Out of the

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Perinatal outcomes in urban and rural areas of Da Nang, Vietnam

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Abstract

Introduction: In Vietnam, neonatal mortality has been paid increasing attention for the past recent years, however other perinatal outcomes including stillbirths, preterm births, congenital anomalies and Caesarean section have not been analysed at the same extent. The present study aimed to describe these outcomes in Da Nang city and to identify associated factors.

Methods: This is a one year prospective cross sectional study. Data collection was conducted from April 2015 to March 2016 based on register books and medical records of 10 hospitals in Da Nang city. There were one tertiary hospital, seven district hospitals and two private hospitals. The classification of rural or urban areas was according to the location of maternal residence.

Results: There were 20,762 births recorded in register books of 10 hospitals. The neonatal mortality rate of neonates whose mother were resident in Da Nang was 4 per 1,000 live births. There were no statistically significant difference in neonatal death rate between urban and rural areas. Three main causes of death in urban areas in descending order were prematurity, congenital anomalies and infections. Three main causes of neonatal deaths in rural areas were the same as in urban areas but congenital anomalies accounted for the highest proportion. The stillbirth rate was 9.7 per 1,000 live births. Additionally there were 5% preterm births. The congenital anomaly rate among inborn newborns at the Da Nang Hospital for Women and Children was 384.4 per 10,000 live births and the most common anomaly was congenital heart defect. The Caesarean section rate among live births in 10 hospitals was 58.6% and this rate was significant higher in private hospitals compared to public hospitals.

Conclusion: The neonatal mortality rate in Da Nang is lower than the national neonatal mortality rate; but both neonatal mortality rate and stillbirth rate remain higher compared to developed countries**.** The extremely high rate of Caesarean sections needs to be paid more attention. Exploring factors associated with increased risk of neonatal mortality, stillbirths, preterm births, congenital anomalies and Caesarean section and difference in causes of death between rural and urban areas in Da Nang are essential to identify strategies to reduce these outcomes.

Contents

1. Introduction

Neonatal mortality and stillbirths remain common adverse pregnancy outcomes in low- and middle-income countries (1) (2) (3). Globally, 2.5 million neonatal deaths (3) and 2.65 stillbirths were estimated annually (1). Almost all (97-99%) neonatal mortality and stillbirths occurred in developing countries (4) (5), 67% of stillbirth worldwide arose in rural areas and 55% in rural sub-Saharan Africa and south Asia (1). However, most epidemiological research focus on the deaths in developed countries and stillbirths remain uncounted on the global platform and country level (1). Worldwide, the main risk factors for stillbirths were estimated to be maternal conditions such as hypertension, diabetes or infection leading to growth restriction as well as congenital abnormalities and childbirth complications (1).

Globally, infection (36%), preterm birth (28%) and asphyxia (23%) are three main direct causes of neonatal deaths (6). Congenital anomalies were related to 7% of deaths in neonatal period. These causes vary from country to country and even within the countries. In settings with very high rate of neonatal mortality, the majority of deaths is due to infection. In contrast, in settings with decreasing neonatal mortality rate, prematurity becomes the major problem (2).

Congenital anomalies contribute significantly to neonatal mortality and under-five mortality, chronic illness and long-term disability (7). Globally, there were 303,000 neonatal deaths annually due to congenital anomalies. The contribution of congenital anomalies to infant death has increased gradually (8) (9). Identifying the exact causes of congenital anomalies is difficult, however simple prevention methods including vaccination, adequate intake of folic acid and antenatal care can prevent some congenital anomalies (7).

Caesarean section can be lifesaving for mothers and babies and an essential surgery that contributes to reduce maternal and child mortality (10). There is no consensus on optimal Caesarean section rate, however, according to the World Health Organisation (WHO), the Caesarean section rate should not exceed 10 to 15% at national level (11). The relationship between Caesarean section and neonatal mortality was not consistent across studies. Recent data showed that the national rate of Caesarean section up to 19 per 100 live births reduced neonatal mortality (10). Worldwide, Caesarean section has increased dramatically especially in middle- and high-income countries (12) (13).

High quality data on perinatal outcomes is barely available in low- and lower-middle-income countries where most of neonatal deaths and stillbirths occurred (14). Causes and risk factors of neonatal deaths and stillbirths in these countries were estimated mostly based on Demographic and Health Survey data and may not reflex a comprehensive situation of the country (15). Therefore, improving quality of data on pregnancies, births and newborn deaths is essential to plan health policy and health service accurately. This will further reduce adverse pregnancy outcomes in limited-resource settings.

2. Rationale and objectives

Vietnam reduced under-five mortality from 53 per 1000 live births to 22 per 1000 live births between 1990 and 2015 and is therefore listed as one of 10 impressive countries in reducing child mortality (16). To speed up progress in reducing child mortality, focusing on neonatal health is crucial because neonatal mortality in Vietnam accounted for 50% of under-five mortality and 60% of infant mortality and these sharing is increasing (17). National data on perinatal outcomes in Vietnam are usually based on estimation of WHO or United Nations International Children's Emergency Fund (UNICEF). Currently neonatal mortality rate is estimated about 11 per 1000 live births (18). Stillbirths have not been paid adequate attention and these data are rarely available in Vietnamese context.

Rural-urban disparities in neonatal mortality has been a challenge in Vietnamese child health and these inequities have increased (19). A study in Quang Ninh showed that while neonatal mortality in urban areas was 10 per 1000 live births, neonatal mortality rate in remote and mountainous areas was three to five time higher (20). In addition, under reporting of births and deaths will be misleading for decision makers and health plans are unable to meet the need (21).

Da Nang is the third largest city in Vietnam in term of urban population, with 87% population lived in urban areas (22). There is currently limited data on perinatal outcomes including stillbirths, preterm births, congenital anomalies, and mode of delivery. Moreover, data on the disparity in neonatal mortality between urban and rural areas in Da Nang is lacking.

In an effort to provide information on perinatal outcomes in Da Nang, the objectives of this thesis were as follows:

- To determine the neonatal mortality rate in urban and rural areas and factors associated with neonatal mortality
- To report the proportion of stillbirths and preterm births
- To determine the prevalence and pattern of congenital anomalies in neonates
- To describe Caesarean section rates, indications and associated factors

Each of the mentioned objectives was presented as a separate manuscript. All of three manuscripts are part of this thesis, presented as

- Manuscript 1: “Stillbirth and preterm birth and associated factors in one of the largest cities in central Vietnam” by journal Acta Paediatrica (Oslo, Norway: 1992) (2018 August 11)

- Manuscript 2: “Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam” under review
- Manuscript 3: “Monitoring and interventions are needed to reduce the very high Caesarean section rates in Vietnam” by the journal Acta Paediatrica (Oslo, Norway: 1992) (2018 April 29)

3. Method

This is a one year prospective cross sectional study. From April 2015 to March 2016, data was collected at 10 health facilities in Da Nang city, Vietnam, including one tertiary hospital, seven district hospitals and two private hospitals.

3.1. Study setting

Da Nang is a port city located in central Vietnam. Over the last two decades, Da Nang has recorded a significant achievement in economic development (23) (24). In 2017, the population in Da Nang reached more than one million with nearly 90% of citizens living in urban areas.

The structure of public health care system in the city is divided into three level according to national plans: 56 commune health centres, seven district hospitals, one tertiary hospital. There are five private hospitals in Da Nang providing pregnancy and childbirth services. Nearly all deliveries are performed in health facilities with the presence of midwives or obstetricians or both. In Da Nang, delivery in commune health centres occurs rarely. Medical insurance covers about 80% of the costs of antenatal care, delivery and postnatal care (25). However, for those women who do not own an insurance, out-of-pocket payments prevent them from seeking care. Vietnam's national guideline for reproductive healthcare recommends at least four antenatal care visits during pregnancy: first antenatal care visit occurs in the first trimester, second visit during the second trimester, and third and fourth visits during the third trimester (26).

The Da Nang Hospital for Women and Children (DHWC) handles approximately 15,000 deliveries yearly. The number of deliveries in this hospital constitute nearly 70% of deliveries in the whole city. The hospital is also a referral hospital for high risk pregnancy from surrounding provinces. Neonatal Intensive Care Unit in DHWC (NICUDN) provides care for approximately 3,000 babies with low birth weight, preterm, or illness each year.

3.2. Case report form

Three case report forms were developed to collect data. One form was designed to get information from hospital birth register books on total number of live births, stillbirths, gestational age, and mode of delivery. Another two forms were designed to collect data on neonatal mortality and congenital anomalies (Annex 9.6).

3.3. Study procedure

A trained data collector with a medical educational background visited 10 health facilities every month to collect the information on all births in birth register books using a case report form designed for this study (Annex 9.6) (27). Other two nurses in the NICU and delivery room in DHWC were responsible for filling the case report form whenever there was a case of neonatal death or congenital anomalies. The principle investigator (Hoang Thi Nam Giang) trained the data collectors and research nurses at DHWC. After checking for accuracy of data, copies of completed and checked report forms were used to enter data, and original files were saved as authenticated data for later referral. The data entry from the form to the database was completed by two people, one was a paramedical professional. If inconsistencies were detected upon data entry, the principle investigator checked and corrected them. After entering data, the cleaning process was undertaken comprehensively to detect any outlier results and inconsistent data. The final database in Excel was anonymous and information could not be related to individual women or infants.

3.4. Data analysis

Categorical variables will be presented as frequency and percentages. Continuous variables will be presented as mean and standard deviations (SD) if data is normally distributed, otherwise median and interquartile range.

Logistic regression model was used to identify the factors associated with neonatal mortality, stillbirths, preterm births and mode of delivery. Odd ratios (ORs) and adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were calculated for all predictor variables. Statistical significance was considered if $p<0.05$.

Data was analysed using R Statistical Language version 3.3.2 (31 Oct 2016) (R Foundation for Statistical Computing, Vienna, Austria)

3.4.1. Neonatal mortality rate in urban and rural areas and factors associated with neonatal mortality

Neonatal mortality rate was calculated for infants whose mother was resident in Da Nang according to Residence registration system in Vietnam.

3.4.2. Stillbirths and preterm birth rate

Stillbirth rate was expressed as number of stillbirths per 1,000 live births (27). Stillbirth was defined as a baby born with no signs of life at a gestational age of at least 22 completed weeks or a weight of more than 500g if the gestational age was not known (28).

The rate of preterm births was defined as number of babies born before 37 completed weeks of gestational age divided by total live births.

3.4.3. Prevalence and pattern of congenital anomalies in neonates

The prevalence of congenital anomalies was presented as the number of congenital anomalies per 10,000 live births. The calculation was done by dividing total number of newborns with congenital anomalies born in the DHWC during the research period by total number of live births who were born in the DHWC during the research period.

3.4.4. Caesarean section rates, indications and associated factors

Rate of Caesarean section was calculated by dividing the number of Caesarean deliveries by total number of live births.

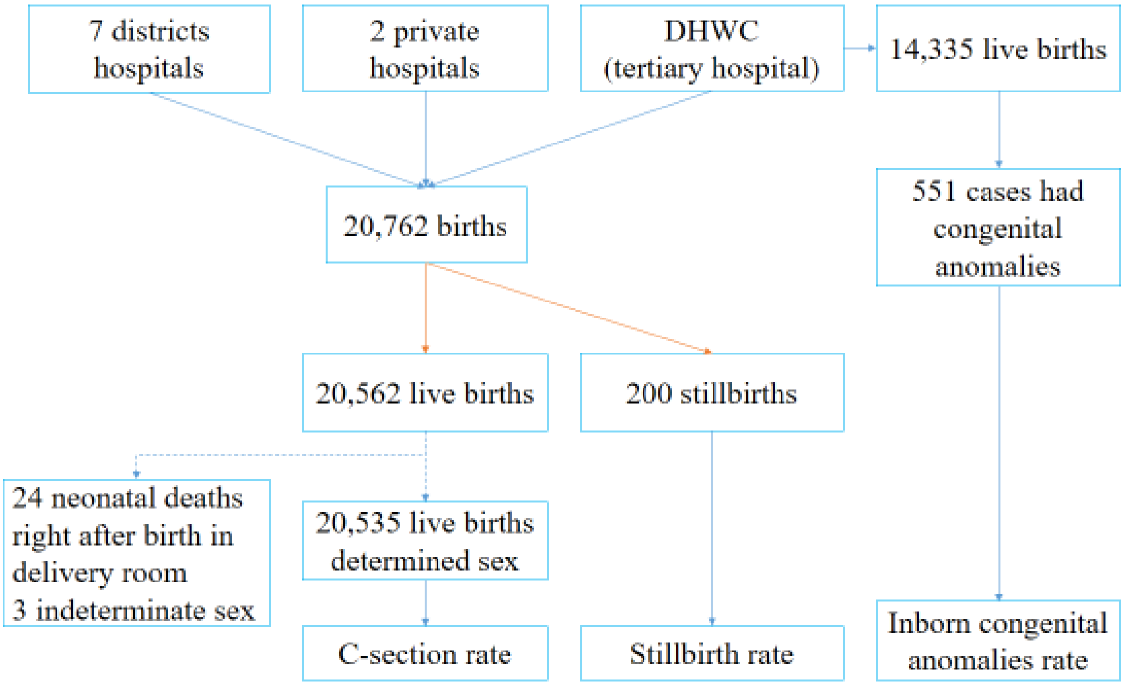

Figure 1. Data flow of the study over one year period

3.4.5. Ethical approval and consent to participate

Approval for the project was given by the Scientific and Ethics Board of Da Nang Hospital for Women and Children and by the Ethics Committee of the Ludwig Maximilian University. Individual informed consent was not required.

4. Results

Over a one year period, there were 20,762 births from register books. Among those, 20,538 were live births, 200 stillbirths, 24 neonates died in the delivery room (Figure 1). Among live births, three (0.01%) were ambiguous genitalia. Regarding to live births whose mother was resident in Da Nang, there was 13,211 live births, 24 neonates died in the delivery room, 29 neonatal deaths in NICU (Figure 2).

4.1. Neonatal mortality rate in urban and rural areas and factors associated with neonatal mortality in Da Nang city

Over one year, there were 13,211 live births whose mother was resident in Da Nang based on the residence registration system. Among those, there were 53 death cases (24 cases in delivery room and 29 cases in NICU) in the neonatal period corresponding a neonatal mortality rate of 4.0 per 1000 live births (Figure 2). The neonatal mortality rate in urban areas was 3.97 per 1000 live births and in rural areas 4.3 per 1000 live births. There was no statistical difference in neonatal mortality rate between urban and rural areas (p=0.5). Of the deaths, 47.2% occurred in the first 24 hour of life, and 73.6% occurred in the first seven days of life. Neonates less than 28 weeks of gestational age accounted for 52.0% of all deaths, and neonates more than 37 weeks of gestational age accounted for 22.0% of all deaths. There were 16 among 53 death cases (30.2%) with congenital anomalies.

Four main causes of neonatal deaths were preterm births 30 (61.2%), congenital anomalies 10 (20.4%), infection (8.2%) and asphyxia (4.1%). The causes of deaths were different between urban and rural areas. While prematurity was dominant in urban areas with 67.5%, congenital anomalies were dominant in rural areas with 57.1%.

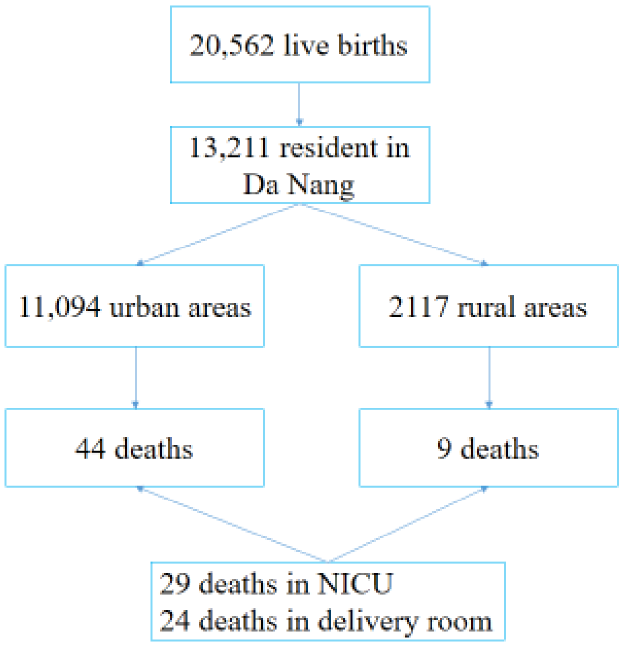

Figure 2. Data flow of data on neonatal mortality in Da Nang

4.2. Stillbirths and preterm birth rate

There were 200 stillbirths corresponding a stillbirth rate of 9.7 per 1,000 live births (95% CI 8.5-11.2 per 1,000 live births) for the whole city within a one-year period. Nearly half (47.0%) of the cases occurred between 22 to 28 weeks of gestational age and a third (31%) occurred after 34 weeks of gestation. Maternal age over 35, maternal occupation as a farmer, having abortion history, and living in other provinces were related to an increased risk of stillbirths.

There were 988 preterm infants corresponding a preterm birth rate of 4.8%. Preterm birth occurred in 35% of multiple births and 4% of singleton births. Maternal age over 35 and under 20, maternal occupation as a farmer, having abortion history, having a previous preterm birth and living in other provinces were related to an elevated risk of preterm births.

4.3. Prevalence and pattern of congenital anomalies in neonates

A total of 551 infants among 14,335 live births born in DHWC had congenital anomalies. The rate of congenital anomalies for inborn infants of DHWC was 384.4 per 10,000 live births (95% CI 353.8-417.5). Prevalence of all main categories of congenital anomalies and fifteen major anomalies are presented in Table 1 and Table 2.

Table 1. **Prevalence (per 10,000 live births) of main congenital anomalies categories in Da Nang, 2015-2016 (n=14,335), taken from the manuscript titled "Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam" (29)**

Congenital anomalies category	No. of case	Prevalence (95 % CI)	Proportion (%)
Total	**551**	**384.4 (353.8-417.5)**	**100**
Multiple congenital anomalies	93	64.9 (52.7-79.8)	16.9
Single congenital anomalies	458	319.5 (291.6-349.9)	83.1
Congenital heart defect	288	200.9 (178.9-225.6)	52.3
Musculoskeletal system	42	29.3 (21.4-40)	7.6
Digestive system	32	22.3 (15.5-31.9)	5.8
Cleft lip and palate	15	10.5 (6.0-17.7)	2.7
Genital organs	12	8.4 (4.5-15.0)	2.2
Nervous system	11	7.7 (4.0-14.2)	2.0
Chromosomal anomaly	10	7.0 (3.5-13.3)	1.8
Urinary system	5	3.5 (1.3-8.6)	0.9
Eye, ear, face and neck	5	3.5 (1.3-8.6)	0.9
Respiratory system	3	2.0 (0.5-6.7)	0.5
Congenital tumor	10	7.0 (3.5-13.3)	1.8
Congenital adrenal hyperplasia	1	0.7 (0.04-0.5)	0.2
Congenital hypothyroidism	1	0.7 (0.04-0.5)	0.2
Other congenital anomalies	15	10.5 (6.0-17.7)	2.7

(29)

Table 2. **Prevalence of the selected congenital anomalies in Da Nang (per 10,000 live births), taken from the manuscript titled "Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam" (29)**

Congenital anomalies subtypes	Da Nang (Prevalence per 10,000 live birth)
Atrial septal defect	175.09

Patent ductus arteriosus	119.98
Ventricle septal defect	41.15
Cleft lip and palate	23.02
Down's syndrome	13.95
Hirchsprung disease	12.6
Polydactyly	11.9
Syndactyly	11.9
Clubfoot	11.2
Ano-rectal atresia and stenosis	11.2
Pulmonary atresia/stenosis	8.4
Gastroschisis	4.9
d-Transposition of great arteries	3.5
Diaphragmatic hernia	3.5
Anencephaly	3.5

(29)

4.4. Caesarean section rate, indications and associated factors

There were 12,035 Caesarean deliveries among 20,535 live births with determined sex. The rate of Caesarean section for the participating hospitals over the study period of one year was 58.6%. Caesarean section rate for public hospitals was 57.9% and 70.6 % for private hospitals ($p < 0.0001$). There were 60.1% of primiparous women and 56.7% of multiparous women giving birth by Caesarean section. The indications for Caesarean section were available in register book for only 10,069 live births. Among those, previous Caesarean sections, cephalopelvic disproportion and foetal distress were three main indications for the Caesarean sections in descending order.

Factors found to be independently associated with Caesarean sections were maternal age greater than 30, maternal occupation as officer, having a history of abortion. Higher birth weight and being a male baby were two characteristics of infants associated with increased risk of Caesarean sections.

5. Discussion

This thesis described the main perinatal outcomes including rate of neonatal death, stillbirths, preterm births, congenital anomalies and the rate of Caesarean sections in neonates in the biggest city in central Vietnam.

The neonatal mortality rate of 4 per 1000 live births in Da Nang is lower than the estimated national neonatal mortality rate of 11 per 1000 live births in 2015 (30) and approximated the level of high-income countries (2). The low neonatal mortality rate in our setting is largely due to a number of steps and interventions that have been implemented to improve care and outcomes in the NICUDN since 2013 (31). This low rate of death may also reflect the remarkable changes in social and economic development over the past five years in Da Nang. The proportional distribution of four main causes of deaths in the neonatal period in Da Nang differed from global and national estimations (2) (32). Birth asphyxia was responsible for a small proportion of neonatal death in our study compared to global average of 23% (32). This may reflects appropriate resuscitation care for neonates right after birth in delivery rooms as a result of rolling out early essential newborn care in DHWC since 2014. As higher proportions of deaths are due to prematurity, ensuring more skilled health workers in the care of preterm babies and live-saving equipment in delivery room are needed. Also, prevention of preterm births and congenital anomalies should be paid more attention. Preterm births and congenital anomalies are two major causes of neonatal mortality in Vietnam. In order to continue reducing the rate and the number of neonatal death annually, available preventive strategies need to be applied. In Da Nang, a high proportion of congenital anomalies among inborn infants in DHWC was recorded and congenital heart defect was the most common anomaly. A previous study on neonatal mortality in DHWC showed a significant contribution of congenital anomalies in primary causes of neonatal death of 24% (31). This study once more highlighted the importance of including congenital anomalies prevention strategies to further reducing neonatal mortality in Vietnam.

Rural-urban difference in neonatal mortality rate was not significant in our study. However, the contribution of primary causes of deaths were different in urban and rural areas. It is important to understand the difference in these causes of deaths between rural and urban population to identify and address health needs of the population.

As other developing countries, Vietnam has not paid sufficient attention to stillbirths and has not included stillbirths in vital statistics report systems. There were sparse studies and data on stillbirths in Vietnamese context so far. The stillbirth rate of 9.7 per 1,000 live births in our study was comparable with the rate reported in Southeast Asia region nearly 20 years ago and significant higher than in high income countries (5). This may reflex inequities in access to good quality antenatal care and care at birth for women in different settings (33) (34). Number of pregnant women receiving at least four antenatal care visits and giving birth with a skilled birth attendant were lower in developing countries compared to developed countries (33) (34). Inconsistence in the definition of stillbirths and the misclassification of stillbirths and early neonatal mortality makes it difficult to obtain accurate data on stillbirths from register books.

Prevalence of congenital anomalies found in this hospital-based prospective study of 384.4 per 10,000 live births is higher than reported from developed countries (35) (36) (37) and lower than the estimated prevalence for South-East Asia (38). The prevalence of congenital anomalies can be affected by many factors including definition of the cases, time of examination, study population and diagnostic capability. We found a higher prevalence of congenital heart defect (200.9 per 10,000 live births) than in other studies (35) (36) (39), primarily because of the large number of atrial septal defect. In this study, we were unable to distinguish between isolated atrial septal defect in preterm infants and fullterm infants and all of the cases were included in the final calculation. This may lead to ascertainment bias. The Caesarean section rate of 58.6% reported by this study is higher than in both rich and poor countries (40) (41) (42). This rate is far greater than the recommended Caesarean section rate at population level by WHO of 10 to 15% and Caesarean section rate worldwide estimated from 150 countries of 18.6%. We could not find medical reasons to justify the high rate of Caesarean sections in Da Nang. Current lacking of specific systems for monitoring and controlling Caesarean sections at national and local levels may contribute to this high rate. In addition, culture-related social concerns and women’s fears may be further factors influencing this current scenario. More high-quality research exploring factors contributing to the rise of Caesarean section rate is needed in order to search for interventions to reduce Caesarean sections in Vietnam.

This study had several limitations. The accuracy of the data collection may be affected by lacking of uniformity in the register books between hospitals. Also, there was a lack of full information from the register books of the included hospitals like exact gestational age of infants at birth. Inconsitancy in the definition of stillbirths and early neonatal deaths may lead to misclassification of cases. We were unable to fully address this limitation as this study was based on register books. We aimed to provide information on perinatal outcomes in Da Nang, however, factors associated with these outcomes have not comprehensively explored, which are essential to search for interventions to improve these outcomes.

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7. Accepted articles

7.1. Article 1 - Monitoring and interventions are needed to reduce the very high Caesarean section rates in Vietnam

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REGULAR ARTICLE

Monitoring and interventions are needed to reduce the very high Caesarean section rates in Vietnam

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ABSTRACT

Aim: The aim of this study was to estimate the prevalence of Caesarean sections in the third largest city in Vietnam and identify the associated risk factors.

Methods: This descriptive study was conducted in Da Nang from April 2015 to March 2016 and the hospital-based sample comprised 20 535 women who delivered during this period. Caesarean section cases were categorised into private and public hospitals and groups of primiparous and multiparous women.

Results: We recruited 10 of the 12 hospitals in the City and they covered 90% of births during the study period. The overall Caesarean section rate was 58.6%: 57.9% in public hospitals and 70.6% in private hospitals. The three main indications for Caesarean sections were previous Caesarean sections, cephalopelvic disproportion and foetal distress. The factors that increased the likelihood of Caesarean sections were the mother being over 30, having an office job, a history of abortions, having a male infant and a higher neonatal birth weight.

Conclusion: Our study demonstrated an extremely high rate of Caesarean section and associated factors in public and private hospitals in one of the biggest cities in Vietnam. The findings highlight the need for monitoring and interventions to reduce the Caesarean section rates.

INTRODUCTION

There has been a rapid rise in Caesarean sections since the first documented operations (1) and they are now the most common surgery in both low-middle income and high-income countries (2). They can save the lives of mothers and babies, but some studies have shown that Caesarean sections above a certain level could even be linked to adverse health consequences (3–6). Other studies have shown no impact on reducing maternal, infant and neonatal mortality when the Caesarean section rate was higher than 10% at a population level (7–9). In 1985, the World Health Organization stated that there was no justification for any region to have Caesarean section rates higher than 10–15% (6,10). In 2015, based on the available data and evidence, the World Health Organization concluded that Caesarean sections were only effective only when they were required for medically indicated reasons.

The Caesarean section rate for developed regions has been estimated to average 21.1% and range from 6.2% to 36% and for less developed countries the respective figure is 14.3%, with a range from 0.4% to 40.5% (6). There is currently limited data on the rate of Caesarean sections at the population level in Vietnam. Therefore, the aims of this study were to describe Caesarean section rates, indications and associated factors in Da Nang city, the largest city in central Vietnam.

METHODS

Study setting

Da Nang is the third largest city in Vietnam in terms of the urban population. The healthcare system in the city is structured according to the national plans. During the study period, perinatal services were provided in various health

Key notes

- This study estimated the prevalence of Caesarean sections in the third largest city in Vietnam and identified the associated risk factors.
- Our analysis of 20 535 deliveries over a one-year period showed that the overall Caesarean section rate was very high at 58.6%: 57.9% in public hospitals and 70.6% in private hospitals.
- The three main indications for Caesarean sections were previous Caesarean sections, cephalopelvic disproportion and foetal distress.

facilities: 56 communal health stations, seven district hospitals, five private hospitals and one tertiary hospital. Deliveries are performed in hospitals, by midwives and obstetric specialists.

Data collection

The data collection for this cross-sectional study was performed over 12 months, from April 2015 to March 2016. Every two weeks, the principal investigator visited the tertiary hospital, seven district hospitals and two of the private hospitals to collect the data. All the live births in these hospitals during the study period were included in this study. There were three private hospitals who refused to provide data for the study. Data on maternal age, occupation, modes of delivery, indications for Caesarean section, birth weight and gender of the newborn were collected from the health registration database at all 10 participating health facilities. The Caesarean section indications were retrieved from clinical indications on the basis of medical records. Missing data were coded as not available.

The outcome measures included the overall rate of Caesarean sections and the rates in the public and private sectors. The deliveries that took place in tertiary hospitals and district hospitals were classified as public sector care.

The independent factors that were evaluated were maternal age and occupation, place of residence, parity, namely primiparous or multiparous, multiple births, birth weight and the infant's sex.

Data analysis

The data were collected into a spreadsheet and analysed using R Statistical Language (R Foundation for Statistical Computing, Vienna, Austria). Frequencies and percentages were used to describe the categorical data and means and standard deviations were used to describe continuous data. Caesarean section rates were calculated by the number of Caesarean births divided by the total number of live births (11).

Univariable logistic regression model was used to explore contributing factors associated with modes of birth. Then, the multivariable logistic regression model was applied to assess the independent impact among all of those factors on the mode of delivery. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated for all predictor variables. $p < 0.05$ was considered statistically significant.

Ethical approval and consent

This study only used anonymous data and individual informed consent was not required. Approval for the project was provided by the Scientific and Ethics Board of Da Nang Hospital for Women and Children (9 February 2015) and by the Ethics Committee of the Ludwig Maximilian University (15 June 2015).

RESULTS

During the study period, there were 20 535 live births and 12 035 births were Caesarean sections, corresponding to a rate of 58.6% for the participating hospitals.

The Caesarean section rate was 57.9% for the public hospitals: 43.7% in the district hospitals and 62.9% in the tertiary hospitals. The percentage of Caesarean deliveries in the private hospitals was 70.6% ($p < 0.0001$). The Caesarean section rate was 60.1% and 56.7% for primiparous and multiparous women, respectively, but ($p < 0.0001$) we had no information on parity in 57 women. The data are presented in Figures 1 and 2.

The indications for 10 069 (83.7%) Caesarean section births were recorded and the three main indications were a previous Caesarean section, cephalopelvic disproportion and foetal distress, contributing to nearly 65% of all the Caesarean sections. The differences in the numbers and percentages of all the indications between public and private hospitals are shown in Table 1. Previous Caesarean sections accounted for more than one-third of all the Caesarean section cases and for approximately two-thirds of the Caesarean sections in multiparous women. Cephalopelvic disproportion, foetal distress and prolonged labour and dystocia contributed to more than 50% of all indications among primiparous women (Table 1).

The factors associated with Caesarean sections are presented in Table 2. Increased rates of Caesarean section were associated with mothers aged over 30 (aOR 1.24, 95% CI: 1.16–1.32), those who had an office job (aOR 1.27, 95% CI: 1.2–1.35) and a history of abortion (aOR 1.52, 95% CI: 1.39–1.65). Higher birth weights (aOR 1.00, 95% CI: 1.00–1.00) and male sex (aOR 1.10, 05% CI: 1.04–1.17) were also associated with the delivery mode of Caesarean section.

DISCUSSION

The increasing rate of Caesarean sections is a worrying issue, both in high-income and low-income countries because it results in negative economic and health-related outcomes (3,12). Rates of Caesarean section are different from one country to another and depend on the level of the hospitals where deliveries take place. Of the 20 535 births in Da Nang, 58.6% were Caesarean sections. This rate was much higher than those reported from high-income

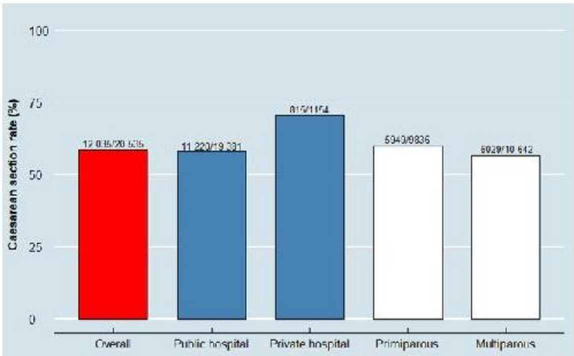

Figure 1 Rate of birth by Caesarean section, by level of hospitals and maternal parity, Da Nang, 2015–2016.

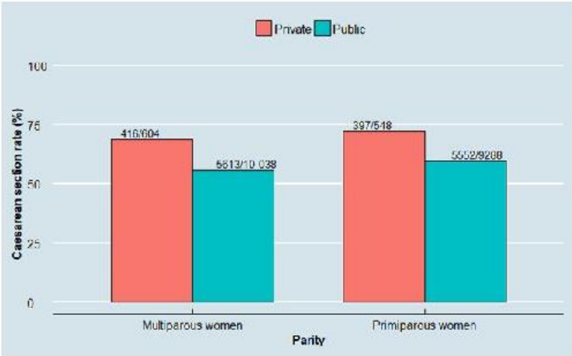

Figure 2 Caesarean section rates by sector (blue bars) and parity (white bars).

countries, such as Germany (30.8%), France (20.8%) (13) and the United States (32.2%) (14) and reports from more resource-rich settings in Asia, such as Thailand (34.1%) and Japan (19.8%) (6). The Caesarean section rate we found in Da Nang was considerably higher than in less developed countries in the South East Asia region, including the Philippines (18.8%) and Cambodia (14.7%) (15). The worldwide Caesarean section rate has increased to unprecedented levels and varies between different regions and countries (11). Betrán et al. reported that the average use of Caesarean sections throughout the world was constant over the 24-period from 1990 to 2014 (18.6%) (11), with the highest rates in Latin America and the Caribbean region (40.5%) and the highest average annual rate of increase in the Asian region. A population-based surveillance in Vietnam's Quang Ninh province from 2008 to 2011 showed a Caesarean section rate of 17% (16), which was one-third of the Caesarean section rate reported in Da Nang. Caesarean section rates may be related to economic determinants (6) and the connection between rising Caesarean section rates and rapid economic development has been discussed in previous studies (17). According to the World Health Organization, Caesarean section rates respond to income or factors strongly related to incomes (12). Vietnam has recorded strong economic growth over the past 30 years and a higher Caesarean section rate may also be found in Quang Ninh now.

The Caesarean delivery rate of 58.6% found in our study was even higher than the rate in China, which has been reported to have the highest Caesarean section rate in the world (46.2%) (15,18) and it was much higher than the World Health Organization recommended threshold of 15% for all deliveries. A systematic review of ecologic studies concluded that Caesarean section rates from 9% to 16% had an impact on reducing maternal, newborn and infant mortality, but the association disappeared when analyses controlled for social-economic factors (19). On the other hand, increasing Caesarean section rates above this

Table 1 Indications for caesarean section (n = 10 069)

		Type of hospital			Parity†		
Indications for caesarean section	Total (n, %)	Private n = 675	Public n = 9394	p Value*	Primiparous n = 9836	Multiparous n = 10 642	p Value*
Previous caesarean section	3574 (35.5)	269 (39.9)	3305 (35.2)	0.01	0	3517 (68.9)	
Cephalopelvic disproportion	1514 (15.0)	77 (11.4)	1437 (15.3)	0.006	1252 (25.5)	262 (5.1)	<0.0001
Foetal distress	1304 (13.0)	61 (9.0)	1243 (13.2)	0.001	1010 (20.6)	294 (5.8)	<0.0001
Prolonged labour and dystocia	602 (6.0)	72 (10.7)	530 (5.6)	<0.0001	518 (10.6)	84 (1.6)	<0.0001
Oligohydramnios	597 (5.9)	79 (11.7)	518 (5.5)	<0.0001	483 (9.8)	114 (2.2)	<0.0001
Maternal condition	517 (5.1)	30 (4.4)	487 (5.2)	0.3	377 (7.7)	140 (2.7)	<0.0001
Pre-eclampsia, eclampsia	472 (4.7)	25 (3.7)	447 (4.8)	0.2	330 (6.7)	140 (2.8)	<0.0001
Multiple pregnancy	425 (4.2)	2 (0.3)	423 (4.5)	<0.0001	236 (4.8)	189 (3.7)	0.006
Foetal malpresentation	415 (4.1)	26 (3.9)	389 (4.1)	0.8	269 (5.5)	146 (2.9)	<0.0001
Foetal macrosomia	229 (4.1)	15 (2.2)	214 (2.3)	0.8	180 (3.7)	49 (1.0)	<0.0001
Premature rupture of membranes, PPROM‡	169 (1.7)	14 (2.1)	155 (1.6)	0.3	117 (2.4)	52 (1.0)	<0.0001
Antepartum haemorrhage§	136 (1.4)	0	136 (1.4)	0.002	63 (1.3)	73 (1.4)	0.6
Polyhydramnios	43 (0.4)	0	43 (0.5)	0.06	28 (0.6)	15 (0.3)	0.02
Post-term pregnancy	32 (0.3)	4 (0.6)	28 (0.3)	0.2	21 (0.4)	11 (0.2)	0.06
Uterine rupture or suspected uterine rupture	15 (0.15)	0	15 (0.2)	0.2	7 (0.14)	8 (0.16)	0.8
Cord prolapse	12 (0.1)	0	12 (0.1)	0.4	6 (0.1)	6 (0.1)	1.0
Congenital anomalies	6 (0.1)	1 (0.1)	5 (0.1)	1.0	4 (0.1)	2 (0.0)	0.02
HELLP syndrome	7 (0.1)	0	7 (0.1)	0.4	5 (0.1)	2 (0.0)	0.02

*Based on Chi-squared test.
†57 women had no information on parity.
‡Pre-term premature rupture of membranes.
§Including lacenta praevia, placental abruption and vasa praevia.

Table 2 Factors associated with modes of delivery

Characteristics	C-section‡ n = 12 035	Vaginal birth n = 8500	Univariable analysis OR (95% CI)§	Multivariable analysis aOR (95% CI)
Maternal characteristics				
Maternal age*	29.3 ± 4.9	28 ± 4.8	1.05 (1.05, 1.06)	1.076 (1.07, 1.08)
<25, n (%)	1815 (15.1)	1988 (23.4)	0.65 (0.60, 0.7)	0.68 (0.63, 0.74)
25–29, n (%)	5155 (42.8)	3644 (42.9)	1	1
≥30, n (%)	5065 (42.1)	2868 (33.7)	1.25 (1.17, 1.33)	1.24 (1.16, 1.32)
Maternal occupation				
Office	4409 (36.6)	2504 (29.5)	1.38 (1.3, 1.47)	1.27 (1.2, 1.35)
Non-office	7626 (63.4)	5996 (70.5)	1	1
Abortion history†	1843 (16)	880 (11.1)	1.52 (1.39, 1.65)	
Neonatal characteristic				
Male	6395 (53.1)	4265 (50.2)	1.13 (1.07, 1.19)	1.10 (1.04, 1.17)
Birth weight (gram)¶	3186.1 (509.0)	3082.6 (478.9)	1.0004 (1.0004, 1.0005)	1.0004 (1.0003, 1.0005)

*Maternal age, mean (SD), year.
†Data on 19454 births only.
‡C-section (Caesarean Section).
§OR (95% CI): Odds ratio (95% confidence interval).
¶Mean (SD).

threshold did not reduce mortality rates further, regardless of adjustment.

To our knowledge, there are currently no specific systems for monitoring and controlling Caesarean sections in Vietnam and this could explain the high prevalence of Caesarean section in Da Nang. Furthermore, culture-related social concerns may contribute to the increasing Caesarean section rate. In Vietnamese culture, the birth hour and day are believed to contribute to determining a person's fate. Also, having a Caesarean delivery is easier than a vaginal delivery and demand from women and families has contributed to rising Caesarean section rates in middle- and high-income countries (20). For example, one study showed that women in Argentina expressed a preference for Caesarean sections in both the public (8%) and private sectors (6%) (21). In addition, the fear of pain and adverse birth outcomes during vaginal birth might be important factors that make women and families choose Caesarean sections. Vietnamese families now tend to have fewer children and many believe that Caesarean sections are safer.

Caesarean section rates varied by the hospitals in our study and were highest in private hospitals (70.6%). A similar disparity was found by a study in Brazil, with 18.9% in public hospitals and 84.3% in private hospitals (22). Our results showed that, even in district hospitals that mostly care for non-risk pregnancies, the Caesarean section rate was also extremely high. The tertiary hospital acts as a referral hospital for the whole city and surrounding provinces for normal and high-risk pregnancies. This could, to some extent, explain the higher Caesarean section rates at the tertiary hospital (62.9%) compared with the district hospitals (43.7%). A survey in Quang Ninh, Vietnam, confirmed a higher 38% Caesarean section rate in tertiary hospitals compared to 15% at district level (16).

When we analysed the main indications for Caesarean sections, we found that they were previous Caesarean sections (35.5%), cephalopelvic disproportion (15%) and foetal distress (13%). These rates were similar to the main indications in nine Asian countries reported by World Health Organization, with previous Caesarean sections (24.2%), cephalopelvic disproportion (22.6%) and foetal distress (20.5%) (15). van Roosmalen and van der Does (23) reviewed the determinants of Caesarean birth and showed that the most frequent reasons to perform Caesarean section included dystocia, repeat Caesarean births, breech delivery and foetal distress, which were consistent with our study. However, the proportion of women with these indications was even higher in Da Nang than in other studies.

In addition, there is no evidence that a Caesarean section is required after a previous Caesarean section delivery (10,24) and the World Health Organization says that vaginal delivery should normally be encouraged after a Caesarean section, as long as emergency surgical intervention is available (10). The high prevalence of this indication for Caesarean sections in Da Nang could be due to previous complicated births, which are common in developing countries (25). In addition, women may not be well informed about the option of vaginal delivery after as previous Caesarean section and the limited knowledge and skills of obstetricians may also make another Caesarean more likely. Previous Caesarean sections seem to be considered as an absolute indication for further Caesarean sections in Vietnam and the knowledge, skills and altitude of healthcare professionals needs to be addressed.

The high rate of Caesarean sections in Vietnam was likely to be associated with demographic factors as well as medical indications, as it was significantly higher in mothers over 30 years. This finding was consistent with studies from

China (26,27) where the Caesarean section rate is higher in mothers aged 25 years or more. One explanation could be that increasing maternal age may be associated with higher neonatal mortality and stillbirths (28,29).

It was interesting that male babies were more likely to be delivered by Caesarean section in our study, which was consistent with another study from Vietnam (16) that showed that the gender of newborn infants was associated with mode of delivery. One interpretation is that some families knew the gender of the baby in advance, using of prenatal ultrasound, and demanded that boys were delivered by Caesarean section. Vietnamese families have traditionally preferred sons because of their potential to carry on the family name and lead ancestor worship. Another interpretation could be that male foetuses have been reported to have more potential complications in pregnancies than female foetuses (30) and boys were more likely to be delivered by Caesarean section.

Another socio-economic factor associated with Caesarean sections was the mother's occupation, as women who worked in offices were more likely to have their babies delivered by Caesarean section. Caesarean sections are two to three times more expensive than vaginal deliveries in Vietnam and the cost of giving birth in private hospitals is four to ten times higher than public hospitals. It is possible that office workers were more likely to have the income to pay for them.

To our knowledge, these are the first comprehensive data from the third largest city in Vietnam on elevated levels of Caesarean sections and their associated factors. This study should raise awareness among community and policy makers to pay more attention to Caesarean section rates. The high-risk groups for Caesarean sections identified in this study should be followed further for interventions to reduce the Caesarean section rate in the future. Using the Robson classification, a system that classifies women into 10 groups based on their obstetric characteristics would help to analyse Caesarean section rates within, and across, groups and further identify priority target groups. These Robson classification groups include parity, previous Caesarean sections, gestational age, onset of labour, foetal presentation and the number of foetuses (31). It is clear from our study that the primary Caesarean section rate needs to be lowered in Vietnam. Furthermore, transferring evidence-based guidelines and recommendations regarding Caesarean sections into clinical practice to promote normal vaginal deliveries is an important task in our setting.

LIMITATIONS OF THE STUDY

The present findings must be interpreted in the context of a number of potential limitations. First, data were extracted from the hospital records and we were not able to confirm the absence of unrecorded risk factors and we lacked sufficient information to code indications for Caesarean sections using the Robson classification. Second, the Caesarean section rates found in Da Nang should not be seen as representative of the entire country. Two private hospitals refused to provide data, so an even higher rate of Caesarean sections could be possible. An American study found that maternal requests accounted for 8% of the total increase in primary Caesarean rates (32), but this could not be addressed in our study, as the indication for surgery was not always indicated in the medical records. Future studies should take this into account.

CONCLUSION

Our prospective study demonstrated an extremely high rate of Caesarean sections and associated risk factors in Da Nang, one of the biggest cities in Vietnam. These findings highlight the need for monitoring and interventions to reduce the Caesarean section rates at all levels of the health system.

FUNDING

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COMPETING INTERESTS

All authors declare that they have no competing interests.

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7.2. Article 2 - Stillbirth and preterm birth and associated factors in one of the largest cities in central Vietnam

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Stillbirth and preterm birth and associated factors in one of the largest cities in central Vietnam

Running title: Stillbirth and preterm birth in Vietnam

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ABSTRACT

Aim

Little is known about the rate of stillbirths, preterm births and associated risk factors in resource-limited settings like Vietnam. This study reports those rates for Da Nang, which is one of the largest cities in central Vietnam.

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Methods

Data on 20,762 births including stillbirths and preterm births and associated risk factors were prospectively collected from health facilities from April 2015 to March 2016.

Results

The data represented 85% of the total births in Da Nang during the study period and a stillbirth rate of 9.7 per 1,000 live births was recorded. The preterm rate for live births was just under 5%. Independent factors associated with an increased risk of stillbirth and preterm births were mothers aged 35 plus, working as farmers, living in the provinces and a history of abortion. Mothers under 20 years with previous preterm births faced a higher risk of another preterm birth.

Conclusion

The stillbirth and premature birth rates in Da Nang were higher than rates in high-income countries. Developing registration programmes in Vietnam will provide improved data that will enable researchers and policy makers to identify strategies to reduce the number of stillbirths and premature births.

Key words

Fetal death, lower middle-income country, preterm, stillbirth, Vietnam

Key notes

- This study identified rates of stillbirth and preterm births and associated factors in Da Nang, Vietnam.
- A stillbirth rate of 9.7 per 1,000 live births was recorded and preterm births accounted nearly 5% of live births.
- Independent risk factors for stillbirths and preterm births were mothers aged 35 plus, working as farmers, living in the provinces and a history of abortion.

INTRODUCTION

Globally, birth outcomes have shown impressive improvements over recent decades. However, a large gap remains between the outcomes in high-income countries and low and middle-income countries (1). It has been reported that 97-99% of adverse birth outcomes including stillbirths, neonatal deaths and preterm births occur in resource-limited settings (1,2). Stillbirth is one of major adverse birth outcomes, as there are nearly 3.2 million stillbirths each year worldwide (3). Preterm birth is another adverse birth outcome in which complications can lead directly to neonatal mortality. Preterm birth and its complications have been reported to account for approximately 27% of neonatal mortality annually across the world (4) and in almost all countries with reliable data, preterm birth rates are increasing. Most of the epidemiologic research regarding stillbirths and preterm births has been conducted in high-income countries, despite the likelihood that risk factors might differ in low resource areas. In addition, risk factors in rapidly industrialising countries may be different from those in poor resource settings.

Vietnam, which has a population of 91.7 million, is a lower middle-income country in the Western Pacific Region. Nearly 1.5 million babies are born every year, corresponding to a birth rate of 16.2 births per 1,000 of the population (5). Vietnam has made remarkable progress in reducing child mortality over the last 20 years. Maternal and neonatal health has been given a high priority by the Vietnamese Ministry of Health. However, stillbirths and preterm births have not received adequate attention and the capacity and resources for implementing maternal and stillbirth audits are inadequate. Statistics on stillbirths, preterm births and other unsatisfactory pregnancy outcomes are unavailable. The aim of this study was to report the proportion of preterm births and stillbirths in the Da Nang area of central Vietnam, as not much is known about the epidemiology of adverse pregnancy outcomes in this region.

METHODS

Data collection was conducted from April 2015 to March 2016 at 10 health facilities in Da Nang city, Vietnam: one tertiary hospital, seven district hospitals and two private hospitals.

Study setting

Da Nang is one of the most populated cities and the largest urban centre in central Vietnam. In recent years, Da Nang has recorded remarkable progress in economic development. Its average gross domestic product per capita has been reported to be 2,506 US dollars, which was above the average national outcome of 2,185 US dollars (6,7). The city has a population of more than one million and three ethnic groups, with the Kinh accounting for 90% of inhabitants. Da Nang is subdivided into eight districts: two rural and six urban. Nearly 90% of Da Nang's population lives in urban areas, with the other 10% in rural areas containing 11 rural communes. According to the national plan, the healthcare system in Da Nang has three levels - community health centres, district hospitals and tertiary hospitals. The Da Nang Hospital for Women and Children is the largest maternity and children's hospital in central Vietnam and the major referral hospital for the city and surrounding provinces. It handles approximately 14,000 deliveries each year, accounting for nearly 70% of deliveries in the whole city. The local guidelines recommend that preterm births of less than 35 weeks of gestation are transferred to Da Nang Hospital for Women and Children. Many hospitals with a low capacity tend to transfer women at less than 37 weeks of gestation if there is a risk of preterm birth and the majority of clinicians follow this rule. Despite this, some cases of imminent preterm delivery may occur at peripheral hospitals.

According to Vietnam's national guideline for reproductive healthcare (8), four antenatal care visits during pregnancy are recommended, one during the first and the second trimester and two during the third trimester. A typical minimum antenatal care consultation in Vietnam includes body weight, blood pressure, height, fetal heart rate, vaginal examination, blood test, urine test, ultrasound, tetanus toxoid immunisation, provision of tablets or advice on iron or folate supplements, malaria prevention, preparation for a safe delivery, health promotion and education, resting and nutrition (8,9). Gestational age is calculated by the first ultrasound in most patients and used for the rest of the pregnancy. Sometimes, the woman's last menstrual period is used for this calculation and in a few cases the Ballard Score is used to assess gestational age after the baby is born (10). Health insurance covers 80% the cost of antenatal visits for most women (11). However, those who are self-employed, housewives or unemployed, don´t have a health insurance and it is possible this prevents them from seeking prenatal care (10).

Procedure and study variables

All the births in the 10 hospitals and their outcomes were recorded in the birth registers, including maternal age at delivery, maternal occupation, place of residence, sex of infants and birth weight. Outcomes, including stillbirth, preterm birth and neonatal deaths occurring in the delivery room, were extracted from the hospital records. Maternal occupation was divided into office worker, factory worker, farm worker, housewife and others. The place of residence was classified as Da Nang city or province on the basis of the mother's residence. Stillbirth was defined as a baby born with no signs of life at a gestational age of at least 22 completed weeks or a weight of more than 500g if the gestational age was not known (12). To account for cases not recorded as stillbirths, we determined an Apgar score of zero at one minute and five minutes as a stillbirth. Preterm birth was defined as a live birth before 37 completed weeks of gestation.

Birth weight was categorised into four groups: very low birth weight (lower than 1,500g), low birth weight (1,500g to 2,499g), normal birth weight (2,500g to 4,499g), and high birth weight (higher than 4,500g) (13).

Data collection and verification

A trained data collector with a medical educational background visited the health facilities every month to collect information on all births. The data entry was carried out by two people, any inconsistencies were checked by the lead author (HTNG) and the data cleaning process detected any outliers and inconsistent data. We anonymised the Excel database (Microsoft Corp, Washington, USA) to protect the identities of the individual women, but an identification number was included to trace the original data if needed.

Statistics

The primary outcomes were stillbirth and preterm births. In the descriptive analyses, the stillbirth rate was defined as the number of stillbirths per 1,000 live births. The preterm birth rate among live births was defined as the percentage of babies born before 37 completed weeks of gestation. As the district hospitals did not routinely record gestational age, the preterm birth rate was calculated on the assumption that district hospitals did not have preterm births, except for a few cases of imminent preterm delivery with information on gestational age. The rationale for this assumption was that in Da Nang, hospitals with low capacity transfer women at less than 37 weeks of gestation. In these analyses, the outcomes of stillbirths and preterm were recorded as binary variables. The explanatory variables included maternal and infant characteristics, covering maternal age at delivery, maternal occupation, place of residence, sex of the babies, and weight at birth. Univariable logistic regression was conducted to examine the risk of potential predictors of stillbirth and preterm births without adjusting for other covariates. Multivariable logistic regression was then performed to identify the significant independent determinants of stillbirths and preterm births. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. Maternal age was divided into five subgroups: less than 20, 20-29, 30-34, 35-39 and 40 plus years. We selected women aged 20-29 years as the reference group because this group was at the lowest risk of several adverse birth outcomes, including stillbirths and preterm births compared with the remaining groups (14-16). The reference categories for maternal occupation and residence were having an office job and being resident in Da Nang, respectively. Da Nang is the municipality with the highest urbanisation ratio among the provinces in Vietnam and its average gross domestic product per capita is higher than surrounding provinces in the central region. This urban area has a lower rate of adverse birth outcomes and consumption of prenatal care (1).

The sex ratio at birth was defined as the number of males born per 100 females (17).

All of the statistical analyses were performed using R statistical language (R Foundation for Statistical Computing, Vienna, Austria). P values equal to, or less than, 0.05 were considered statistically significant.

Ethical approval and consent to participate

Approval for the project was given by the Scientific and Ethics Board of Da Nang Hospital for Women and Children and by the Ethics Committee of the Ludwig Maximilian University. Individual, informed consent was not required.

RESULTS

Maternal socio-demographic and obstetric characteristics

From April 2015 to March 2016, a total of 20,762 births were registered. There were 541 (3%) multiple births. The number of mothers was 20,489 because there were 263 pairs of twins (12.8 per 1,000 mothers) and five sets of triplets (0.2 per 1,000 mothers).

The mean maternal delivery age was 28.8 ±4.9 years with a range of 14-49 years. Approximately, 2% of mothers were younger than 20 years of age and 3% of mothers were older than 40 years of age. The majority (59%) worked in offices and factories.

Nearly 80% of the women had a maternal gravidity of 0-1 and 14% of mothers had a history of abortion (Table 1).

Sex and birth weight of live births

During the study there were 20,538 live births: 52% were male and three (0.01%) had a disorder of sex differentiation. The sex ratio at birth was 108 male per 100 female. The means of the birth weight for male and female infants were 3,153.7 ± 545.1 (range 500g to 5,300g) and 3,094.49 ± 530.1 (range 600g to 5,300g), respectively. There was a significant difference in birth weight between males and females ($p<0.0001$). Overall, 7% of the babies had a low birth weight: 2% at term and 5% preterm (Table 2).

Stillbirths

A total of 200 stillbirths were identified, resulting in a stillbirth rate of 9.7 per 1,000 live births (95% CI 8.5-11.2 per 1,000 live births) for the whole city. Of those stillbirths, 91 (46%) were female and six (3%) had ambiguous genitalia.

The majority (47%) of all stillbirths occurred between 22 and 28 weeks of gestation, 22% were registered between 28 and 33.9 weeks of gestation and 31% from 34 weeks onwards (Figure 1).

Preterm birth

The preterm rate in live births was just under 5% and preterm births occurred in 35% of multiple births and 4% of singletons births. Data on gestational age could only be accurately collected from the tertiary hospital, but this covered 99% of the births.

Risk factors for stillbirth and preterm birth

Table 3 presents the association between maternal socioeconomic characteristics and infant factors with stillbirth and preterm births. A full analysis is presented in Table S1.

A number of factors were independently associated with an increased risk of stillbirth and preterm birth, as measured by odd ratios (OR) and 95% confidence intervals (95% CI). These were women who were over 35 years of age (OR 1.97, 95% CI 1.22-3.2 and OR 1.33, 95% CI 1.04-1.71), those who worked on a farm (OR 3.54, 95% CI 1.71-7.32 and OR 2.93, 95% CI 2.03-4.24), those who lived in the provinces (OR 3.23, 95% CI 2.34-4.44 and OR 2.43, 95% CI 2.1-2.81) and a history of abortion (OR 1.55, 95% CI 1.09-2.21

and OR 1.25, 95% CI 1.04-1.52). Being under 20 years of age at delivery (OR 1.99, 95% CI 1.24-3.2) and having had a previous preterm birth were independently associated with an elevated risk of preterm birth (OR 1.99, 95% CI 1.24-3.2).

DISCUSSION

This prospective survey provided data on the high stillbirth and preterm birth rates in central Vietnam and identified the risk factors, which included age, occupation, home location and previous pregnancy outcomes. Strategies are clearly needed to reduce these rates.

Data on live births, stillbirths, preterm births and associated information were collected from hospitals and clinics within one month of the birth. The number of stillbirths in our study was 9.7 per 1,000 live births which was more than double the stillbirth numbers reported for high income countries of four per 1,000 live births (4). However this rate was nearly the same as the stillbirth rate in the Southeast Asia region in 2000 (12.7 per 1,000 live births, 95% CI 10-16 per 1,000 live births) (3). Compared to data from a multi-centre study in a similar setting (12.5 per 1,000 live births) (18) and a population study from Ha Tay Vietnam (19 per 1,000 live births) (14), the incidence of stillbirths in our study was lower. In the Ha Tay study, the stillbirth rate was high among adolescent mothers aged from 15 to 19. Young maternal age as well as older age are well-known factors for an increased risk of stillbirths and other adverse birth outcomes (19-23). In the current study, although the mother's age ranged from 14 to 49, the majority were aged between 20 to 34 years and that might explain the lower risk compared with the study population in Ha Tay. Maternal age has been found to be a strong independent risk factor in many studies at both ends of the age distribution, including below 20 years, 35-39 years and over 40 years (23,24). Also maternal age matters when it comes to preterm births. In our study, young maternal age was associated with an almost two-fold increased risk for preterm birth, which was the same as stated in the studies of Hediger et al and Gardosi and Francis (15,25). In the current study women aged 20-35 years had significant lower rates of preterm births than women under 20 years of age and women who were 40 years of age or older.

The stillbirth rate varies widely, even between high-income countries, ranging from 1.3 to 8.8 per 1,000 births, with six countries having a stillbirth rate of 2.0 per 1,000 births (1). This shows that further reductions are is possible. In the present study, 47% of stillborn babies were born at 22-27.9 weeks of gestation. The high rate of stillbirths before 28 weeks of gestation was consistent with a study at a tertiary referral hospital in Ho Chi Minh city, Vietnam (12).

Our finding that just under 5% of the births in Da Nang were preterm births was lower than previous figures Vietnam and fairly low when compared with international rates. In a hospital-based, urban study in Vietnam, nearly 12% were delivered preterm. Estimated preterm delivery rates worldwide range from 5% in high-income countries to 25% in low- income countries (4). Obtaining accurate information on the duration of gestation remains a challenge in perinatal research.

Living in the provinces outside city has been strongly associated with an increased risk for adverse birth outcomes, including neonatal mortality, stillbirth and preterm birth in other studies (12,26). In our study women resident outside Da Nang also had an increased risk of both preterm and stillbirth deliveries. Women living in Da Nang, which is a modern city in central Vietnam, have much better living conditions and educational opportunities than women in most of the other provinces in the region. Another factor that may be related to high adverse birth outcomes among women from the other provinces may be that high-risk pregnancies from the other provinces tend to come to the tertiary hospital, Da Nang Hospital for Women and Children, for delivery. The high number of adverse pregnancy outcomes, including stillbirths, may reflect inequities in access to reproductive healthcare services and highlight disparities between women living in rural and urban areas and between those with high and low incomes (1). Globally, rural areas account for a larger proportion of stillbirths than urban areas (1,27). The quality of antenatal care that pregnant women received is another determinant that has been reported to affect stillbirths (28) and rural residence has been associated with lower antenatal care quality (29). A study conducted with 2,132 pregnant women in Ha Noi, northern Vietnam, showed that the use of antenatal care was significantly lower in rural areas compared to urban areas. This included both the quantity, number and timing of the visits and the content of the visits (30).

Although some occupational or environmental hazards may predict stillbirth and preterm births, the occupation of the women probably reflected their low socio-economic status in our study. A study on rural farming women in Vietnam found that they were at increased risk of giving birth to preterm infants (31). Although farming did not account for a really large proportion of the mothers in this study, or in the current Da Nang population, the association between preterm birth and stillbirth and the mother working as a farmer was in the same odds ratio range previously reported from Vietnam, but in a smaller population sample (31). The reasons for that could be that agriculture in Vietnam is still physically demanding, often with little mechanisation, and that farm workers may have insufficient access to antenatal care. A history of preterm birth and abortion was strongly associated with an increased risk of preterm birth in our study and this was consistent with nearly all the previous studies (25,32,33).

Limitations of the study

This study had several limitations. A lack of uniformity in the birth register between hospitals made the data collection difficult and not all the information could be generated. Misclassification of cases regarding stillbirths and early neonatal deaths was another possible limitation and the substitution of an APGAR score may not have fully addressed this deficit.

There was a major confounding bias in our data on all preterm birth rates. The number of preterm births could have been underestimated, because this information is not required by the official health information system. We only had data from the tertiary hospital. In contrast, the records for the 6,202 births in the district hospitals noted the infants' birth weights, but did not record their exact gestational age. In addition, we did not have any data on how prematurity was treated in rural hospitals.

Another concern was that we collected data from hospital registers, therefore we may have missed some cases from 22 to 27.9 weeks that were recorded as stillbirths but were actually born alive. These live births were also missed if the infants who were examined showed initial signs of life but then died and were not recorded as live births in the register books.

CONCLUSION

This study presented relatively comprehensive background data on stillbirths, preterm births and associated risk factors in central Vietnam. Independent factors associated with an increased risk of stillbirth and preterm births were mothers aged 35 plus, working as farmers, living in the provinces and a history of abortion. Mothers under 20 years with previous preterm births faced a higher risk of another preterm birth. The rate for stillbirth and premature birth in Da Nang was still higher in comparison with highly industrialised countries and there is a need to record and register quality data on all births, stillbirths and preterm births in Vietnam. Improved data can help healthcare providers to target interventions that reach women and infants who experience stillbirths and preterm births. Regular antenatal care visit is another need to improve pregnancy and neonatal outcomes. Identifying the priorities for interventions, care and outcomes in a resource-limited setting like Vietnam will hopefully reduce the numbers of stillbirths and preterm births.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Figure 1. Distribution of stillbirths according to gestational age at delivery

Table 1. Characteristics of the 20,489 study mothers

Maternal characteristic	n (%)
Mother's age, mean (standard deviation), standard error of mean, (min, max)	28.8 (4.9), 0.034, (14-49)
Maternal occupation	
Office	6,855 (33.0)
Factory worker	5,357 (26.0)
Farmer	302 (2.0)
Housewife	5,143 (25.0)
Other	2,832 (14.0)
Place of residence	
Da Nang city	13,109 (64.0)
Provinces	7,380 (36.0)
Place of delivery	
Stillbirths (n=200)	
Tertiary hospital	200 (100)
Preterm (n=990)	
Tertiary hospital	979 (99.0)
District hospitals	11 (1.1)
Abortion history*	2,727 (14.0)
Preterm history*	515 (3.0)

*Data on only 19,413 mothers

Table 2. Characteristics of all 20,762 births over the one-year study period

Characteristics	Live births (n=20,538)	Stillbirths (n=200)	Deaths in first 30 minutes (n=24)
Male, n (%)	10,660 (52.0[a])	103 (52.0[b])	13 (54.0[c])
Birth weight (grams), mean (standard deviation), standard error of the mean, (min, max)	3,143.1 (499.5) 3.49 (500, 5300)	-	-
>4,500, n (%)	80 (0.4)	1 (0.5)	1 (4.0)
2,500-4,499, n (%)	19,077 (92.9)	42 (21.0)	5 (21.0)
1,500-2,499, n (%)	1,185 (5.8)	42 (21.0)	1 (4.0)
<1,499, n (%)	196 (0.9)	115 (57.5)	17 (71.0)
Multiple birth, n (%)	515 (3.0)	26 (13.0)	0
Preterm, n (%)	988 (5.0)	-	-
Multiple births	181 (35.0)	-	-
Singleton	807 (4.0)	-	-

[a,b,c]Proportion of male infants among live births, stillbirths, death cases respectively

Table 3. Risk factors for stillbirth and preterm birth, Da Nang, Vietnam, 2016

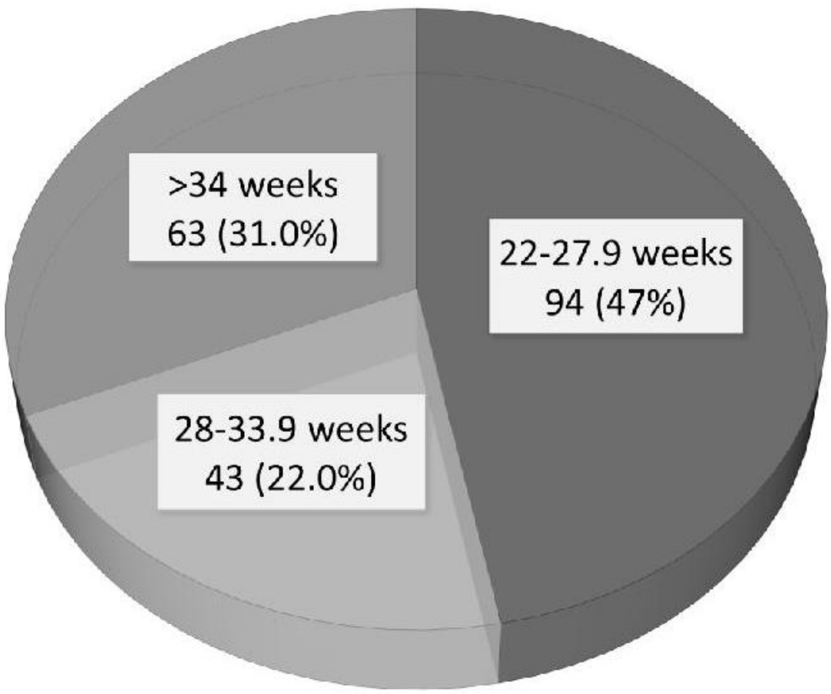
Characteristics	**Stillbirth** n=174[d] n (%)	Multivariable analysis odds ratio	**Preterm** n=807[d] n (%)	Multivariable analysis odds ratio
Maternal age, n (%)				
<20	4 (2.0)	1.99 (0.72-5.54)	20 (3.0)	1.99 (1.24-3.2)
20-29	89 (51.0)	1	469 (58.0)	1
30-34	42 (24.0)	1.2 (0.82-1.75)	188 (23.0)	0.97 (0.81-1.16)
35-39	26 (15.0)	1.97 (1.22-3.2)	90 (11.0)	1.33 (1.04-1.71)
≥40	13 (8.0)	2.32 (1.19-4.51)	40 (5.0)	1.63 (1.13-2.35)
Maternal occupation				
Office	35 (20.0)	1	243 (30.0)	1
Factory	45 (26.0)	1.76 (1.12-2.75)	172 (21.0)	0.93 (0.76-1.14)
Farmer	11 (6.0)	3.54 (1.71-7.32)	42 (5.0)	2.93 (2.03-4.24)
Housewife	42 (24.0)	1.68 (1.06-2.66)	191 (24.0)	1.07 (0.88-1.31)
Other	41 (24.0)	2.42 (1.52-3.84)	159 (20.0)	1.51 (1.22-1.86)
Place of residence				
Da Nang city	63 (36.0)	1	344 (43.0)	1

Province	111 (64.0)	3.23 (2.34-4.44)	463 (57.0)	2.43 (2.1-2.81)
Male	103 (52.0)	1.15 (0.85-1.56)	464 (58.0)	1.25 (1.08-1.44)
Abortion history[a,b]	38 (22.0)	1.55 (1.09-2.21)	135 (17.0)	1.25 (1.04-1.52)
Preterm history[c]	5 (3.0)	1.10 (0.45-2.68)	79 (10.0)	4.55 (3.54-5.85)

[a]Data on 19,124 mothers; [b]Univariable analysis; [c]Data on 18,951 mothers: 26 cases of stillbirths and 181 cases of preterm were excluded from this analysis because of multiple pregnancy

Additional file

Table S1. Risk factors for stillbirth and preterm birth, Da Nang, Vietnam, 2016.



8. Conclusions

- There were no significant difference in neonatal mortality rate between urban and rural areas of Da Nang
- Preterm births and congenital anomalies were two important causes of neonatal deaths. Neonatal mortality in urban and rural areas were different regarding these causes.
- The rate of stillbirths in Da Nang was higher than reports from rich countries. Registration programmes may be the first essential step to provide high quality data on stillbirths followed by interventions to reduce the stillbirths.
- Risk factors for adverse pregnancy outcomes identified from this study were maternal age over 35 or under 20, working as farmers, living in the provinces and a history of abortion. Risk factors of the adverse outcomes for stillbirths, preterm births and congenital anomalies in Vietnam need to be further explored to identify proper interventions.
- This study highlighted an extremely high rate of Caesarean sections in Da Nang, Vietnam and a need for monitoring and interventions to reduce the rate of Caesarean sections in both public and private settings.

9. Annex

9.1. Manuscript 3. Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam

Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam

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Article category: Original article

Running title: Congenital anomalies in central Vietnam

Abstract

Burden and pattern of congenital anomalies are insufficiently reported in Vietnam. This study aims to determine the prevalence and pattern of congenital anomalies in neonates in a tertiary hospital in central Vietnam. A prospective cross sectional study recruited all newborns with congenital anomalies in Da Nang Hospital for Women and Children – where nearly 60% neonates in the city are delivered. Congenital anomalies were diagnosed based on clinical evaluation, imaging examination and blood test. Over a one-year period, 551 out of 14,335 registered live births were found to have congenital anomalies, equivalent to an overall prevalence of 384.4 per 10,000 live births. Congenital heart defects were the most common type (52.3%) with the prevalence of 200.9 per 10,000 live births, followed by anomalies of musculoskeletal system, digestive system, cleft lip and cleft palate (29.3, 22.3, and 10.5 per 10,000 live births respectively). There were significantly more newborns with congenital anomalies delivered by women with a university degree or higher than by women with lower level of education. This study revealed a high prevalence of congenital anomalies with the most common type being congenital heart defects in central Vietnam compared to both higher income countries and resource-limited settings.

Key words

Birth defect; congenital anomalies; congenital malformation; congenital heart defect; Vietnam

Key note

- Little is known about the prevalence and pattern of congenital anomalies in Central Vietnam
- A high prevalence of congenital anomalies was documented in this study with the most common types of congenital anomalies are congenital heart defects, musculoskeletal anomalies, digest system anomalies, cleft lip and cleft palate.
- More studies on risk factors associated with congenital anomalies in Vietnamese context are needed

INTRODUCTION

Congenital anomaly is a serious global public health problem because it is a major cause of child mortality and morbidity worldwide. Congenital anomaly causes lifelong disability and considerable impacts on the health care system. In 2015, congenital anomaly is responsible for nearly 276,000 neonatal deaths around the world; 95% of the deaths come from low-middle income countries (World Health Organization. 2015, March of Dimes. 2006). Prevalence and pattern of congenital anomalies have been reported in developed countries. However, there are surprisingly few data on this matter in countries with limited resources.

Vietnam is a low-middle income country with a population of approximately 90 million people and the accurate birth prevalence of congenital anomalies is difficult to obtain because the health report system is being developed and the diagnostic capability is limited.

Central Vietnam was toxic contaminated from Agent Orange during the Vietnam War and Da Nang Airbase has been confirmed as a significant dioxin hotspot (Hatfield Consultants. 2009, The Aspen Institute. 2017, World Bank. 2017). More than fifty years after the use of Agent Orange during Vietnam War, the concentration of dioxin remains elevated indicating extremely high contamination (Hatfield Consultants. 2009). Data and information related to congenital anomalies in Vietnam are still insufficient. Central Vietnam is identified as the region with the highest prevalence of congenital heart defects and a recent study conducted in 2011 in the neonatal unit of Da Nang Hospital for Women and Children showed that congenital heart defect was the commonest defect of admission and death (Tran. 2015). We hypothesized that the prevalence of congenital anomalies and subgroups connected to Agent Orange are higher than in other parts of Vietnam.

The current study was conducted to determine the prevalence and patterns of congenital anomalies in newborn infants in Da Nang Hospital for Women and Children.

METHODS

Study design

This is a cross-sectional study over one year from April 2015 to March 2016, recruiting all newborns with congenital anomalies born in Da Nang Hospital for Women and Children.

Study setting

The study was conducted in the neonatal unit and delivery room at Da Nang Hospital for Women and Children. The hospital was established in 2011 to offer health care for children and women. Every year there are around 14,000 pregnant women from different parts of Da Nang and surrounding provinces including Quang Nam and Quang Ngai. There are approximately 4,000 admissions to the neonatal unit, mainly neonates with different diseases, among those congenital anomalies are a big part. Da Nang has a population of about one million people. The surrounding provinces of Quang Ngai and Quang Nam have a population of approximately three million people. During the Vietnam War, in central Vietnam, Da Nang, Quang Nam and Quang Ngai were heavily contaminated from Agent Orange (The Aspen Institute. 2017, Wikipedia. 2017).

Study procedure

Data was collected prospectively after birth using a structured form designed for this study. Information collected includes sex, type of congenital anomalies, maternal and perinatal history, and parents' demographic information, including highest educational qualification, the occupation of mother and father, smoking, alcohol consumption, pesticide exposure and chronic diseases. Information related to newborns with congenital anomalies was extracted from medical records at the time of discharge by two research nurses. If the newborn had visible congenital anomalies and severe health problems, they were transferred to the neonatal unit and information was recorded in the neonatal unit. If the newborn had minor congenital anomalies and no need to admit to the neonatal unit, information was recorded in the delivery room. Data were checked to avoid duplicated cases between neonatal unit and delivery room.

For those babies that were obviously healthy, they were examined at least one time by health professionals (doctor, nurse, or midwife) before leaving the hospital. Only newborns with suspected problems were checked by a pediatrician. Newborns stayed three days in hospital if they were vaginally born and five days if they were born with caesarean section.

Measurement of endpoints

Congenital anomalies were diagnosed based on clinical evaluation, imaging examination and blood tests, this information was documented in the medical records by doctors. Categories of congenital anomalies were described according to the International Classification of Disease, version 10 (ICD-10) (ICD 10. 2016). Isolated or single congenital anomaly or multiple anomalies within the same body system was counted as one anomaly. Multiple congenital anomalies are two or more unrelated structural anomalies (British Isles Network of Congenital Anomalies Registers. 2012).

Data analysis

Data were rechecked and entered into Microsoft Excel sheet. Statistical analysis was conducted using R Statistical Language (R Foundation for Statistical Computing, Vienna, Austria).

Primary outcome is the presence of congenital anomalies. As congenital anomalies occur during intrauterine life, total births should be denominator in congenital anomaly statistics (Kim. 2012).

However, it is difficult to obtain accurate data on congenital anomalies in stillbirth in hospitals in Vietnam background. Therefore, in the descriptive analyses, the prevalence of congenital anomalies, defined as the number of congenital anomalies per 10,000 live births, was calculated as the total number of infants with congenital anomalies per total number of live births who were born in the hospital during the research period. The independent variables included parental demographic factors, neonatal factors. Categorical variables were described as proportion and Chi-squared or Fisher exact test were performed to compare proportion between individual items. Poisson distribution was used to calculate 95% confident interval (CI) of congenital anomalies and their subgroups prevalence. The alpha level was set at $\alpha = 0.05$. For analyzing congenital anomaly characteristics, a newborn with multiple congenital anomalies was counted as one unit. For specific analysis of a particular defect or system defect, each anomaly was counted as one unit.

Ethical approval

The study was approved by the Scientific and Ethics Board of Da Nang Hospital for Women and Children and the Ethics Board of the Medical Center of Ludwig Maximilian University. Individual informed consent was not required. Our research have complied with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects.

RESULTS

Congenital anomalies characteristics

Among 551 newborns with congenital anomalies, there were 241 (43.7%) male. Multiple births accounted for 16 (2.9%) of the deliveries. There was 458 (83.1%) newborns had a single congenital anomaly and 93 (16.9%) had multiple anomalies. Thus, there were a total of 796 anomalies among 551 newborn babies. Mother's abortion history was presented in 122 cases (22.1%) and maternal history of giving preterm birth was presented in 19 cases (3.4%).

Prevalence of congenital anomalies of inborn newborns

Over a full calendar year, 551 inborn newborns were found to have congenital anomalies out of 14,335 live births registered at Da Nang Hospital for Women and Children within the study period. This corresponds to an overall prevalence of 384.4 per 10,000 live births (95% CI 353.8-417.5). Prevalence of all main categories of congenital anomalies is presented in Table 1.

Congenital heart defects were the most common congenital anomaly with the prevalence of 200.9 per 10,000 live births (95 % CI 178.9-225.6) and it accounted for 52.3% of all congenital anomalies. The second most common anomaly was musculoskeletal system anomalies 29.3 per

10,000 live births (95 % CI 21.4-40.0), digestive system anomalies 22.3 per 10,000 live births (95 % CI 15.5-31.9) and cleft lip and cleft palate 10.5 per 10,000 live births (95% CI 6.6-17.7). The prevalence of anomalies of respiratory and urinary system were less than five per 10,000 live births.

Prevalence of single congenital anomaly was 319.5 per 10,000 live births (95% CI 353.8-417.5), accounting for 83.1% of all congenital anomalies. The prevalence of multiple congenital anomalies was 64.9 per 10,000 live births (95% CI 52.7-79.8).

Among the newborn infants with congenital heart defect, atrial septal defect was the most common with 251 (48.5%) cases. Among those with musculoskeletal system anomalies, polydactyly, syndactyly and clubfoot were the most commonly defects with 50 (74.6%) cases. Hirschsprung disease accounted for 18 (38.3%) and ano-rectal atresia/stenosis accounted for 16 (34%) of all digestive system anomalies.

Indeterminate sex, anencephaly, congenital cystic adenomatoid malformation of lung and congenital posterior urethral valves were found to be the most common anomalies of genital anomalies, nervous system anomalies, respiratory system anomalies and urinary system anomalies with 37.5%, 27.7%, 50% and 42.9% respectively.

The prevalence of chromosomal anomalies was seven per 10,000 live births. Down syndrome was the most common chromosomal anomaly and it accounted for 83.3% of chromosomal anomalies. The fifteen major anomalies were presented in Table 2.

DISCUSSION

Congenital anomalies cause both early mortality and long term disability. Their impact in low-middle income countries is much higher than in high income countries (World Health Organization. 2013). Recognizing the burden of congenital anomalies and associated disabilities is essential to identify priorities for care and prevention of congenital anomalies. In this hospital-based prospective study, we investigated the prevalence and pattern of congenital anomalies in Da Nang.

Vietnam is a low-middle income country. The prevalence of congenital anomalies in Vietnam has been estimated 1%-3% (Vy. 2005, Dung. 2004). The high prevalence of congenital anomalies of 384.4 per 10,000 live births is higher than the report from the EUROCAT (261.5 per 10,000 births) and Korea (286.9 per 1,000 live births) (Kim. 2012), and higher than recent report from the more resource-rich setting in the region such as Thailand (261.2 per 10,000 live births) and Singapore (239.9 per 10,000 live birth) (Tan. 2005). The high prevalence of this recent study may be explained by the fact that Da Nang hospital for Women and Children is a referral hospital for high risk pregnancy and sick children.

In terms of environmental agents, central Vietnam including Da Nang was highly contaminated by Agent Orange, Da Nang airbase was determined as a “dioxin hotspot”. In addition, the high prevalence calculated could also be attributed to the classification of congenital anomalies using ICD-10 which does not differentiate major and minor anomalies.

However, the prevalence of congenital anomalies found in this study was lower than the prevalence estimated to the South-East Asia Region by the World Health Organization 510 per 10,000 live birth (congenital anomalies: 310 per 10,000 live and chromosomal disorders: 39 per 10,000 live births, single-gene disorders: 14.7 per 10,000 live births) (World Health Organization. 2013), Indonesia 593 per 10,000 live birth, Bangladesh 586 per 10,000 live birth. Limited diagnostic capability might attribute to underestimate the prevalence of congenital anomalies in the current study. Although most of the births were attended by medical staffs, only suspected cases were examined by pediatricians, therefore less severe anomalies could be missed.

Among all congenital anomalies, congenital heart defect was the most common defect, followed by anomalies of musculoskeletal system and digestive system.

Studies in Korea (Kim. 2012) and UK (Dastgiri. 2002) reported similar data. However, a study from India (Sarkar. 2013) reported mainly musculoskeletal anomalies, followed by gastro-intestinal and central nervous, while Mashuda et al (2014) reported in Tanzania the highest number of congenital anomalies was related to nervous system and musculoskeletal system. The prevalence of atrial septal defect was particularly high in Da Nang, approximately 10 times higher than in United States and 2.5 times higher than in Korea. The prevalence of cleft lip and cleft palate was also three times higher than that in United States and two times higher than in Korea. When considering the overall prevalence of congenital heart defects, the prevalence of 200.9 per 10,000 live births represents the prevalence of insolated congenital heart defects only. The birth prevalence of congenital heart defect in Da Nang reported in our study was particularly higher than that in the EUROCAT (82.16 per 10,000 births) (EUROCAT. 2016), Korea (124.5 per 10,000 live births) (Kim. 2012), United States (108 per 10,000 live births) (Egbe. 2015), and China (52.41 per 10,000 live births) (Wu. 2014). Other regions in Vietnam also reported a prevalence of congenital heart defect significantly lower than in Da Nang, 1.6 per 10,000 live births in Ho Chi Minh (six cases with congenital heart defects out of 37,530 births) (Dung. 2004), 17.6 per 10,000 live births in Binh Dinh (29 cases with congenital heart disease out of 16,444 live births), and 3.1 per 10,000 live births in Ha Noi (six cases with congenital heart disease out of 18,834 live births)

(Hoan. 2001). The difference in frequency may be due to difference in environmental and genetic factors, time and method of collecting data, difference in diagnostic ability and diagnostic criteria (Penchaszadeh. 2002). Da Nang city was exposed to Agent Orange during the War, this might be a possible cause of high prevalence in congenital anomaly.

Regarding fetal number, the finding in our study is similar with previous study, that congenital heart defect in twins is more common than in singletons (63% increase in the odds for congenital heart defect for twins) (Herskind. 2013).

The relationship between parental occupational exposures and educational qualification with adverse reproductive outcomes in epidemiological studies is often inconsistent and limited (Shi. 2001). Parental educational qualification and occupation have been considered as factors at socio-economic level influencing the occurrence of congenital anomalies. The occurrence of congenital anomalies has been found to decrease in the higher maternal educational qualification groups in a study in Singapore (Shi. 2002). In this study, the relationship between parental education and congenital anomalies does not mean that maternal and paternal education themselves influence on congenital anomalies. Education is considered as an indirect risk factor for congenital anomalies (Hoang. 2013). Our results show a higher prevalence of congenital anomalies occurring among mothers with university degree and higher education. The prevalence of congenital anomalies was not significant different between mother involved in factory work and mother involved in office work, while the difference was significant higher in father worked in factory compared with fathers worked in office.

The limitation of the study

An important limitation of hospital-based studies such as recent study is that they will not represent the full spectrum of congenital anomalies of general population.

CONCLUSION

In conclusion, this study highlighted the prevalence of congenital anomalies in one year in the largest hospital for women and children in central Vietnam. It revealed a high birth prevalence of congenital anomalies in central Vietnam compared to high income countries, resource-limited setting, and high risk countries. Among those, congenital heart defect is the most common anomalies. These findings have informed and raised awareness about the high prevalence of congenital anomalies including congenital heart defect in a population in central Vietnam possible due to late effects of environmental contamination two to three generations ago.

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Table 1. Prevalence (per 10,000 live births) of main congenital anomalies categories in Da Nang, 2015-2016 (n=14,335)

Congenital anomalies category	No. of case	Prevalence (95 % CI)	Proportion (%)
Total	**551**	**384.4 (353.8-417.5)**	**100**
Multiple congenital anomalies	93	64.9 (52.7-79.8)	16.9
Single congenital anomalies	458	319.5 (291.6-349.9)	83.1
Congenital heart defect	288	200.9 (178.9-225.6)	52.3
Musculoskeletal system	42	29.3 (21.4-40)	7.6
Digestive system	32	22.3 (15.5-31.9)	5.8
Cleft lip and palate	15	10.5 (6.0-17.7)	2.7
Genital organs	12	8.4 (4.5-15.0)	2.2
Nervous system	11	7.7 (4.0-14.2)	2.0
Chromosomal anomaly	10	7.0 (3.5-13.3)	1.8
Urinary system	5	3.5 (1.3-8.6)	0.9
Eye, ear, face and neck	5	3.5 (1.3-8.6)	0.9
Respiratory system	3	2.0 (0.5-6.7)	0.5
Congenital tumor	10	7.0 (3.5-13.3)	1.8
Congenital adrenal hyperplasia	1	0.7 (0.04-0.5)	0.2
Congenital hypothyroidism	1	0.7 (0.04-0.5)	0.2
Other congenital anomalies	15	10.5 (6.0-17.7)	2.7

Table 2. Prevalence of the selected congenital anomalies in Da Nang (per 10,000 live births)

Congenital anomalies subtypes	Da Nang (Prevalence per 10,000 live birth)
Atrial septal defect	175.09
Patent ductus arteriosus	119.98
Ventricle septal defect	41.15
Cleft lip and palate	23.02
Down’s syndrome	13.95
Hirchsprung disease	12.6
Polydactyly	11.9
Syndactyly	11.9
Clubfoot	11.2
Ano-rectal atresia and stenosis	11.2
Pulmonary atresia/stenosis	8.4
Gastroschisis	4.9
d-Transposition of great arteries	3.5
Diaphragmatic hernia	3.5
Anencephaly	3.5

9.3. List of publication

1. **Giang HTN**, Bechtold-Dalla Pozza S, Tran HT, Ulrich S. Stillbirth and preterm birth and associated factors in one of the largest cities in central Vietnam. Acta paediatrica (Oslo, Norway : 1992) 2018.
2. **Giang HTN**, Ulrich S, Tran HT, Bechtold-Dalla Pozza S. Monitoring and interventions are needed to reduce the very high Caesarean section rates in Vietnam. Acta paediatrica (Oslo, Norway : 1992) 2018.
3. **Giang HTN**, Banno K, Minh LHN, Trinh LT, Loc LT, Eltobgy A, et al. Dengue hemophagocytic syndrome: A systematic review and meta-analysis on epidemiology, clinical signs, outcomes, and risk factors. Rev Med Virol 2018:e2005.
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5. Hanifah A, Pratomo H, **Giang HTN**. Husband’s Support for Their Wives in Antenatal Care Visit. 2018 2018:9 (DOI: http://dx.doi.org/10.21109/kesmas.v13i1.1565).

9.4. Statement on pre-release and contribution

Parts of this thesis have been already published in the form of manuscripts:

1. Giang HTN, Ulrich S, Tran HT, Bechtold-Dalla Pozza S. Monitoring and interventions are needed to reduce the very high Caesarean section rates in Vietnam. *Acta paediatrica (Oslo, Norway : 1992)* 2018; 107 12:2109-14.
2. Giang HTN, Bechtold-Dalla Pozza S, Tran HT, Ulrich S. Stillbirth and preterm birth and associated factors in one of the largest cities in central Vietnam. *Acta paediatrica (Oslo, Norway : 1992)* 2018 (published ahead of print)

The remaining part of thesis titled “Prevalence and pattern of congenital anomalies in a tertiary hospital in central Vietnam” was submitted to peer reviewed journal.

9.5. Acknowledgments

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My PhD colleagues at CIH (2014 batch) could not be forgotten. I have learned a lot from each one of them.

Last, but not least I would like to express my gratitude towards my supervisors, without whom this project would not have been possible. I thank you all for your contributions!

9.6. Case report form

NEONATAL MORTALITY IN URBAN AND RURAL AREAS OF DANANG, VIETNAM

Information required for all neonatal death

Study ID: ……..................

CIH LMU

Neonatal mortality: A neonatal death is defined as death of a live birth during the first 28 days of life

General information		
1	Name of baby	…………………………………………………………………………..
2	Mother name	
3	Mother age at birth	………………….years
4	Address	Village/Street:………Commune:………...District:…………Da Nang
5	Telephone	…………………………………………………………………………...
Around delivery		
6	Date of birth	Date ……..month…….year………… , ………..hour…….minute
7	Gender	1. Female 2. Male
8	Birth weight	……………….grams
9	Gestational age at birth	……….............weeks
10	APGAR	1. Apgar/1 minute: ………………………………………………. 2. Apgar/5 minute: ……………………………………………….
11	Did the baby need any resuscitation right after birth?	1. Oxygen 3. Ventilation via face mask 2. Intubation & chest compression 4. Drugs
12	Was baby kept skin to skin contact with mother immediately after birth?	1. Yes 2. No
13	When was breast-feeding initiated (or attempted to be initiated)?	1. Within 1 hour after delivery 2. Later than 1 hour after delivery *How long:* …………………………………………….......................... 3. Without breast-feeding after delivery
14	Was the baby discharged and gone home after birth or referred to the other hospitals?	1. Baby was discharged after birth and go home *go to question (15)* 2. Baby was referred to other hospital *go to question (16)*
Admission		
15	Which symptoms/signs of the illness led to admission	1. Diarrhea 5. Unconscious 9. Difficult breathing 2. Cough 6. Convulsions 10. Cyanosis 3. Fever 7. Yellow skin 11. Other: ……………… 4. Rash 8. Reducing activities

	before the baby's death?	
16	Why was the baby transferred?	………………………………………………………………………......
17	Date of admission	Date………month………year
18	Treatment of the infant during illness until the baby died	1. Respiratory support 4. Kangaroo Mother Care 2. Phototherapy 5. Medication 3. Transfusion 6. Incubation 7. *Other*: ………………………………………………………………
19	Date of discharge/dealth	Date …….. month …...year…………., ……….hour ……….minute
20	Final diagnosis	Main diagnosis: ………………………………………………… Associated diagnosis 1: …………………………………………… Associated diagnosis 2: ……………………………………………

CONGENITAL ANOMALIES OF NEWBORN BABIES AT DANANG HOSPITAL FOR WOMEN AND CHIDREN

Study ID: ………………..

<table>
<tr><td>1</td><td>Name</td><td colspan="3">…………………………………………………………………………………………
…….</td></tr>
<tr><td>2</td><td>Address</td><td colspan="3">Village/Street:…………Commune…………….District……………………Da Nang</td></tr>
<tr><td>3</td><td>Gender</td><td colspan="3">1. Female 2. Male</td></tr>
<tr><td>4</td><td>Congenital heart disease</td><td colspan="3">1. Yes 2. No
If yes, please give detail below:
1. Atrial septal defect 3. Patent ductus arteriosus
2. Ventricular septal defect 4. Other:
……………………………………
Method of diagnosis:
1. Fetal ultrasound 3. Echocardiography
2. Examination for heart sound and murmurs</td></tr>
<tr><td>5</td><td>Other congenital anomalies</td><td colspan="3">1. Yes 2. No
If yes, please give detail below:
1. Down syndrome 3. Cleft lip and palate
2. Bowed legs 4. Congenital disorder anomalies
3. Other:
……………………………………………………………………</td></tr>
<tr><td>6</td><td>Do other people in baby's family present congenital anomalies?</td><td colspan="3">1. Yes 2. No
If yes, what's kind of congenital anomalies:
………………………………………………
If yes, please give detail about the relationship of those people with the baby
1. Father 2. Mother 3. Sibling
4. Other:
………...</td></tr>
<tr><td>7</td><td>PARA</td><td colspan="3">…….. ……… ……… ……….</td></tr>
<tr><td>8</td><td>Did baby's mother have any health problem during pregnancy?</td><td colspan="3">1. Yes 2. No 3. Don't know
If yes, please give detail below:
1. Fever 2. Rash 3. Gestational diabetes
4. Other:
…………………………………………………………...............................</td></tr>
<tr><td rowspan="2">9</td><td rowspan="2">Did baby's mother take medications during pregnancy?</td><td>Iron</td><td>Acid folic</td><td>Other</td></tr>
<tr><td>1. Yes 2. No</td><td>1. Yes 2. No</td><td>…………………………........
...</td></tr>
</table>

	General information	Mother	Father
11	Highest grade of education	1. Illiterate 2. Read/write only 3. Primary completed 4. Secondary completed 5. Tertiary completed 6. University/college degree 7. Postgraduate	1. Illiterate 2. Read/write only 3. Primary completed 4. Secondary completed 5. Tertiary completed 6. University/college degree 7. Postgraduate
	General information	**Mother**	**Father**
12	Main occupation	1. Government officer 2. Worker ………………………… 3. Farmer 4. Student 5. Housewife 6. *Other*: …………………………	1. Government officer 2. Worker …………………………... 3. Farmer 4. Student 5. Housewife 6. *Other*: ……………………………
13	Does she/he smoke?	1. Yes 2. No *If yes, number of cigarettes per day* …………………………………………....	1. Yes 2. No
14	Does she/he drink alcohol?	1. Yes 2. No *If yes, give detail about kind of alcohol?* ………………………………………….… *Number of ml per day:* …………………	1. Yes 2. No
15	Is she/he exposed to pesticide?	1. Yes 2. No	1. Yes 2. No
16	Does she/he have chronic disease?	1. Yes 2. No *If yes, give detail about kind of chronic disease*……………………………………....	1. Yes 2. No

DATA FROM REGISTER BOOK

Month: ……

No.	Mother's name	Address	Year of birth	Occupation	PARA	Mode of delivery	Indicator of Caesarean section	Gender	Birth weight	Multiple birth	Outcome
1											
2											
3											
4											