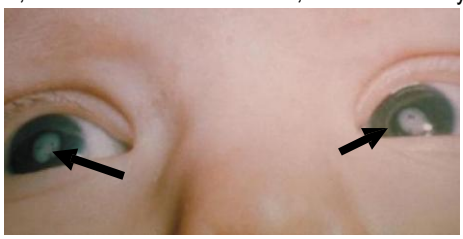


Note: Often are accompanied by malformations of the brain and face, and frequently are components of genetic syndromes.

2. CONGENITAL CATARACT *(ICD10:Q12)*

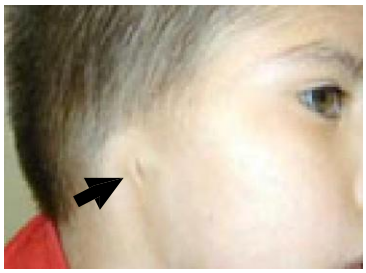
Description: Alteration in the transparency of the crystalline lens.

Note: The presence of a congenital cataract is usually first suspected on physical exam by the lack of a red reflex and the presence of leukokoria (white pupillary reflex). Approximately 50% of cases are unilateral and 50% bilateral. They may be seen with metabolic disorders,; genetic syndromes; chromosomal abnormalities, such as Trisomy 21; intrauterine infection, such as congenital rubella.



3. MICRO/ANOTIA *(ICD10:Q16)*

Description: *Anotia*: Absent pinna, with or without atresia of ear canal. *Microtia:* Malformation or hypoplasia of the external ear.



Note: Any infant with an abnormality of the external ear should have a careful physical examination to identify other craniofacial anomalies, facial asymmetry, dysmorphic features, or other physical abnormalities

III.RESPIRATORY SYSTEM

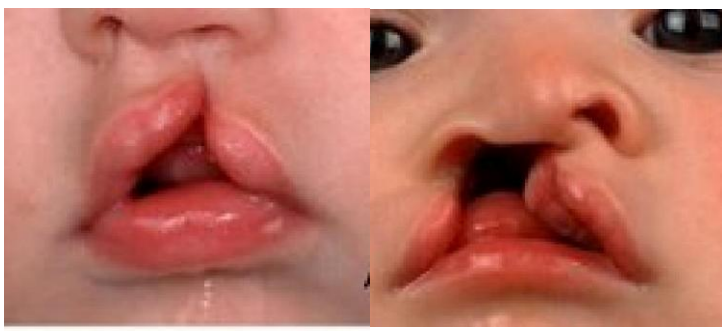
CHOANAL ATRESIA *(ICD10:Q30)*

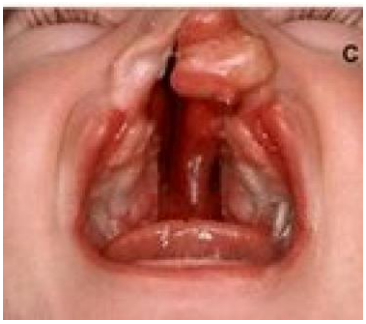
Description: Bony or membranous choanae with no passage from nose to pharynx.
It can be diagnosed by failure to pass a small 3- to 4-mm thick nasogastric catheter through the nose into the nasopharynx. The condition may be unilateral (40–50%) or bilateral (50–60%).Approximately 75% of patients with bilateral choanal atresia has other associated congenital abnormalities. Other nasal anomalies, cleft palate and other palatal defects, and craniosynostosis syndromes are often seen in patients with choanal atresia.

IV.ORO-FACIAL CLEFTS

1. CLEFT LIP WITH /WITHOUT CLEFT PALATE *(ICD10:Q36/37)*

Description: Clefting of the upper lip with or without clefting of the maxillary alveolar process and hard and soft palate.

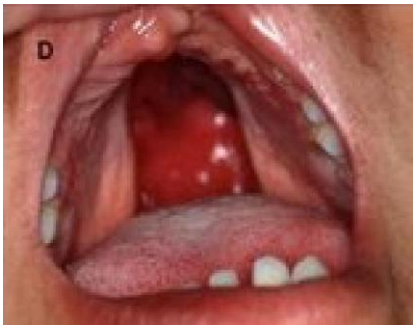




Note: Cleft lip (CL) may be unilateral (80%) or bilateral (20%) and when unilateral, it is more common on the left side (70%) Approximately 85% of cases of bilateral CL and 70% of unilateral CL are associated with cleft plate.

2. ISOLATED CLEFT PALATE *(ICD10:Q35)*

Description: Fissure defect of the soft and/or hard palate(s) or submucous cleft without cleft lip.

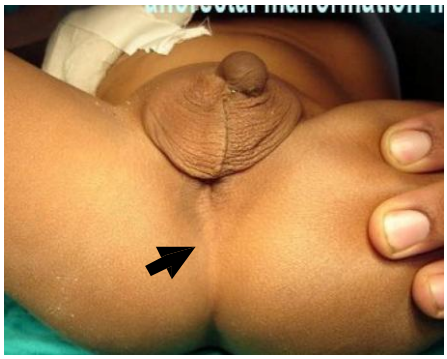


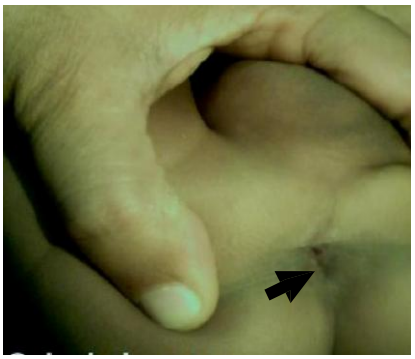
Note: The opening may involve the hard palate only, the soft palate only, or both. The most frequently observed features of this disorder are congenital heart defects. Cleft palate is one component of the Pierre Robin sequence, which also includes micrognathia and glossoptosis (when the tongue falls backward into the posterior pharynx).

V.DIGESTIVE SYSTEM

1. ANO-RECTAL ATRESIA AND STENOSIS *(ICD10:Q42)*

Description: Imperforate anus or absence or narrowing of the communication canal between the rectum and anus.

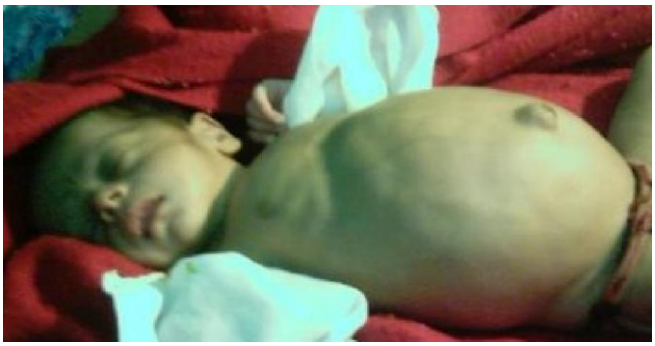




Note: Most infants are diagnosed at or soon after birth when no anal opening is noted on physical examination
Anal atresia is one of the defects reported as part of the VATER, or VACTERL, association, which may also include vertebral and cardiac defects, TE fistula, renal defects, and limb anomalies.

2. HIRSCHSPRUNG'S DISEASE (Congenital megacolon) *(ICD10:Q43)*

Description: Absence of the parasympatic ganglion nerve cells (aganglionosis) of the wall of the colon or rectum. May results in congenital megacolon.



Note: 99% of healthy term infants pass meconium within 48 hours of birth. Hirschsprung's disease and rectal atresia or stenosis may be suspected by the clinical presentation of failure to pass meconium or stool. Approximately 3% of infants with Down syndrome have mega colon.

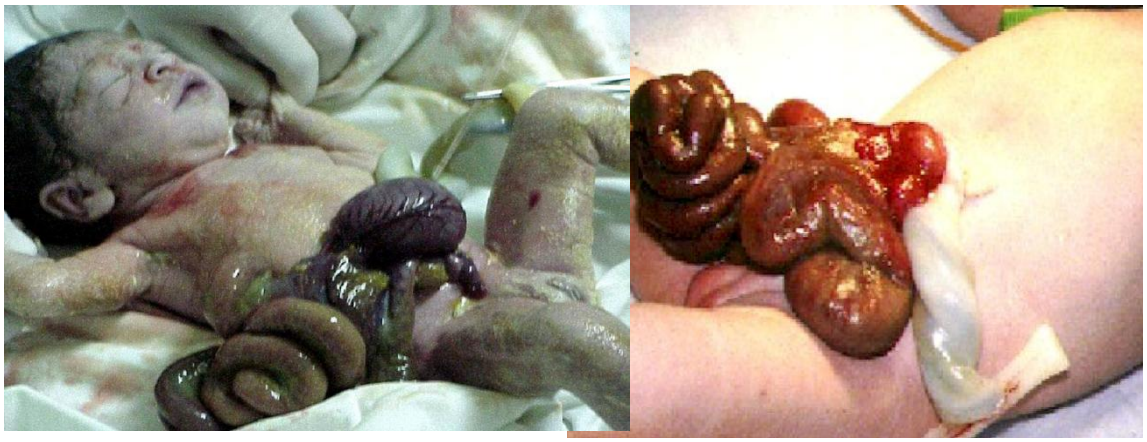
3. ESOPHAGEAL ATRESIA *(ICD10:Q39)*

Description: The esophagus ends in a blind pouch and fails to connect with the stomach. Esophageal atresia is suspected by the clinical presentation of polyhydramnios, vomiting after every feeding, or respiratory distress and Levin tube blocked at about 10 cm.

VI.ABDOMINAL WALL DEFECTS

1. GASTROSCHISIS *(ICD10:Q79.3)*

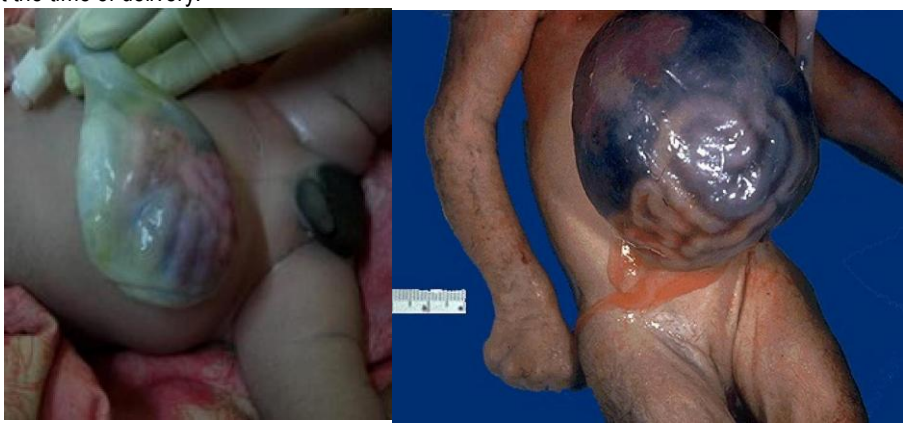
Description: Protrusion of abdominal contents through an abdominal wall defect lateral to an intact umbilical cord and not covered by a membrane.



Note: Unlike omphalocele, gastroschisis is usually an isolated malformation and is not known to be a part of any reported syndrome.

2. OMPHALOCELE *(ICD10:Q79.2)*

Description: Herniation of abdominal content through the umbilical ring, the contents being covered by a membrane sometimes ruptured at the time of delivery.

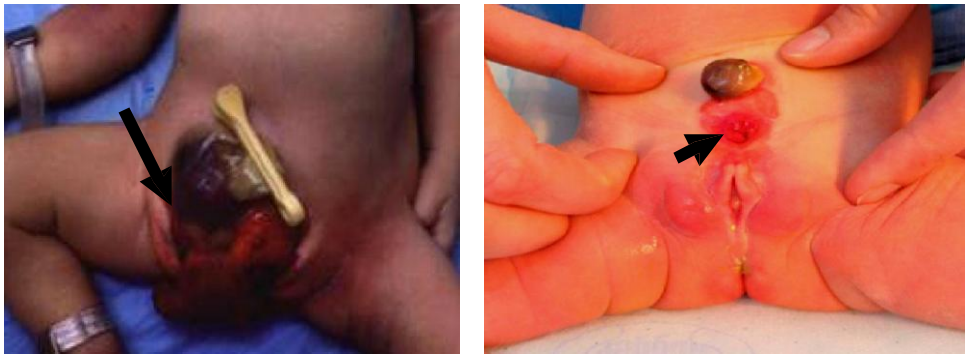


Note: Associated congenital malformations are frequently seen in infants with omphalocele and their incidence varies widely from 40% to 90%: Central nervous system, cardiovascular system, genitourinary system. Omphalocele is one of the defects reported as part of the Omphalocele- Exstrophy-Imperforate Anus-Spina Bifida (OEIS) complex.

VII.URINARY SYSTEM

1. BLADDER EXTROPHY *(ICD10:Q64)*

Description: Defect in the closure of the bladder and lower abdominal wall.

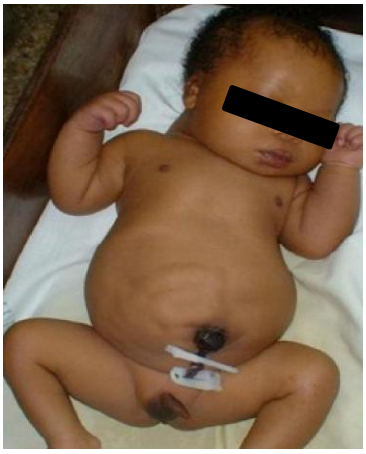


Note: In the classic form of bladder exstrophy, the entire urinary tract is open anteriorly from the urethral meatus to the umbilicus. The pubic bones are widely separated, as are the abdominal muscles and fascia. The classic form of bladder exstrophy occurs

more frequently in males. It is often associated with epispadias and structural anomalies of the pubic bones.

2. POSTERIOR URETHRAL VALVE AND/OR PRUNE BELLY SYNDROME *(ICD10:Q79.4)*

Description: Urethral obstruction with dilatation of bladder and hydronephrosis. In severe cases also distended abdomen.
Prune belly syndrome: Triad syndrome: 1.Agenesis of abdominal wall muscles; 2.Bladder outflow obstruction and 3.Bilateral undescended testes.

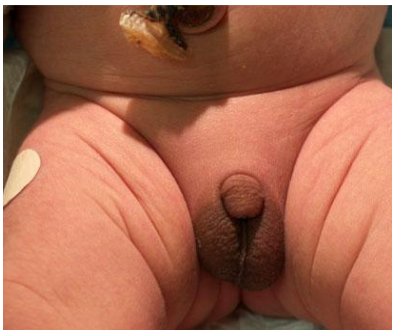


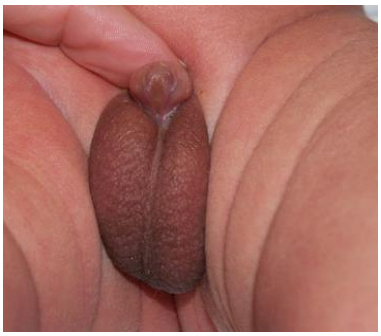
Note: Prune belly syndrome is associated with trisomy 18 and 21. Patients with prune belly syndrome also have an increased incidence of tetralogy of Fallot and ventriculoseptal defects.

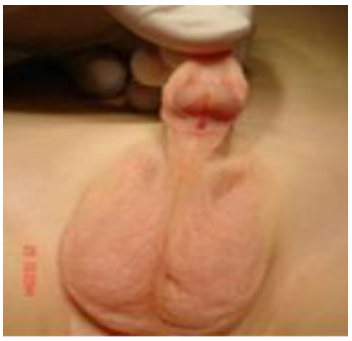
VIII.GENITAL SYSTEM

1. HYPOSPADIAS (ICD10:Q54)

Description: The urethral meatus is abnormally located and is displaced proximally on the ventral surface of the penis.



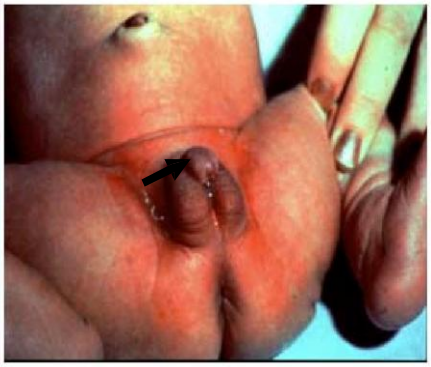




Note: Hypospadias usually is an isolated anomaly. However, hypospadias is common in boys with multiple congenital anomalies.
Associated malformation: undescended testis, cleft lip, heart defects, cleft palate, syndactyly, and polydactyly.

2. INDETERMINATE SEX (ICD10:Q56)

Genital ambiguity at birth that does not readily allow for phenotypic sex determination.



IX.LIMBS

1. UPPER LIMB REDUCTION *(ICD10:Q71)*

Description: Complete or partial absence of the upper arm (humerus), lower arm (radius and/or ulna), wrist (carpals), hand (metacarpals), or fingers (phalanges).

2. LOWER LIMB REDUCTION *(ICD10:Q72)*

Description: Complete or partial absence of the upper leg (femur), lower leg (tibia and/or fibula), ankle (tarsals), foot (metatarsals), or toes (phalanges).

3. COMPLETE ABSENCE OF A LIMB *(ICD10:Q71-72-73)*

Description: Complete absence of a limb: the upper limb (humerus, radius, ulna, wrist, hand and fingers) or the lower limb (femur, tibia, fibula, ankle, foot, and toes).

Upper limb reduction includes:

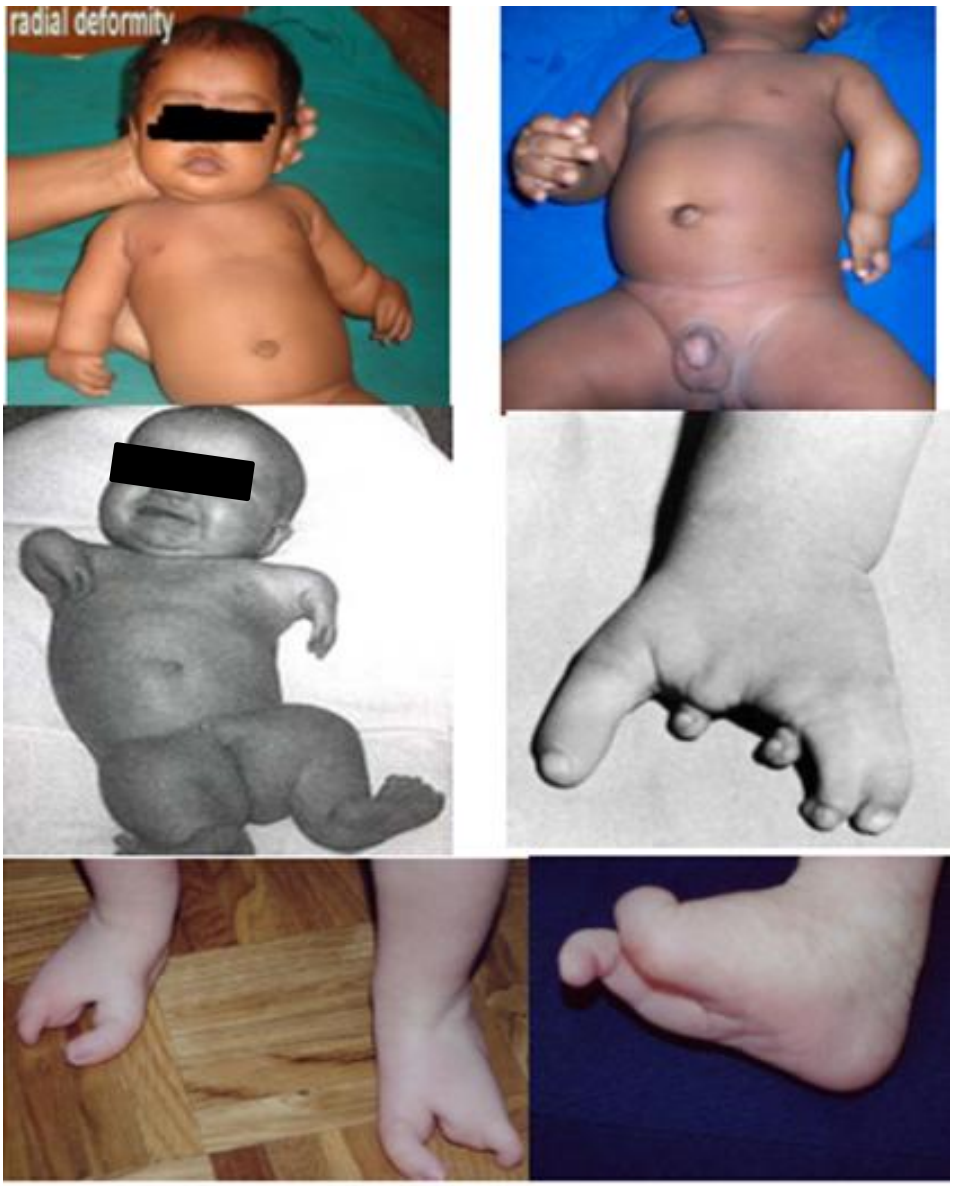
Transverse limb reduction: Absence of a hand, Absence of digits (fingers), Absence of phalanges.

Longitudinal limb reduction: Partial absence of the arm in parallel with the long axis of the arm: Isolated missing thumb, middle digit is missing, Ulnar aplasia or hypoplasia, Radial aplasia or hypoplasia, complete or partial of second through fourth fingers and their associated metacarpal bones of the hand.

Lower limb reduction includes:

Transverse limb reduction: Absence of digits (toes); Absence of phalanges.

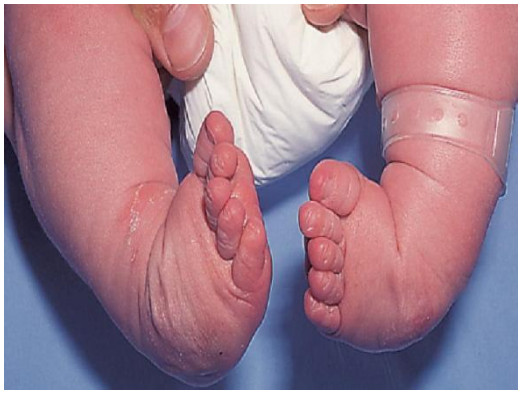
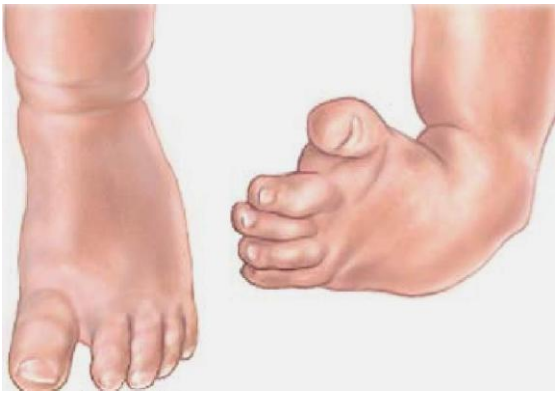
Longitudinal limb reduction: Partial absence of the arm in parallel with the long axis of the leg: Middle digit is missing; Tibia aplasia or hypoplasia; Fibularl aplasia or hypoplasia; complete or partial of second through fourth toes and their associated metacarpal bones of the foot.



Note: Upper limb defects are more common than lower limb defects (60–80% versus 25–40%). The most common anomalies seen in infants with limb reduction defects are cryptorchidism, ventricular septal defect, cleft lip with or without cleft palate, club feet, syndactyly, renal agenesis, imperforate anus, and hydrocephalus.

4. CLUB FOOT - TALIPES EQUINOVARUS *(ICD10:Q66)*

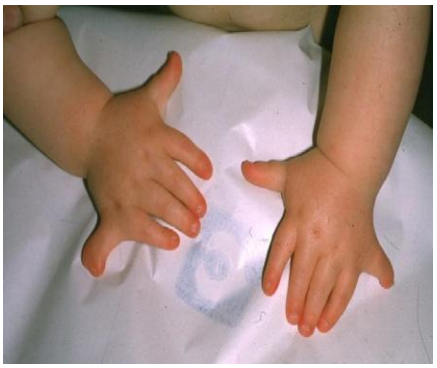
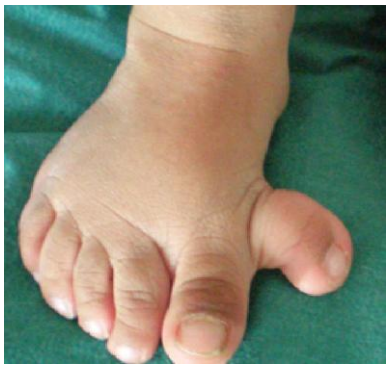
Description: Foot anomaly with equinus of the heel, varus of the hindfoot and adductus of the forefoot.

Note: Club foot may be associated with other birth defects such as spina bifida cystica, trisomie 18, Edwards syndrome, congenital hip dislocation.

5. POLYDACTYLY *(ICD10:Q69)*

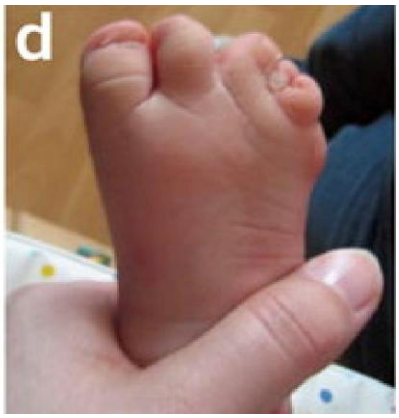
Description: Having more than the normal number of digits in the hands and/or feet.

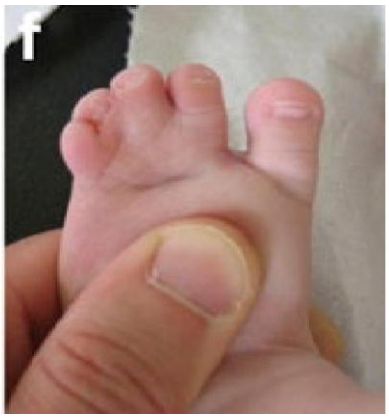



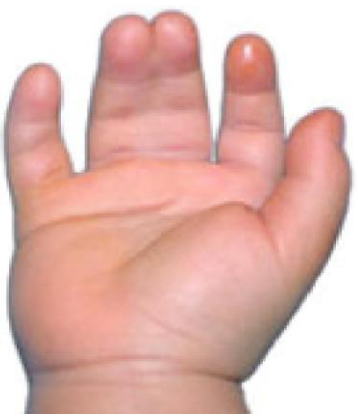
Note: Polydactyly is usually an isolated malformation (in 85% and 88% of the cases).Many different anomalies of all major organ systems have been reported in association with polydactyly : Limb Anomalies, Central Nervous System, Cardiovascular, Gastrointestinal, Genitourinary, Cleft lip and palate Anophthalmia, Microtia.

6. SYNDACTYLY *(ICD10:Q70)*

Description: A condition where two or more digits are fused together.



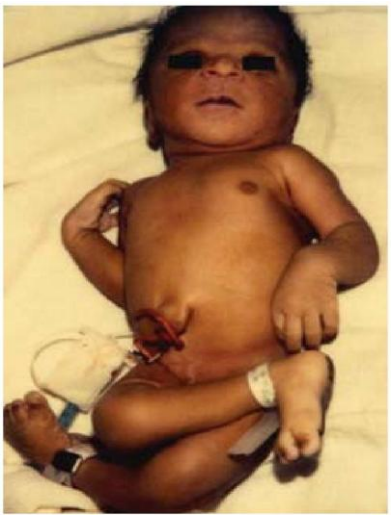
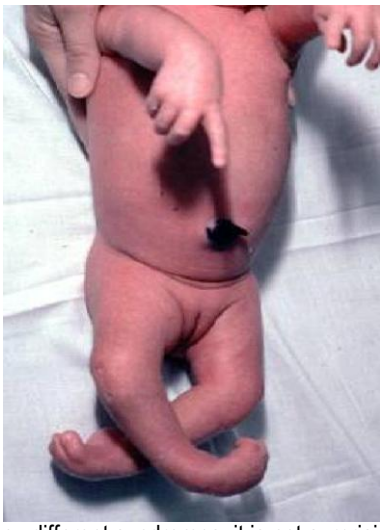




Note: Syndactyly is frequently bilateral. Unlike polydactyly, a*ssociated anomalies* are reported in nearly half of all cases with syndactyly. Musculoskeletal and craniofacial anomalies are most common followed by genitourinary anomalies.

7. ARTHROGRYPOSIS MULTIPLEX CONGENITA *(ICD10:Q74)*

Description: Multiple congenital contractures, some times caused by neurological disease. The term arthrogryposis is used to describe pre- natal onset of joint contractures with associated limitation of movements in two or more joints in different body areas.

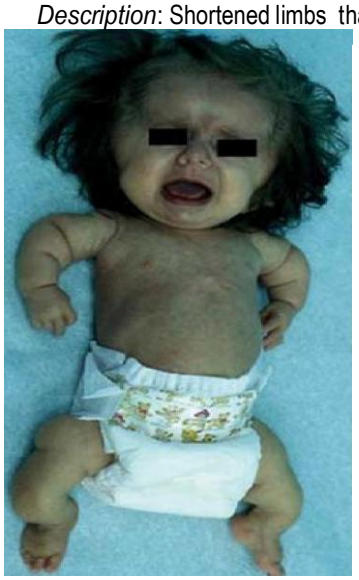



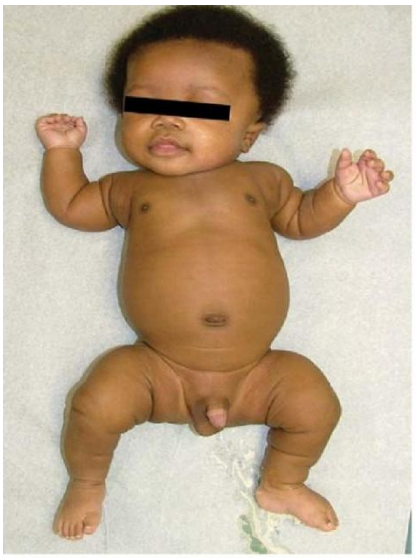
Note: Since multiple congenital contractures are part of many different syndromes, it is not surprising that the congenital anomalies of other organ are frequently associated with arthrogryposi. The CNS malformations are most frequently a sociated, followed by skeletal, renal, and cardiac anomalies.

X.MUSCULO-SKELETAL SYSTEM

1. DWARFISM *(ICD10:Q77.4)*

Description: Shortened limbs that have all of their component parts.

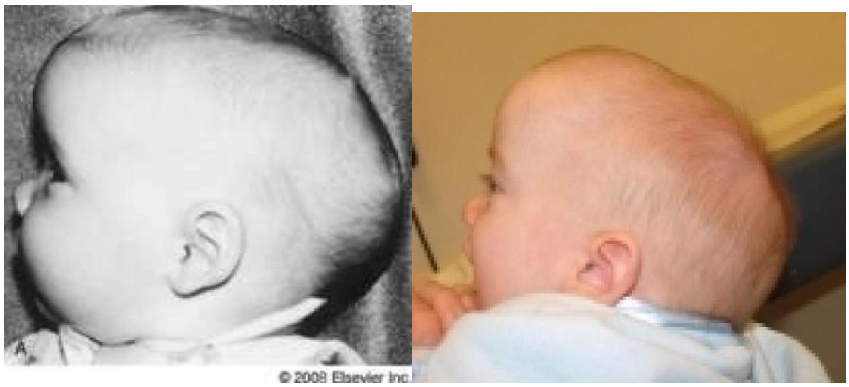




Note: Short upper limb: A simple guide to evaluating relative extremity length is to determine where the fingertips are in relation to the thighs when the upper extremities are adducted alongside the body. In the normal infant, the fingertips fall below the hip joint in the midthigh region. When the upper extremities are short, they align with the hip joint or above.

2. CRANIOSYNOSTOSIS *(ICD10:Q75)*

Description: Premature closure of cranial sutures.



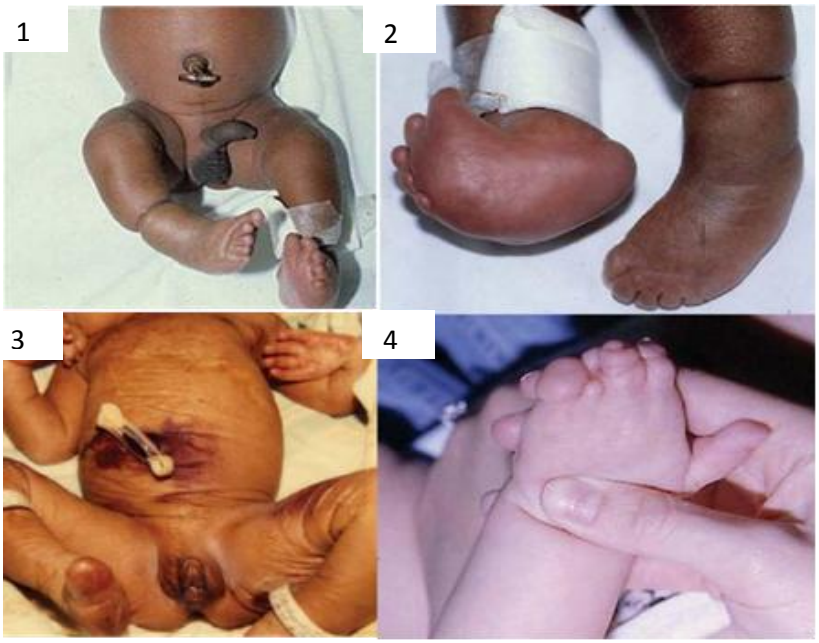
Note: Premature closure of cranial sutures causing problems with normal brain and skull growth (skull deformity).
The diagnosis of craniosynostosis is typically suspected shortly after birth on the basis of the abnormal head shape. The shape of the head will vary depending on the suture or sutures involved. Sagittal synostosis, elongated in the anteroposterior (AP) dimension with a prominent forehead and occiput. It is representing approximately 50–60% of all cases. Coronal craniosynostosis, decreased AP diameter to the skull and a high, is the second most common type, accounting for 20–30% of cases. Craniosynostosis can be associated with a wide range of chromosome anomalies, with several teratogenic syndromes.

3. CONGENITAL CONSTRICTION BANDS/AMNIOTIC BAND *(ICD10:Q79.8)*

Description: Bands in the amniotic fluid that causes constriction of part of the brain, body or limbs, including limb-body-wall complex.

Note: Often the bands are detected indirectly because of the constrictions, amputationand swelling upon limbs, digits. Bands which wrap around fingers and toes can result in syndactyly or amputations of the digits. In other instances, bands can wrap around limbs causing restriction of movement resulting in clubbed feet.
Triad of amniotic band syndrome: **a**. Amnion-denuded placenta **b**. Fetal attachment or entanglement by amniotic remnants **c**. Fetal deformation, malformation, and/or disruption.

Image 1-2. An infant with deep constricting groove around the lower one third of both legs. *Image 3:* Infant with constriction bands of leg with amputation and club left hand .*Image 4*: A hand of an infant with constriction bands of the fingers with amputation

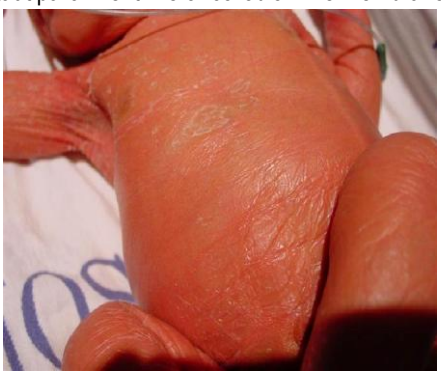
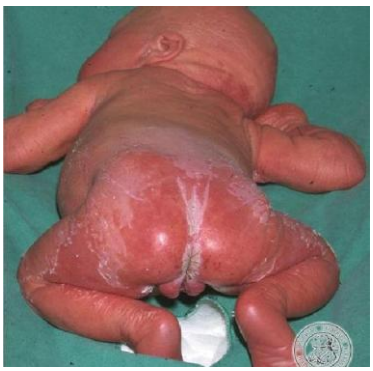


XI.OTHER MALFORMATIONS

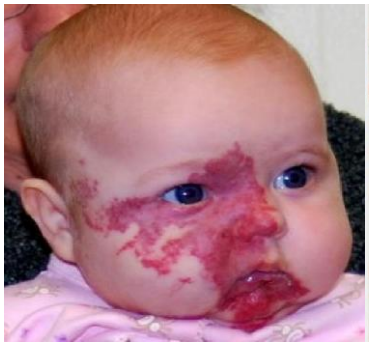
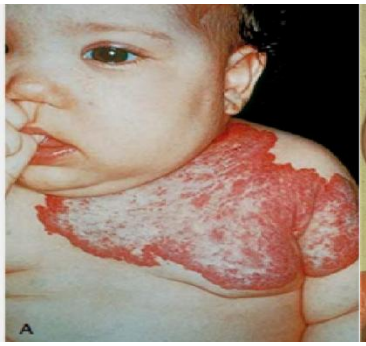
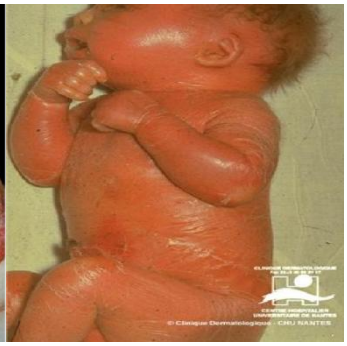
1. DISORDERS OF SKIN *(ICD10:Q80)*

Congenital ichthyosis lammellaris: *(ICD10:Q80.2*)

This is a rare manifestation of the inherited ichthyoses, a group of conditions in which the skin is dry and scaly. Infants are born with a taut parchment-like or collodion-like membrane.

Hemangioma *(ICD10: D18)*: characterized by a growth phase, which is marked by endothelial proliferation and hypercellularity, and by an involutional phase..

Note: Most cutaneous hemangiomas are benign. Generally, superficial hemangiomas have reached their maximum size by 6 to 8 months, but deep hemangiomas can proliferate for 12 to 14 months or, rarely, up to 2 years.

2. CONJOINED TWINS *(ICD10:Q89.4)*

ANNEX:

ILLNESS BEFORE PREGNANCY: Any illness whether chronic or acute with onset before pregnancy and that may affect fetal development (eg. childhood cancer, metabolic disease). Main illness: TB, Hyperthyroidism, Diabetes, Epilepsy, Asthma, Chronic alcoholism, Drug addict

ILLNESS DURING PREGNANCY: Illnesses with chronic or acute onset during first half of the pregnancy including asymptomatic maternal infections.

DRUG TAKEN DURING PREGNANCY: Any drug taken by the mother during the first trimester of pregnancy (from the 1st day of last menstrual period up to the 12th week of gestation).

CONSANGUINITY: Restrictive definition of consanguinity: where the parents of the malformed case have one or more ancestors in common no more remote than a great-grandparent (second cousins)

CONGENIALE ANOMALIES OF MOTHER'S FAMILY: Include mother herself as well as mother's family. Restrict the family to first, second and third degree relatives (mother, father, siblings, grandparents, aunts, uncles, half-siblings, first cousins).

REPRODUCTIVE HISTORY: Total number of previous pregnancies: include all previous abortions whether spontaneous or induced. Multiple pregnancies count as1 in the total.

MOTHER'S OCCUPATION: Mother's occupation at time of conception. Main groups: Office staff, Worker, Farmer, Fisherman, Forestry worker, Seller (Agricultural chemical, petrol, pesticide), other seller, Barber-Hairdresser, House wife.

MAJOR ANOMALY: A congenital abnormality that requires medical or surgical treatment, has a serious adverse effect on health and development, or has significant cosmetic impact. Individual major anomalies occur in less than 1 percent of the population. Together, they are seen in approximately 3 percent of births. Examples include cleft lip and tracheo-esophageal fistula.

MINOR ANOMALY: A congenital abnormality that does not require medical or surgical treatment, does not seriously affect health and development, and does not have significant cosmetic impact.

FETAL DEATH (STILLBIRTH): Spontaneous delivery of an infant or fetus at 20 weeks or greater gestation that does not exhibit signs of life.

SPONTANEOUS ABORTION (MISCARRIAGE): spontaneous delivery of a fetus at less than 20 weeks gestation.

TERM INFANT: An infant born after 37 completed weeks and before 42 completed weeks of gestation.

PRETERM INFANT: An infant born before 37 completed weeks of gestation. Low birth weight birth weight less than 2,500 grams, regardless of gestational age.

VERY LOW BIRTH WEIGHT: Birth weight less than 1,500 grams, regardless of gestational age.

2.CHECK LIST OF CONGENITAL ANOMALIES ON NEWBORNS

	Checklist of Congenital Anomalies on Newborns				
No	If « Yes or Suspected », fill (X) in the blank	ICD10	No	If « Yes or Suspected », fill (X) in the blank	ICD10
	Anomalies of the nervous system			**Abdominal wall defect**	
1	Does the newborn's skull present an abnormal form or a defect? (*Anencephaly*)	Q00		**Abdominal wall defect**	
2	Does the newborn present a tumefaction between the eyes or on the back of the skull (occipital region) ? (*Encephalocele , Meningocele*)	Q01	22	Are the newborn's abdominal content herniated through the umbilical ring ? (*Omphalocele*)	Q79.2
3	Does the newborn's spine present a tumefaction or an opening in the back at any level?(*Spina bifida*)	Q05	18	Does the newborn have a partial or complete lack of abdominal muscles and a lack of amniotic fluid with palpable tumor in the lower belly? (*Prune belly syndrome*)	Q79.4
4	Is the circumference of the head over 38 cm? (*Hydrocephaly*)	Q03	23	Are the newborn's abdominal content herniated any where in the abdominal wall? (*Gastroschisis*)	Q79.3
5	Is circumference of the head under 32 cm? (*Microcephaly*)	Q02		**Anomalies of the musculoskeletal system**	
6	Does the newborn show one of the following signs: *Are the eye very close to one another? Absence of nose? Presence of a median labial defect? Presence of a single nostril? Presence of one median eye ?*(*Arhinencephaly/horoprosencephaly*)	Q04	24	Does the newborn have complete absence of upper limb ? (*Complete absence of a upper limb*)	Q710
	Anomalies of eye, ear, face and neck		25	Does the newborn have a hand only without upper arm and forearm? (*Uper limb reduction*)	Q711
7	Is the eye absent or very small? (*Microphtalmos/Anophthalmos*)	Q11	26	Does the newborn have absence of both forearm and hand (*Upper limb reduction*) ?	Q712
8	Presence of a small white stain visible in the iris centrum?(*Cataract*)	Q12	27	Does the newborn have absence of hand and finger? (*Uper limb reduction*)	Q713
9	Does the newborn have no pinna,only one pinna or a too small pina?(*Anotia/microtia*)	Q16		Does the newborn have fewer 5 fingers ? (*Upper limb reduction*)	Q718
10	Is the nasal tuble through the nose into the nasopharynx blocked at about 4 cm ? (*Choanal astresia*)	Q30	28	Does the newborn have only shortening of arm but with normal aspect of this ?(*Uper limb reduction*)?	Q714-Q718
	Anomalies of the circulatory system (or Blue Child)		29	Does the newborn have complete absence of lower limb ? (*Complete absence of a lower limb*)	Q720
11	Does the newborn have cyanosis around his/her lips and at fingers with oxygen supplementation	Q20-26	30	Does the newborn have absence of thigh and lower limb with foot present ? (*Lower limb reduction*)	Q721
	Cleft lip and cleft palate		31	Does the newborn have absence of foot and toes ? (*Lower limb reduction*)	Q723
12	Does the newborn have cleft lip?(*cleft lip*)	Q37	32	Does the newborn have absence of both lower leg and foot ? (*Lower limb reduction*)	Q722
13	Does the newborn have cleft lip associated with cleft palate?(*cleft lip with cleft palate*)	Q36		Does the newborn have fewer 5 toes ? (*Split foot: Lower limb reduction*)	Q72.7
14	Does the newborn cleft palate alone (buccal examination) without associated cleft lip? (*Isolated cleft palate*)	Q35	33	Does the newborn have only shortening of legs with normal aspect and structures of this ? (*Lower limb reduction*)	Q724-Q728
	Anomalies of the digestive system		34	Does the newborn have an abnormal ankle? (*Club foot*)	Q79.8
15	Is the oro-gastric tube blocked at about 10 cm?(*Oesophageal Atresia or stenosis*)	Q39	35	Does the newborn have more than 5 digits in each hand or each foot ? (*Polydactyly*)	Q69
16	Does the newborn have an imperforate anus?(*Anorectal atresia or stenosis*)	Q42	36	Does the newborn have any fusion of the fingers or of the toes? (*Syndactyly*)	Q70
17	Does the newborn have a dilated abdomen or no pass meconium within 48 hours of birth? *(Hirschsprung's disease, or intestinal obstruction*)	Q443	37	Does the newborn have (multiple) abnormal deformity of ankles, knees and wrist ? (*Arthrogryposis multiplex congenita*)	Q74
	Anomalies of genital organ		38	Was the newborn much too small ? (*Darwfism*)	Q77.4
19	Is the male newborn's squirt of urine abnormal?(*Hypospadias or Epispadias*)	Q54	39	Does the newborn have very deformed skull (too long, too large or too high) (*Craniocytosis*) ?	Q750
20	Is the newborn's sex definitely unidentified?(*Indeterminate sex*)	Q56	40	Does the newborn have multiple amputations ? (*Congenital constriction band/ amniotic band*)	Q79.8
21	Does the newbonr present a defect in the closure of the bladder and lower abdominal wall through wich the urine flows? (*Bladder extrophy*)	Q64	41	Is the newborn's skin too smooth (ichtyose, collodion baby) and with a too « polish » aspect ? (*Congenital ichthyosis*)	Q80.2

3. NOTIFICATION FORM FOR EXTERNAL BIRTH DEFECT STUDY

N⁰	MOTHER'S DETAIL							STT	BABY/INFANT'S DETAIL
1	Surname:							1	Sex: 1.boy 2.girl 3.unknown
2	First name:							2	Date of delivery:: / / (dd/mm/yy)
3	Addresss:							3	Birth order :
4	Mother's age (years)							4	Number of baby delivered (in multiple set):
5	**Mother's occupation:** 1. Office staff 2. Seller (Agricultural chemical, pesticide) 3. Worker 4. Barber-Hairdresser 5. Farmer 6. Fisherman 7. House wife 8. Others(write)							5	Mode of delivery: 1. Normal 2.Forcep 3. Caesarean
								6	Apgar Score after 5 minutes:
6	Ethnic group::							7	**Size and Weight**
7	**Educational level:**: 1. Illiteracy 2. Primary 3. Primary 4. High school 5. Higher education								Length (cm)::
8	**Economic status *:** 1.Very poor 2.Poor 3.Well 4.Wello to do							8	Weight (gram)
9	**Reproductive history* *:**							9	Total previous pregnancy 's number
	Previous delivery in term's number		Total living child's number					10	Head circumference (cm):
	Previous abortion's number							11	Malformation present (see checklist and atals for details)
	Prevous delivery preterm's number		2.						1.
10	**History of Illnesses before pregnancy*: *?** 1. Diabetes 2.Hypertension 3. Epilepsy 4. Hyperthyroidism 5. Asthma 6. Tuberculosis 7.Other (write) :								3.
									4.
									Clinical description (write) :
11	Illness during pregnancy *?								
12	Drugs taken during first trimester pregnancy*: *?								
13	Delivery complication:								
14	Gestational age (weeks):							Name of interviewer::	
	Family history:								
15	Consanguinity* *: yes no							Date and working place::	
16	On congenital anomalies		System involved						
	1.Husband's close relative*:							Date:...../...../.....	**see intstruction*
	2. Wife's close relatives								
	3. Previous sons' or daughters								

4. NOTIFICATION FORM FOR FOLLOW UP STUDY

Notification form for follow up study			
Baby's name:			
Mother's name:			
Place of birth (in details):			
Address:			
Baby's sex:	1Boy	2.Girl	3.Unknown
Date of birth:			
Examinations	**First time**	**Second time**	**Third time**
Examination date	…../……/	…../……/	…../……/
Length (cm)			
Head circumference (cm)			
Weight (gram)			
Malformation :			
• Hear murmur			
• Cyanosis.			
• Other			
Registration number *Working place* *Investigator:*	*Date:*		

5. INFANT DEATH REGISTRATION APPLICATION

Infant death registration application			
1. Baby's name:			
2. Mother's name:			
3. Place of birth (in details):			
4. Address:			
5. Baby's sex:	1Boy	2.Girl	3.Unknown
6. Date of death			
7. Date of birth			
8. Place of death			
9. Suspected cause of death	1.Preterm or low birth weight 4..Birth asphyxia or hypoxia	2.Infection 5.Others	3.Malformation
Registration number			
Working place *Investigator:*	*Date:*		