School of Public Health

Maternal Lifestyle, Gestational Diabetes Mellitus and Pregnancy Outcomes: A Prospective Cohort Study in Vietnam

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The study protocol was approved by the Curtin University Human Research Ethics Committee (approval number: HR32/2015) and the Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number: No. 05/HPUMPRB/2015).

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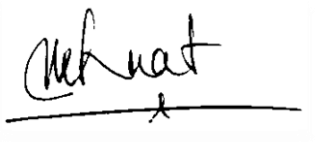
Signature: 

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Abstract

Background

Maternal lifestyle and dietary intake are known to be associated with metabolic disorders such as gestational diabetes mellitus (GDM). In turn, these conditions increase the risk of adverse pregnancy outcomes. Particularly, over-nutrition or sedentary behaviours during pregnancy have been positively associated with GDM risk. Women with GDM and their offspring tend to have higher risks of adverse health outcomes including preeclampsia, preterm birth, caesarean section, macrosomia, neonatal hypoglycaemia, type 2 diabetes and cardiovascular disease later in life. Globally, over 18 million live births were affected by GDM in 2017 and 88.0% of them occurred in low and middle income countries. In East and Southeast Asia, about one in ten pregnant women experience GDM. While approximately 1.5 million babies are born every year in Vietnam, the available data on the relationship between maternal lifestyle, GDM and pregnancy outcomes are sparse. This project updates our knowledge of this problem in Vietnamese women who become pregnant.

Objectives

The aims of this study were: 1) to undertake a systematic review of GDM prevalence in Eastern and Southeastern Asia including Vietnam; 2) to conduct a cohort study in Vietnamese women with the following objectives: 2.1) to investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index (BMI); 2.2) to evaluate the prevalence of GDM and adverse pregnancy outcomes (e.g. stillbirth, preterm delivery, low birthweight, macrosomia, caesarean section); 2.3) to ascertain the association between physical activity during pregnancy and GDM; and 2.4) to examine the association between GDM and pregnancy outcomes.

Methods

The PRISMA and MOOSE guidelines were followed in reviewing the prevalence of GDM in Eastern and Southeastern Asia. GDM prevalence and the corresponding 95%

confidence intervals were calculated according to fixed effects and random effects models.

A prospective cohort study was conducted in six hospitals in three cities across the length of Vietnam, namely, Ha Noi, Hai Phong, and Ho Chi Minh City from August, 2015 to December, 2016. Participants were recruited early in their pregnancy at a prenatal care visit. Eligibility criteria were: (1) permanent residency in the study locations; (2) ≥18 years of age; (3) at 24-28 weeks of gestation; (4) singleton pregnancy; (5) no serious pre-existing health condition such as cancer or ischemic heart disease; and (6) ability to read the information sheet and sign the consent form. Participants were invited to attend a baseline interview at 24-28 weeks of gestation to provide their lifestyle information including dietary intake, physical activity, smoking, alcohol drinking, demographics and medical history, before the determination of their GDM status. Dietary information was collected using an interviewer-administered food frequency questionnaire, and nutrient intakes were estimated using the Vietnamese food composition tables. Physical activity was assessed during the past 3 months before the baseline interview using the interviewer-administered Pregnancy Physical Activity Questionnaire. A single-step 75-g oral glucose tolerance test was conducted at 24-28 weeks of gestation to diagnose GDM using different international diagnostic criteria. Participants were then followed up to delivery to assess maternal and neonatal outcomes using hospital medical records. The data were summarised by means, percentages, and interquartile ranges accordingly. Besides descriptive statistics and univariate analyses, logistic regressions were performed to ascertain the associations between each outcome and its influencing factors. All analyses were mainly conducted using STATA version 12.0 (StataCorp, College Station, USA).

Results

The review of 48 studies found that approximately one in ten women in Eastern and Southeastern Asia had GDM. The prevalence of GDM varied substantially among countries. Lower- and upper-middle income countries had higher prevalence of GDM than high-income nations. The prevalence of GDM may be overestimated when using one-step screening approach compared with two-step screening method.

2030 out of 2248 (90.3%) eligible women consented to participate in the study. They were interviewed at the baseline and followed up until delivery. After delivery, complete information on birth and neonatal outcomes were available for 1909 mothers, with 121 dropouts due to history of diabetes before pregnancy (n=7), termination of pregnancy (n=1), human immunodeficiency virus (n=2), and loss to follow-up (n=111).

Rice, fruits, and vegetables were the main food sources consumed. The mean total energy intake was 2004 kcal/day (SD = 625), with 15.9%, 31.8%, and 52.2% of energy coming from proteins, fats, and carbohydrates, respectively. Over half of the women did not meet the Vietnamese recommended nutrient intakes (RNI) for total energy intake. The intakes of essential micronutrients including folate, calcium, iron, and zinc were below the RNI, and almost all of pregnant women failed to meet the recommendations for these micronutrients. Women with GDM were less physically active in terms of total PA (mean 116.6 vs. 125.0 MET-hrs per week) and had significantly lower levels in moderate-intensive activity (12.6 vs. 19.3 MET-hrs per week) as well as household/caregiving activity (46.2 vs. 49.7 MET-hrs per week) compared to non-GDM counterparts. No differences in sitting time, light, vigorous, occupational, recreational, and commuting activities were found between the two groups. Very few participants engaged in vigorous activity (2.9%), and only one-fifth of the pregnant women met the recommended guideline for PA (17.4% for GDM and 21.5% for non-GDM groups).

The prevalence of GDM varied according to the diagnostic criteria used: 6.4% by the America Diabetes Association (ADA), 7.9% by the European Association for the Study of Diabetes (EASD), 22.8% by the International Association of the Diabetes and Pregnancy Study Groups/ World Health Organization (IADPSG/WHO), and 24.2% by the National Institute for Health and Care Excellence (NICE) criteria. The estimates of preeclampsia, postpartum haemorrhage, and caesarean section were 0.3%, 1.1%, and 38.1%, respectively. The mean birthweight was 3142.7 grams (SD = 405.5). There were 0.4% of stillbirth and 5.2% of preterm labour. The proportions of macrosomia, low birthweight, jaundice requiring phototherapy, and admission to neonatal intensive care unit were 1.3%, 4.1%, 9.6%, and 3.0%, respectively.

Women undertaking the highest level (upper tertile) of PA during pregnancy appeared to have a lower risk of GDM (odds ratio (OR): 0.70, 95% confidence interval (CI): 0.53 to 0.94, P_{trend}: 0.017) when compared to those at the lowest tertile of PA. Similarly, women with increased levels of moderate-intensive activity and household/caregiving activity during pregnancy were associated with reduced risks of GDM (OR: 0.66, 95% CI: 0.50 to 0.86, P_{trend}: 0.002 and OR: 0.72, 95% CI: 0.55 to 0.95, P_{trend}: 0.020, respectively). These apparent inverse associations were not attenuated by their sitting time. There were no significant associations between sitting time, light-intensity activity, vigorous-intensity activity, occupation, sports/exercise, commuting, or meeting exercise guidelines and GDM risk.

Women with GDM according to the EASD criteria were more likely to have macrosomic infants (OR 4.35, 95% CI: 1.49 to 12.72), despite no apparent increase in risk under other criteria. Babies born to mothers with GDM appeared to be large-for-gestational age by the ADA criteria (OR 2.10, 95% CI: 1.10 to 4.02) or EASD criteria (OR 2.15, 95% CI: 1.16 to 3.98), when compared to their counterparts in the normal group. No significant differences in maternal and other neonatal outcomes were found between the GDM and normal groups.

Conclusions

Global consensus guidelines are essential to developing screening strategies and diagnostic criteria of GDM to enable early detection as well as effective prevention and management of GDM. It is also necessary to accelerate nutrition programs targeting pregnant women in Vietnam to ensure they get sufficient essential nutrients. In addition, pregnant women should be advocated to adopt an active lifestyle to help reduce the risk of GDM.

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Statement of Contribution of Others

The School of Public Health at Curtin University provided the research environment that supported the PhD candidate to undertake this research. The PhD candidate was responsible for designing the methodology, undertaking recruitment, implementing data collection and analysis, and writing all publications presented as part of the thesis, with input from co-authors. Details are summarised as follows.

• **Professor Andy H. Lee** contributed as a PhD main supervisor and provided ongoing close support and involvement with the study. He involved in the study design, revising manuscripts, and giving comments to improve all four publications.

• **John Curtin Distinguished Professor Colin W. Binns** contributed as an associate supervisor. He also involved in the study design, revising manuscripts, and giving comments to improve all four publications.

• **Dr. Dat Van Duong** contributed as an associate supervisor. He involved in the study design, revising manuscripts, and giving comments to improve all four publications.

• **Dr. Ngoc Minh Pham** contributed as an associate supervisor. He involved in the data analysis, revising manuscripts, and giving comments to improve all four publications.

Signed statements of the contribution of each co-author are provided in Appendix A.

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List of publications

1. **Cong Luat Nguyen**, Phung T.H. Nguyen, Tan Khac Chu, et al. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794 *[Impact factor: 2.413]*

2. **Cong Luat Nguyen**, Ngoc Minh Pham, Colin W. Binns, Dat Van Duong, and Andy H. Lee. 2018. Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis. *Journal of Diabetes Research*, Article ID 6536974, 10 pages. https://doi.org/10.1155/2018/6536974 *[Impact factor: 2.885]*

3. **Cong Luat Nguyen**; Dong Van Hoang; Phung T.H. Nguyen, et al. 2018. Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam. *Nutrients*, 10(8), 1025. https://doi.org/10.3390/nu10081025 *[Impact factor: 4.196]*

4. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, et al. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol*, 55(9): 955-962. https://doi.org/10.1007/s00592-018-1174-3 *[Impact factor: 3.126]*

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Abbreviations

ADA	America Diabetes Association
ADIPS	Australasian Diabetes in Pregnancy Society
BMI	Body mass index
CI	Confidence interval
C&C	Carpenter and Coustan
CVD	Cardiovascular diseases
EASD	European Association for the Study of Diabetes
FFQ	Food frequency questionnaire
GDM	Gestational diabetes mellitus
HAPO	Hyperglycaemia and Adverse Pregnancy Outcome Study
HDP	Hypertensive disorders in pregnancy
IADPSG	International Association of the Diabetes and Pregnancy Study Groups
LGA	Large-for-gestational age
MET	Metabolic equivalent task
MetS	Metabolic syndrome
NDDG	National Diabetes Data Group
NGT	Normal oral glucose tolerance test
NICE	National Institute of Health and Clinical Excellence
OGTT	Oral glucose tolerance test
OR	Odds ratio
PA	Physical activity

PCOS	Polycystic ovarian syndrome
PPAQ	Pregnancy physical activity questionnaire
RNI	Recommended nutrient intakes
SGA	Small-for-gestational age
T2DM	Type 2 diabetes mellitus
WHO	World Health Organization

Chapter 1. INTRODUCTION

1.1 Overview

Diabetes mellitus has become a worldwide epidemic. It is a multifactorial disease characterised by chronic hyperglycaemia due to defects in insulin secretion and/or insulin resistance (World Health Organization., 1999). According to the 1999 WHO revised classification of diabetes mellitus based on aetiology, there are four basic types of diabetes - type 1 diabetes, type 2 diabetes, other specific types (e.g., genetic defects of β-cell function or in insulin action, diseases of the exocrine pancreas, endocrinopathies, drug- or chemical-induced diabetes, infections, uncommon forms of immune-mediated diabetes and other genetic syndromes) and gestational diabetes mellitus (GDM) (World Health Organization., 1999). GDM has been linked to type 2 diabetes and type 1 diabetes. Accumulating data suggests that women with GDM have an increased risk of developing type 2 diabetes later in life (Bellamy, Casas, Hingorani, & Williams, 2009; Zhu & Zhang, 2016), and those with autoimmune GDM may subsequently progress to overt type 1 diabetes (Wucher, Lepercq, & Timsit, 2010). Thus prevention and management of GDM can contribute to reducing the burden of diabetes.

Gestational diabetes mellitus is a metabolic health problem that commonly occurs in pregnant women. GDM is defined as any glucose intolerance with first diagnosis during pregnancy (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997) and it has emerged as a global public health concern (Guariguata, Linnenkamp, Beagley, Whiting, & Cho, 2014). The prevalence of GDM varies widely, from 1% to 28%, depending on population characteristics (e.g. maternal age, socioeconomic status, race/ethnicity, or body composition), screening methods and diagnostic criteria (Jiwani et al., 2012). Data in high-income countries (HICs) showed that GDM prevalence ranges from 1.7 to 11.6% while those in low- and middle-income countries (LMICs) are in the range of 0.4 and 24.3% (Kanguru, Bezawada, Hussein, & Bell, 2014). The prevalence of GDM in Asia also varies substantially, between 1.6%-17.8% (J.E. Hirst, Raynes-Greenow, & Jeffery, 2012).

GDM has been associated with short-term and long-term adverse health outcomes for both mothers and their newborns (Farrar et al., 2016). Women with GDM are known to have decreased quality of life and increased risks of caesarean section, gestational hypertension, preeclampsia, type 2 diabetes mellitus (T2DM), and cardiovascular disease (C. Kim, Newton, & Knopp, 2002; Marchetti, Carrozzino, Fraticelli, Fulcheri, & Vitacolonna, 2017; McKenzie-Sampson, Paradis, Healy-Profitos, St-Pierre, & Auger, 2018; Metzger et al., 2008; Yogev, Xenakis, & Langer, 2004). In babies GDM has been found to be associated with macrosomia or large-for-gestational age infants, neonatal hypoglycaemia, subsequent obesity, and T2DM later in life (Clausen et al., 2008; Farahvar, Walfisch, & Sheiner, 2018; Langer, Yogev, Most, & Xenakis, 2005; Metzger et al., 2008). These consequences may be prevented by early detection, particularly at high-risk groups, proper management and treatment of GDM.

There are various risk factors of GDM such as maternal obesity, advanced maternal age, family history of T2DM, prior GDM, history of macrosomia, history of stillbirth or congenital malformations, hypertension prior to 20 weeks gestation, polycystic ovary syndrome, and ethnicity (Cypryk, Szymczak, Czupryniak, Sobczak, & Lewinski, 2008; Xiong, Saunders, Wang, & Demianczuk, 2001). Several modifiable factors including nutritional status and physical activity (PA) may affect the risk of GDM. Particularly, a high intake of fat, a Western dietary pattern with larger amounts of red meat, glycaemic load, and sugar-sweetened beverages, have been positively associated with the GDM risk. In contrast, prudent dietary patterns comprising fruit, vegetables, poultry, fish and dietary fibre are inversely associated with the GDM risk (C. Zhang, Liu, Solomon, & Hu, 2006; C. Zhang, Schulze, Solomon, & Hu, 2006). Coffee and tea are the most popular beverage in the world and Vietnam. Moderate intake of coffee and tea might have a protective effect against GDM (Hinkle, Laughon, Catov, Olsen, & Bech, 2015). The link between smoking or alcohol drinking and GDM remains controversial. On the other hand, a large number of observational studies have shown that PA during pregnancy might decrease the risk of GDM, especially when pregnant women perform PA before or at early pregnancy (Aune, Sen, Henriksen, Saugstad, & Tonstad, 2016; Tobias, Zhang, van Dam, Bowers, & Hu, 2011). All pregnant women without contraindications are advised to engage in appropriate levels

of PA throughout pregnancy to minimise detrimental health risks. It is obvious that healthy lifestyle has a vital role in reducing GDM risk.

Vietnam is a developing country in the Asia-Pacific region with an increased burden of non-communicable diseases (NCDs) (C. T. Nguyen, Pham, Lee, & Binns, 2015). The prevalence of T2DM has tripled in the last two decades and continues to go up (Harper, 2011). However available data on GDM remain limited. A hospital based study conducted in Ho Chi Minh City, Southern Vietnam, reported that the prevalence of GDM ranged considerably from 5.9% using the American Diabetes Association (ADA) criteria to 24.3% using the World Health Organization (WHO) criteria (T. S. Tran, Hirst, Do, Morris, & Jeffery, 2013). The study also found that women with GDM tended to deliver preterm and their newborns had a higher incidence of neonatal hypoglycaemia and labour inductions. The effects of GDM on gestational age, severe birth trauma, maternal and neonatal mortality were not statistically significant. Nevertheless, the associations between maternal lifestyle, dietary habit and GDM were not examined.

1.2 Background of Vietnam and study settings

Vietnam is located Southeast Asia bordering China in the North, Laos and Cambodia in the West, and Eastern Sea in the East. It has diverse geography that three-fourths of the area is mountains and hills, and two main deltas are the Red River Delta in the North and the Mekong River Delta in the South (Ministry of Foreign and Affairs., 2017). The country is divided into six administrative zones including the Red River Delta, the Northern midlands and mountain areas, the North Central and Central coastal areas, the Central Highlands, the South East, and the Mekong River Delta. Vietnam has 63 provinces and 713 districts and equivalents such as cities under provinces, urban districts, towns or rural districts. These districts are further divided into 11,162 wards, town districts, or communes for administrative purposes. Majority of population lives in rural areas with 65.5% and 34.5% of population lives in urban areas (General Statistics Office., 2016). The 2016 Human Development Report

showed that the Human Development Index of Vietnam was 0.683 and it ranked 115th in the world (United Nations Development Programme., 2016).

The population of Vietnam in 2016 was approximately 92.7 million. The sex ratio between males and females was 0.973 (General Statistics Office., 2016). The country has 54 ethnic groups in which the Kinh is a predominant group with over 86% of the Vietnamese people. They mainly live in the low lands and deltas while the remaining ethnic groups are scattered over mountainous areas and the midlands. Over 70% of the population follows the religion of Buddhism, Taoism and Confucianism due to the impact of feudal ideology (Ministry of Foreign and Affairs., 2017). In 2009, the literacy rate of the population aged 15 and older was 93.5%. This rate was slightly higher in males than females (95.8% versus 91.4%) and in urban than rural areas (97.0% versus 92%) (General Statistics Office., 2011).

Despite a lower-middle income country, Vietnam has achieved almost all of Millennium Development Goals (MDGs) and targets (Socialist Republic of Viet Nam., 2015). For the Goal 1, Vietnam has eradicated extreme poverty and hunger. The country has also succeeded in universalising primary education with the enrolment rate of 99.0% in 2014 (Goal 2). Vietnam has attained the MDG 3 target on gender equality and female empowerment. During the period from 1990 to 2014, the infant mortality rate and under five mortality rate dropped two and 2.5 times, respectively. These have made the targets of MDG 4 on track. In addition, maternal health (MDG 5) has been significantly improved by reducing the maternal mortality ratio and improving women's reproductive health. Furthermore, malaria and tuberculosis have been controlled successfully while the spread of HIV/AIDS has been managed and is towards halting. The average life expectancy at birth for whole country was 73.4 years, and females live longer than males (76.1 versus 70.8 years) (General Statistics Office., 2016). In summary, the health care of Vietnam has been implemented successfully although numerous difficulties and challenges still persist.

This study was conducted in Ha Noi, Hai Phong and Ho Chi Minh cities of Vietnam. Ha Noi is the capital located in the North region with an area of around 3.4 thousand km^2 and 7.3 million people. Ho Chi Minh City is the most populated and industrialised city of Vietnam located in the South with approximately 8.3 million. Hai Phong is a coastal city located in the North. It is the third largest city in Vietnam in terms of urban population with nearly 2 million people (General Statistics Office., 2016).

1.3 Study design

A hospital-based prospective cohort study was undertaken in Ha Noi, Hai Phong, and Ho Chi Minh cities during August 2015 and December 2016. Data were collected from face-to-face interviews and medical records by trained female enumerators. Questionnaires used in the study have been validated and standardised for the Vietnamese population. These included demographics, food frequency, physical activity, smoking and drinking, anthropometrics, and blood glucose test. GDM was diagnosed according to international diagnostic criteria which have been widely accepted such as the WHO 2013 (World Health Organization., 2013) and International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria (International Association of Diabetes and Pregnancy Study Groups Consensus Panel. et al., 2010).

1.4 Aims and objectives

1.4.1 Aims of the Study

The aims of this study were to evaluate GDM prevalence and determine modifiable maternal risk factors for pregnancy outcomes in Vietnam. The scope of this thesis focused on the period from first trimester until delivery.

1.4.2 Objectives of the study

The specific objectives of this study were:

1. To undertake a systematic review and meta-analysis of GDM prevalence in Eastern and Southeastern Asia including Vietnam.
2. To conduct a cohort study in Vietnamese women with the following objectives:
    2.1. To investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index (BMI).
    2.2. To evaluate the prevalence of gestational diabetes mellitus and adverse pregnancy outcomes (e.g. stillbirth, preterm delivery, low birthweight, macrosomia, caesarean section).
    2.3. To ascertain the association between physical activity during pregnancy and gestational diabetes mellitus.
    2.4. To examine the relationship between gestational diabetes mellitus and pregnancy outcomes.

1.5 Significance of the study

Information on the association between maternal lifestyle, nutrition and maternal and child health is limited in Vietnam, especially in view of the dynamic nature of lifestyle, changing food habits and their interactions with demographic and socio-economic factors in a developing country such as Vietnam. This study presents the first comprehensive investigation of the topic in Vietnam. It provides the estimates of GDM and adverse pregnancy outcomes. This study also reports the relationship between maternal factors (e.g. pre-pregnancy BMI, dietary intake, physical activity, cigarette smoking, alcohol drinking) and GDM or adverse pregnancy outcomes (e.g. stillbirth, preterm delivery, low birthweight, macrosomia, caesarean section). The findings of this study will contribute to the development of health promotion guidelines and lifestyle intervention programs to enhance maternal and child health in Vietnam. The research is well aligned with the current strategic priority of the Vietnam Ministry of Health.

1.6 Outline of the thesis

This thesis consists of five chapters as follows:

Chapter one provides general background on GDM and an overview of the study location. It also describes the aims and objectives of the study as well includes the significance of the study.

Chapter two presents a summary of the literature review. It shows an up-to-date situation of GDM in the world, Asia, and Vietnam. It also describes previous findings on risk and protective factors of GDM such as habitual diet, physical activity, smoking and drinking. Consequences of GDM for the mother and child are also discussed.

Chapter three describes the methodology used in this cohort study. It includes brief information about study design, study settings, participants and sample size calculation, the procedures and instruments of data collection, statistical analysis, and ethical consideration.

Chapter four includes the results and discussion. It is presented in a mixture of descriptive findings and published papers. The results are organised according to the objectives of the study.

Chapter five briefly summaries the main findings of the thesis and gives some recommendations drawn from the study.

Ethics approval letters, information sheet, consent form, questionnaires, and other relevant documents are enclosed in the Appendices.

Chapter 2. LITERATURE REVIEW

2.1 Overview

This chapter describes a critical review of the literature on primary issues of gestational diabetes mellitus. The review begins with the definitions and historical background of GDM. Section three will briefly summarise an up-to-date status of GDM in the world, Asia, and Vietnam. Section four describes the current understanding about the pathophysiology of GDM. Risk and protective factors of GDM are showed in section five, with an extensive focus on main factors such as maternal age, ethnicity, pre-pregnancy BMI and gestational weight gain (GWG) during pregnancy, family history of diabetes, previous GDM, dietary habit, and physical activity. Section six will provide information on consequences of GDM for both mothers and their offspring, whereas screening approaches and diagnostic criteria for GDM will be updated in section 7. Section 8 and 9 will present the treatment and management of GDM.

2.2 Gestational Diabetes Mellitus

2.2.1 Definitions

GDM is a type of diabetes that occurs during pregnancy. For many years, it has traditionally been defined as any glucose intolerance with first diagnosis during pregnancy (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997). However, this definition has a limitation because the glucose intolerance may have predated or begun concomitantly with the pregnancy. In addition, more women of reproductive age and pregnancy with type 2 diabetes have not been identified due to the ongoing epidemic of obesity and diabetes. Pregnant women who are diagnosed with diabetes in the first trimester would be classified as having pre-existing pregestational diabetes including type 2 diabetes (mainly), type 1 diabetes, or monogenic diabetes (rarely).

The most recent definition proposed by the American Diabetes Association is that GDM is diabetes diagnosed in the second or third trimester of pregnancy (American Diabetes Association, 2018). This definition avoids including pre-existing diabetes as cases of gestational diabetes. This definition is awaiting international acceptance.

The Vietnam Ministry of Health issued the first national guidelines on prevention and control of GDM in August 2018 (Vietnam Ministry of Health., 2018). According to the guidelines, GDM is defined according to the recommendations of the WHO 2013 (World Health Organization., 2013). Specifically, GDM has lower levels of blood glucose than diabetes in pregnancy (overt diabetes).

2.2.2 Historical background of gestational diabetes mellitus

Diabetes mellitus was first described in the Egyptian Ebers papyrus approximately 1500 BC. However, diabetes in pregnancy was first described in 1824 in Germany when Bennewitz recorded a mother with several foetal macrosomia and stillbirth (Bennewitz, 1824). In 1882, a study of Duncan found that the proportions of maternal mortality and perinatal mortality from 16 mothers with diabetes in pregnancy were 60% and 47%, respectively. He took several conclusions and one of them was that diabetes may develop during pregnancy (Duncan, 1882). In 1909, Williams' study showed that most pregnant women had diabetes before the conception and few of them developed diabetes after conception (J. A. Williams, 1909). The classification of diabetes and pregnancy called "White's Classification" was proposed by White in 1949 (White, 1949). In the 1950s, some studies identified risk factors for the development of abnormal carbohydrate metabolism in pregnancy and the term "gestational diabetes mellitus" was introduced (Carrington, Shuman, & Reardon, 1957; Jackson, 1953; Moss & Mulholland, 1951; Wilkerson & Remein, 1957). In 1954, the association between increased obstetrical risk and GDM was first described by Hoet (Hoet & Lukens, 1954). In 1979, the First International Workshop on GDM was held in Chicago and GDM was defined as "carbohydrate intolerance of variable severity recognized for the first time in pregnancy" ("American Diabetes Association Workshop-Conference on gestational diabetes: summary and recommendations,"

1980). Another four workshops were organised in the same place in 1984, 1990, 1997, and 2005 (Metzger, 1991; Metzger et al., 2007; Metzger & Coustan, 1998; "Proceedings of the Second International Workshop-Conference on Gestational Diabetes Mellitus. October 25-27, 1984, Chicago, Illinois," 1985).

2.2.3 Morbidity of gestational diabetes mellitus

2.2.3.1 Current status and trend in gestational diabetes mellitus worldwide

The exact global prevalence of GDM is unknown due to a lack of systematically synthesised data together with unavailable data from many countries (Zhu & Zhang, 2016). However, the prevalence of GDM has been increasing in parallel with a pandemic of type 2 diabetes as a consequence of obesity, overeating, sedentary behaviour and urbanisation (Hunt & Schuller, 2007; Zhu & Zhang, 2016). In 2013, the International Diabetes Federation (IDF) estimated high blood glucose in pregnancy worldwide for the first time with an estimation of approximately 17.9 million live births affected by GDM (International Diabetes Federation., 2013). This number increased to around 18.4 million in 2017 (Cho et al., 2018). Of them, the vast majority of cases came from low- and middle-income countries where maternal care services were limited to access. Results of a recent review paper in Eastern and Southeastern Asia also indicated that lower- and upper-middle income countries had much higher GDM prevalence than high-income countries (C. L. Nguyen, Pham, Binns, Duong, & Lee, 2018).

The prevalence of GDM varies significantly across regions in the world. The highest prevalence of GDM was found in Middle East and North Africa with a median proportion of 12.9%, followed by Western Pacific, Southeast Asia, and South and Central America with median estimates of 11.7%, 11.7%, and 11.2%, respectively. Africa and North America and Caribbean had a comparable median prevalence of GDM (8.9% and 7.0%, respectively), while the lowest prevalence was observed in Europe with a median estimate of 5.8% (Zhu & Zhang, 2016). These findings were relatively consistent with the results of review articles in Africa, Asia, and Europe (Eades, Cameron, & Evans, 2017; J.E. Hirst et al., 2012; Macaulay, Dunger, & Norris,

2014). In Africa, two review papers reported the prevalence of GDM was as high as approximately 14% (Macaulay et al., 2014; Mwanri, Kinabo, Ramaiya, & Feskens, 2015). In Asia, GDM prevalence ranged substantially from 0.6% to 17.8% (J.E. Hirst et al., 2012) and the overall prevalence of GDM in Eastern and Southeastern Asia was around 10% (C. L. Nguyen et al., 2018). In Europe, a review of 40 studies found that the overall prevalence of GDM was 5.4% (range 3.8% - 7.8%) (Eades et al., 2017).

The prevalence of GDM is substantial heterogeneity between countries even in a region. For example, the prevalence of GDM in Japan was 6.1% while this prevalence in Singapore was 18.9% (C. L. Nguyen et al., 2018). Similarly, there was a considerable range of GDM prevalence in Africa, from 0.0% in Tanzania to 13.9% in Nigeria (Mwanri et al., 2015). In Europe, the proportions of GDM in Sweden and Italy were 1.5% and 10%, respectively (Eades et al., 2017). The wide discrepancies in GDM prevalence across countries and regions may be explained by a great variety of screening procedures, diagnostic criteria, and population characteristics. A study in Singapore showed that high-risk screening detected a lower estimate of GDM (9.8%) than universal screening (18.9%) (Chong et al., 2014). The development and adoption of new diagnostic criteria with lower threshold values such as the IADPSG criteria led to an increase in GDM prevalence by several times. A study conducted in Brazilian women indicated that GDM prevalence raised substantially from 2.3% using ADA 2010 to 7.1% using WHO 1999 and 18.0% using the IADPSG criteria (Trujillo et al., 2015). Another hospital-based study in United Arab Emirates showed that the estimates of GDM using the ADA 2004, WHO 1999, and IADPSG criteria were 13.3%, 24.5%, and 45.3%, respectively (Agarwal, Dhatt, & Othman, 2015). In addition, the prevalence of GDM also varies greatly by ethnicity. South and South-East Asian, Pacific Islander, Hispanic, African, and Indigenous Australian women have consistently been found to have a higher risk of developing GDM compared with non-Hispanic white women (Berkowitz, Lapinski, Wein, & Lee, 1992; Dornhorst et al., 1992; Metzger & Coustan, 1998).

2.2.3.2 Prevalence of gestational diabetes mellitus in Eastern and Southeastern Asia

The Eastern and Southeastern Asia Region consists of 18 countries including Vietnam with over 30% of the Asian population (The United Nations., 2017) and accounting for about 80% of the Asian economy (International Monetary Fund., 2017). A large number of studies on GDM have been reported in this subregion, however, no systematic review and estimates of GDM prevalence are available. Therefore, we undertook a systematic review and meta-analysis of GDM prevalence from countries in Eastern and Southeastern Asia (Objective 1 of the thesis). The results of this work have been published on the Journal of Diabetes Research in 2018 as below.

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Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis

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Review Article

Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis

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Aim. To review the prevalence of gestational diabetes mellitus (GDM) in Eastern and Southeastern Asia. *Methods.* We systematically searched for observational studies on GDM prevalence from January 2000 to December 2016. Inclusion criteria were original English papers, with full texts published in peer-reviewed journals. The quality of included studies was evaluated using the guidelines of the National Health and Medical Research Council, Australia. Fixed effects and random effects models were used to estimate the summary prevalence of GDM and the corresponding 95% confidence intervals (CI). *Results.* A total of 4415 papers were screened, and 48 studies with 63 GDM prevalence observations were included in the final review. The pooled prevalence of GDM was 10.1% (95% CI: 6.5%–15.7%), despite substantial variations across nations. The prevalence of GDM in lower- or upper-middle income countries was about 64% higher than in their high-income counterparts. Moreover, the one-step screening method was twice more likely to be used in diagnosing GDM when compared to the two-step screening procedure. *Conclusions.* The prevalence of GDM in Eastern and Southeastern Asia was high and varied among and within countries. There is a need for international uniformity in screening strategies and diagnostic criteria for GDM.

1. Introduction

Gestational diabetes mellitus (GDM), which is defined as diabetes diagnosed in the second and third trimesters of pregnancy [1], has emerged as a global public health concern [2]. It has been associated with short-term and long-term adverse health outcomes for both mothers and their newborns [3]. Women with GDM are known to have decreased quality of life and increased risks of caesarean section, gestational hypertension, preeclampsia, and type 2 diabetes [4–7]. In babies, GDM has been found to be associated with macrosomia or larger than normal gestational-aged infants, neonatal hypoglycemia, and type 2 diabetes mellitus later in life [6, 8, 9]. As such, it is important to understand the burden of GDM in various parts of the world to provide country-specific information to help inform on policy and planning.

The global prevalence of GDM varies widely, from 1% to 28%, depending on population characteristics (e.g., maternal age, socioeconomic status, race/ethnicity, or body composition), screening methods, and diagnostic criteria [10]. In addition, as with the common form of type 2 diabetes [11], GDM can also be influenced by genetic factors, which may differently affect disease prevalence among populations [12]. To date, at least 8 associations have developed their own diagnostic criteria for GDM, namely, the American Diabetes Association (ADA 2004, 2007, 2010, and 2012), Australian Diabetes in Pregnancy Society (ADIPS), Carpenter-Coustan (CC), International Association of the

Diabetes and Pregnancy Study Groups (IADPSG), International Classification of Diseases (ICD), Japan Society of Obstetrics and Gynecology (JSOG), National Diabetes Data Group (NDDG), and World Health Organization (WHO 1998, 1999, 2006, and 2013) [13, 14]. Data in high-income countries (HICs) ranges from 0.6% to 27.5% [15], and those in low- and middle-income countries are in the range of 0.4 and 24.3% [16]. Regional differences exist regarding the distribution of GDM, such as Africa and Asia, after adjusting the data with prevalence reports being 0%–13.9% and 1.6%–17.8%, respectively [17, 18].

Asia is the largest and most populated continent (60% of the world's population), with an increasing prevalence of GDM [19]. While maternal overweight/obesity is an established risk factor for GDM [20], particularly in HICs, recent reviews have found that the prevalence of GDM may be even higher among lean populations than those with a larger body size [2]. This is consistent with the developmental origins of adult disease hypothesis (DOHAD) as undernutrition in the first 1000 days is associated with later diabetes [21–24]. The Eastern and Southeastern subregions include 18 countries, with more than 30% of the Asian population [25] and contributing approximately 80% to the Asian economy [26]. Given the rapid socioeconomic and nutrition transition and the increasing prevalence of GDM in Asia [19, 27], it is of public health importance to provide an overview of this condition in Eastern and Southeastern Asia. However, accessible and systematically organized estimates of GDM prevalence in this subregion are lacking. Moreover, the lack of uniformity in screening methods, definition, and diagnostic criteria for GDM makes it difficult to compare the prevalence of GDM between and within countries. The aim of this study was to undertake a systematic review and meta-analysis of the prevalence and associated risk factors of GDM in selected countries of Eastern and Southeastern Asia.

2. Methods

The present review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [28] and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) protocols [29].

2.1. Search Strategy. The databases (PubMed, Embase, and Scopus) were used to search relevant articles with the following key words: "gestational diabetes mellitus," "GDM," "hyperglycemia in pregnancy," "gestational hyperglycemia," or "diabetes in pregnancy" as well as "name of country" in Eastern and Southeastern Asia. The websites of the World Health Organization (WHO) and International Diabetes Federation were also reviewed to extend our search results. Then the reference lists of included articles were assessed to identify further relevant studies.

2.2. Inclusion Criteria. Studies that met the following criteria were retrieved for assessment: (1) being conducted in Eastern and Southeastern Asian countries classified by the United Nations Statistics Division [30]; (2) being published in English language journals between January 1, 2000, and December 31, 2016; (3) reported primary results (i.e., original studies); (4) provided the prevalence of GDM and associated 95% confidence interval (CI) or total of participants and number of GDM events; and (5) had a sample size of at least 1000 and 50 GDM cases. When multiple publications were derived from analyses of the same or overlapping samples, we used data from the largest or most recent results only.

2.3. Study Selection. Relevant papers identified from the aforementioned databases and websites were imported into an EndNote X7.5, and duplicates were removed. Two reviewers independently screened the titles and abstracts for potentially eligible articles based on the inclusion criteria. If a paper contained insufficient information on GDM in the title and/or abstract, the full text was retrieved for further assessment and any disagreement between the two reviewers was resolved through discussion. Finally, the full text of relevant studies was reviewed.

2.4. Quality Assessment and Data Extraction. The guidelines of the National Health and Medical Research Council were used to assess the quality of searched articles by two independent investigators [31]. Only articles that meet the level III of evidence were included and analysed in this review. An extraction form was developed in Excel to record data from selected papers by one reviewer, and the completeness and accuracy of extracted data were verified by a second reviewer. The following characteristics were extracted from each study: first author, country, year of publication, year of survey, setting, gestational age, screening procedure (one and/or two steps), sample size, GDM cases, prevalence of GDM (including percentage and 95% CI), and diagnostic criteria for GDM. If 95% CIs were not reported, they were calculated based on the sample size and observed proportion of GDM in each selected study [32]. Since we only collected published studies, ethical approval was not required for this work.

2.5. Data Analysis. Diagnostic criteria were aggregated into 8 clusters due to some similarities: (1) JSOG, (2) NDDG, (3) ADA 2004/ADA 2010, (4) ICD10, (5) ADA 2007/CC, (6) WHO 1998–2006, (7) ADA 2012/IADPSG/WHO 2013; and (8) ADIPS98. The prevalences of GDM, with 95% CI, were grouped according to the different diagnostic criteria to perform meta-analyses. The summary prevalence (95% CI) regardless of and by each diagnostic criteria was calculated using the random effects model of the DerSimonian and Laird method [33] to allow for the possibility of real differences in the distribution of GDM between studies that are not solely resulted from sampling error. The heterogeneity among studies was tested with the I^2 index (low is <25%, moderate 25%–50%, and high > 50%), which describes the percent of total variation contributed by between-study variations [34]. The overall prevalence of GDM (95% CI) by each group of diagnostic criteria was depicted graphically in forest plots. Statistically significant heterogeneity was considered present at $P < 0.1$ and $I^2 > 50\%$ [35]. In addition, subgroup analysis according to lower- or upper-middle income countries (LMICs) or HICs, type of GDM screening, and individual country under study was performed to understand the

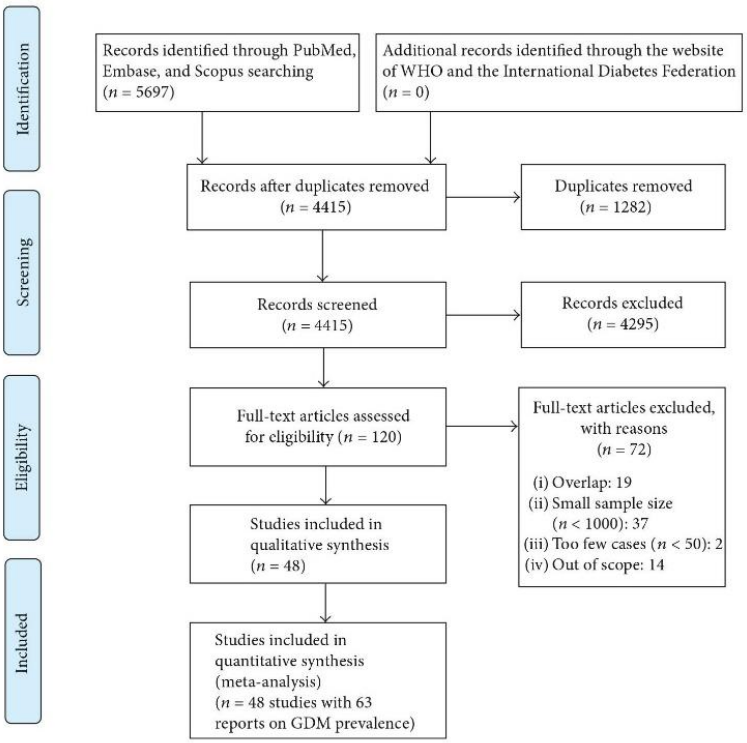

Figure 1: PRISMA flow diagram of selected studies.

impact of economic development and geographical location on the prevalence of GDM. The summary prevalence of GDM for each study that used more than one diagnostic criterion was pooled using a fixed effects model. All analyses were performed using Stata 13.1 (StataCorp LP, College Station, TX).

3. Results

3.1. Description of Included Studies. Figure 1 shows the flow diagram of our systematic literature search. The initial search identified 5697 publications, and after the removal of duplicate records ($n = 1282$), 4415 were retrieved for preliminary assessment. Of these, 120 were potentially relevant after title and abstract screening, and thus, their full texts were obtained and evaluated against the inclusion criteria, resulting in 48 studies reported in 63 observations. No papers were retrieved from the reference list. Of 48 studies, one paper reported four values of GDM prevalence by using four diagnostic criteria [36], 12 papers had two values of GDM prevalence by comparing two different diagnostic criteria or screening types [37–48], and 35 papers only used one diagnostic criterion to estimate GDM prevalence [49–83].

3.2. Characteristics of Included Studies. The main characteristics of the included studies are described in the Supplemental Table (available here). Between the years 2000 and 2016, 48 articles were published with a total sample of 3,594,803 pregnant women (range: 1038–1,824,913) in 7 countries. Of the 48 studies, 21 were conducted in China [41–43, 45, 48–64], 8 in the Republic of Korea [65, 68, 70–72, 74, 75, 77], 6 in Thailand [37, 46, 79–81, 83], five in Japan [39, 47, 73, 76, 78], five in Taiwan (China) [38, 44, 66, 67, 69], one in Malaysia [82], one in Singapore [40], and one in Vietnam [36]. Two-thirds of the studies ($n = 32$) used a two-step screening procedure, that is, women underwent a 1-hour glucose challenge test (GCT) and a 3-hour glucose tolerance test (GTT) if GCT were abnormal. To perform these tests, women were required to drink 50 g of glucose and 75 or 100 g of glucose for GCT and GTT, respectively. Over one-quarter of studies ($n = 13$) followed a single-step screening, where all pregnant women were given a 75 g GTT. Three studies did not specify the screening method used [56, 71, 75]. A total of 20 studies used IADPSG, the 2010 ADA, or the 2013 WHO standards as the GDM diagnostic criteria. The number of studies that employed CC or the 2007 ADA, NDDG, WHO (1998, 1999, and 2006) was 13, 12, and 10, respectively. The remaining 8 studies applied other criteria (see Supplemental

Table 1: Pooled prevalence and 95% confidence interval of gestational diabetes according to the income group, screening type, and country.

	Studies	Subjects	Prevalence	Lower 95% CI	Upper 95% CI	I^2	$P_{\text{heterogeneity}}$
Income level							
High							
JSOG	2	3877	2.80	2.31	3.39	0.00%	0.411
NDDG	4	35,400	4.21	2.15	8.26	99.30%	<0.001
ICD10	1	1,306,281	7.53	7.51	7.56	—	—
ADA 2007/CC	9	1,880,183	7.38	6.03	9.03	98.90%	<0.001
WHO 1999–2006	2	2272	15.37	13.89	17.02	—	—
ADA 2012/IADPSG/WHO 2013	6	16,237	7.48	4.74	11.80	98.60%	<0.001
Subtotal	24	3,244,250	6.66	4.40	10.09	98.30%	<0.001
Lower- or upper-middle							
NDDG	8	79,487	5.83	4.31	7.90	99.10%	<0.001
ADA 2004/ADA 2010	4	28,342	6.59	4.40	9.86	98.50%	<0.001
ADA 2007/CC	4	21,259	11.85	4.94	28.42	99.80%	<0.001
WHO 1999–2006	8	183,545	8.57	5.23	14.06	99.90%	<0.001
ADA 2012/IADPSG/WHO 2013	14	113,656	17.56	15.07	20.47	99.20%	<0.001
ADIPS98	1	2772	20.82	19.34	22.40	—	—
Subtotal	39	429,061	10.84	7.35	15.99	94.40%	<0.001
Type of screening							
One step	13	95,638	15.71	13.88	17.77	98.90%	<0.001
Two-step	32	338,825	7.15	5.63	9.08	99.70%	<0.001
Unspecified	3	3,132,329	7.83	7.39	8.29	99.70%	<0.001
Country							
Mainland China	21	282,086	11.91	8.96	15.83	99.90%	<0.001
Japan	5	12,596	6.08	3.49	10.62	98.70%	<0.001
Korea	8	3,180,515	7.12	6.74	7.53	99.60%	<0.001
Malaysia	1	1538	11.83	10.30	13.60	—	—
Singapore	1	1136	18.93	16.74	21.40	—	—
Taiwan	5	30,944	6.51	4.45	9.54	99.0%	<0.001
Thailand	6	55,205	6.10	4.39	8.48	98.8%	<0.001
Vietnam	1	2772	20.06	19.28	20.87	—	—
All	48	3,566,792	10.07	6.47	15.68	99.3%	<0.001

—: not applicable; ADA: American Diabetes Association; ADIPS: Australian Diabetes in Pregnancy Society; CC: Carpenter-Coustan; IADPSG: International Association of the Diabetes and Pregnancy Study Groups; ICD: International Classification of Diseases; JSOG: Japan Society of Obstetrics and Gynecology; NDDG: National Diabetes Data Group; WHO: World Health Organization.

Table). All studies included in the present review met the level III of evidence of the National Health and Medical Research Council in Australia [31].

3.3. Prevalence of GDM. The overall mean prevalence of GDM, regardless of diagnostic standards, was 10.07 (95% CI: 6.47–15.68) (Table 1). Figure 2 depicts the prevalence of GDM across 8 diagnostic groupings. The highest prevalence of GDM was observed for studies using the IADPSG, ADA 2012, or WHO 2013 criteria (13.77%) while the lowest data was found among Japanese reports that employed JSOG criteria (2.80%). Between that range, the summary prevalence of GDM according to NDDG, ADA 2004 or ADA 2010, ADA 2007 or CC, and WHO (1998, 1999, or 2006) recommendations was 5.24%, 6.59%, 8.54%, and 9.40%, respectively. Only two single data points for GDM prevalence were reported using either ICD 10 [75] or ADIPS 1998 [36], with the respective prevalences being 7.53% and 20.82%, respectively (Table 1). With the exception of studies employing JSOG, there was considerable heterogeneity of GDM prevalence among studies assessed based on various criteria; a measure of heterogeneity varied from 98.5% to 99.8% ($P < 0.001$).

3.4. Prevalence of GDM by Income and Diagnostic Criteria. Overall, the prevalence of GDM was higher in LMICs than HICs, 10.84% versus 6.66%, respectively (Table 1). Except for pooled GDM prevalence according to WHO (1998, 1999, or 2006) criteria, the summary estimates of GDM prevalence based on other diagnostic criteria were greater in LMICs than in HICs. Notably, the prevalence using the most popular criteria, that is, ADA 2012, IADPSG, or WHO 2013, was over twofold higher in the former

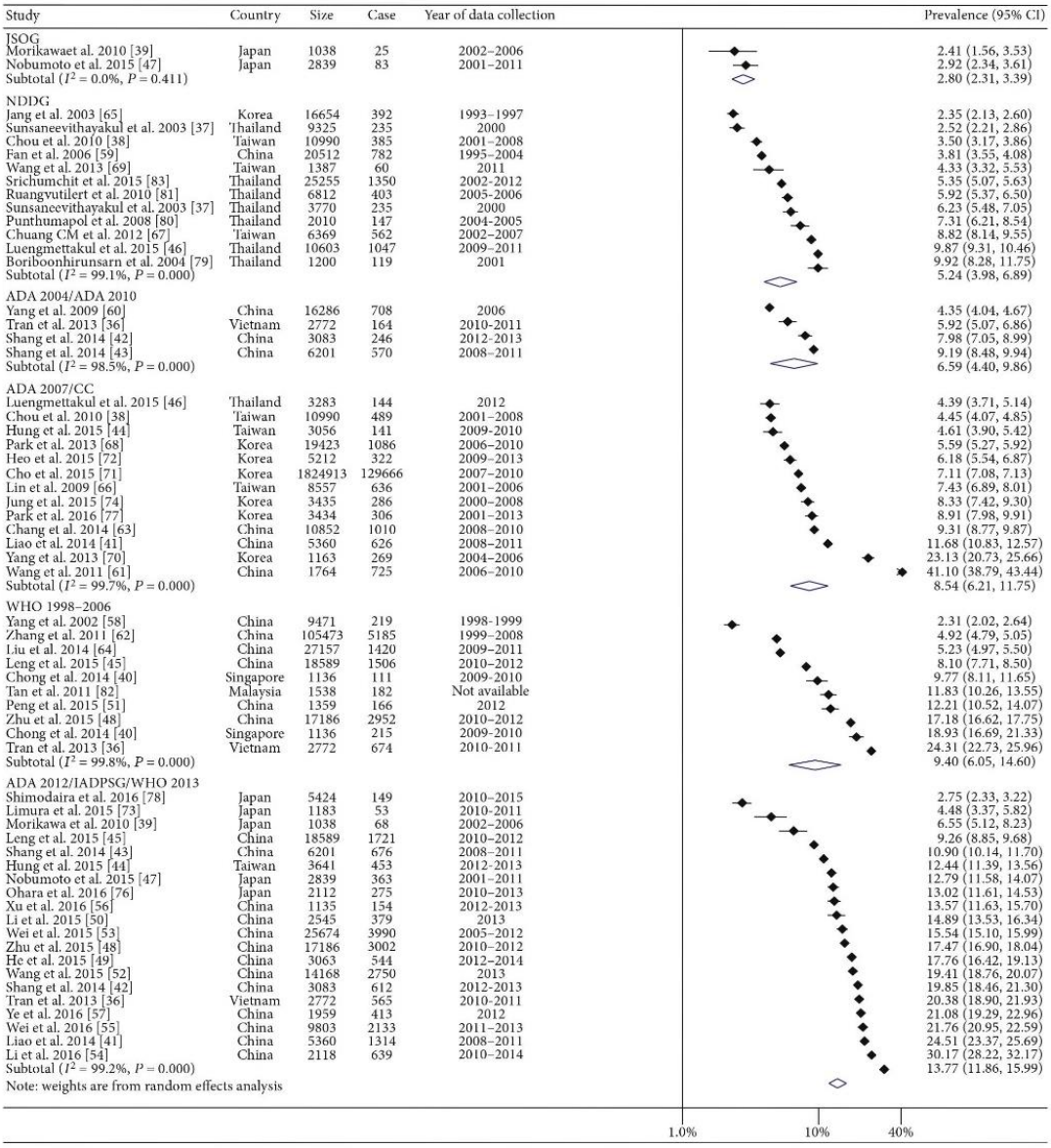

Figure 2: Forest plots presenting the prevalence of gestational diabetes for individual studies and the corresponding pooled prevalence for studies combined according to diagnostic criteria in Eastern and Southeastern Asia. Bars and diamonds indicate 95% confidence interval (CI). The size of each square corresponds to the weight of the study in the meta-analysis using the Der Simonian and Laird method. ADA: American Diabetes Association; CC: Carpenter-Coustan; IADPSG: International Association of the Diabetes and Pregnancy Study Groups; JSOG: Japan Society of Obstetrics and Gynecology; NDDG: National Diabetes Data Group; WHO: World Health Organization.

when compared with the corresponding figure in the latter (17.56% versus 7.48%) (Table 1).

3.5. Prevalence of GDM by Screening Method. The mean prevalence of GDM derived using one-step screening and two-step screening was 15.71% (95% CI: 13.88–17.77%) and 7.15% (95%CI: 5.63–9.08%), respectively; there was substantial heterogeneity among studies using either the one-step screening method or the two-step screening method ($I^2 > 98\%$ and $P < 0.001$) (Table 1).

3.6. Prevalence of GDM by Country. There was variation in the overall prevalence of GDM, with Vietnam and Singapore showing the highest rates (20.06% and 18.93%, resp.). While mainland China and Malaysia had a comparable prevalence of GDM (11.91% and 11.83%), the remaining countries (Japan, Korea, Taiwan, and Thailand) had a GDM prevalence of less than 8.0%. It should be noted that mainland China accounted for nearly 50% of the total studies ($n = 21$) (Table 1).

4. Discussion

The present review included 48 studies with more than three and a half million participants from 7 countries in Eastern and Southeastern Asia, showing a wide variation in the overall prevalence of GDM. The pooled prevalence of GDM was approximately 10%, with a higher estimate in LMICs than in HICs. The discrepancy in the overall estimate also existed according to diagnostic criteria and countries. The most widely used criteria were ADA 2012, IADPSG, or WHO 2013, resulting in a pooled prevalence of GDM of 14% while only a limited number of studies used ADIP 1998, ICD 10, JSOG, ADA 2004, or ADA 2010. The highest prevalence of GDM was found in Vietnam and Singapore, where approximately one in five women were diagnosed with GDM, followed by mainland China and Malaysia where about one in 9 women had GDM. The remaining countries had no more than one in 14 women with GDM. To the best of our knowledge, this is the first study that systematically synthesised data on the prevalence of GDM in important subregions of Asia, Eastern and Southeastern, and provided accessible evidence to formulate locally feasible strategies for effective and efficient prevention of GDM in Asia.

Overall, approximately one in 10 pregnant women in Eastern and Southeastern Asia had GDM. This finding is higher than African countries, where the average prevalence of GDM is about 6.0% [17]. Similarly, our data is greater than results reported in Western countries including Europe, US, and Australia, with the prevalence of GDM being 5.4%, 9.2%, and 5.7%, respectively [84–86]. We have no clear reason for such a discrepancy, but we speculate that it may be due to socioeconomic, racial/ethnic, or lifestyle disparities. For instance, Asian women were reportedly having a higher risk of GDM compared with their Caucasian, African-American, and Hispanic counterparts [87]. This observation suggests that the development of GDM may be shaped by early-life exposure to poor nutrition, that is, under- or overnutrition, and/or epigenetics according to the DOHAD theory [88]. Another factor may be the different screening regimes and testing methods that will be discussed below.

The lack of consensus regarding the use of diagnostic criteria for GDM is largely attributable to the heterogeneity of GDM prevalence. Of diverse diagnostic criteria such as NDDG [89], CC [90], ADA [91], and WHO [92], the IADPSG criteria based on the Hyperglycemia and Adverse Pregnancy Outcome Study (HAPO) has recently become more accepted [93]. Indeed, the use of IADPSG criteria may produce an estimated prevalence of GDM two to threefold even up to 7-fold higher than other criteria [13, 94]. In a Brazilian study, for instance, the prevalence of GDM was only 2.3% and 7.1% according to ADA 2010 and WHO 1999, respectively, but it increased to 18.0% following the IADPSG criteria [94]. An alternative explanation for the variation in GDM prevalence may be ascribed to different screening methods, that is, the one-step or two-step approach. Similar to our review, a recent meta-analysis of 40 studies in Europe reported that the one-step screening method resulted in a higher prevalence of GDM compared with the two-step procedure [86]. Although a one-step screening type is simpler, less laborious, and of low lost, it typically overestimates the prevalence of GDM [95]. However a two-step screening method is more accurate and could accordingly reduce personal and societal costs despite its inconvenience for patients and increased workload for healthcare professionals [96]. Given the lack of international consensus in screening and diagnostic methods for GDM, it is imperative to develop a standardised approach to allow for comparison of GDM burdens worldwide.

The high prevalences of GDM in less wealthy countries reviewed here are consistent with studies from other parts of Asia and Africa [17, 18]. Likewise, around 90% of cases of hyperglycemia during pregnancy occur in low- and middle-income nations as reported by the International Diabetes Federation in 2015 [27]. This discrepancy may be associated with limited access to maternal health care and/or low socioeconomic status in low- and middle-income economies [27, 97, 98]. It is evident from this review that the prevalence of GDM in Vietnam, a lower-middle income country, at least tripled the corresponding data in HICs such as Japan, Taiwan, and South Korea. It can also be speculated that the difference in lifestyle factors (e.g., diet and physical activity), acculturation, and urbanisation may explain the variation in GDM prevalence between the two aforementioned country-income groups [99]. This finding implies that improvement of socioeconomic conditions may contribute to the prevention of GDM.

On the other hand, more epidemiological studies on GDM in the remaining countries of Eastern and Southeastern Asian regions including Mongolia, Indonesia, Philippines, Myanmar, Cambodia, and Laos need to be conducted to add information to the current evidence. These studies should be performed in both urban and rural populations in order to compare and evaluate the effects of urbanisation on GDM in particular and public health in general.

The present review has the advantages of a large sample size with studies involving over three and a half million women, using different methods for screening and diagnosis of GDM and consistency of method, quality, and focus. There are several limitations that need to be considered when interpreting the results of this work. Our review indicated substantial heterogeneity of GDM prevalence across studies, making direct comparison difficult. Such variation may be attributable to the potential influence of screening procedures (i.e., selective or universal) for GDM and its diagnostic criteria, population characteristics, or other socioenvironmental factors. Nonetheless, those possible modifiers were not taken into account in this review due to the lack of data

available from included studies. In addition, the inclusion of only English publications may have resulted in publication bias. Our review did not address GDM situations in other countries in the region including Indonesia, Philippines, Myanmar, Cambodia, and Laos due to the lack of data, and thus, the findings may not be generalisable to the whole Eastern and Southeastern Asia.

5. Conclusion

A large-scale review of literature shows that around one in 10 pregnant women in Eastern and Southeastern Asia had GDM and the number of women with GDM varied substantially between and within countries. The prevalence of GDM was highest according to ADA 2012, IADPSG, or WHO 2013 criteria, greater following a one-step screening procedure and higher in LMICs. The findings suggest the need for developing an international uniformity regarding screening and diagnostic methods for GDM.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Cong Luat Nguyen and Ngoc Minh Pham designed the study and wrote the manuscript. Cong Luat Nguyen systematically searched the literature and extracted data. Ngoc Minh Pham reviewed the included studies and conducted statistical analyses. Colin W. Binns and Andy H. Lee critically commented and substantially revised the manuscript. Dat Van Duong contributed to literature review and discussion. All authors participated in drafting the manuscript and approved the final version.

Supplementary Materials

Supplemental Table: characteristics of selected studies. *(Supplementary Materials)*

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2.2.3.3 Prevalence of gestational diabetes mellitus in Vietnam

2.2.3.3.1 Literature Search

Three strategies were used to identify primary research studies reporting prevalence of GDM among Vietnamese women in Vietnam. First, a literature search was conducted in PubMed for articles published before 31 December 2017. The following search terms and combinations were used: ("gestational diabetes" or "gestational diabetes mellitus" or "diabetes in pregnancy") AND (Vietnam or Vietnamese). Second, we searched a number of commonly medical websites in Vietnam including Vietnam Journal of Preventive Medicine, Vietnam Journal of Public Health, Journal of Practical Medicine, and Ho Chi Minh City Medicine Journal for any publications about GDM prevalence. We used both Vietnamese and English search terms with each website ("dai thao duong thai ky" or "gestational diabetes mellitus") as almost all of articles had their titles and abstracts in both Vietnamese and English. Third, we checked the reference lists and citations of selected articles to identify further relevant studies.

Search results from the database and websites were downloaded into Endnote X7.5 for removing duplicates. The titles and abstracts of all publications were screened based on the following inclusion criteria: (1) being conducted in Vietnam; (2) being published in English or Vietnamese; and (3) providing the prevalence of GDM. The full texts of all papers potentially meeting the inclusion criteria were reviewed and assessed to finalise the studies for review. Data were extracted and summarised from each study using a standardised data extraction form. Confidence intervals were calculated where possible for publications that did not present them. If multiple articles were published from the same population, the most complete and detailed publication was selected. If a paper reported multiple prevalence estimates of GDM according to different diagnostic criteria, all prevalence estimates were included in the review. Data were extracted from each included study regarding title, first author, journal name, year of publication, study period, study design, timing of screening, sample size, number of GDM cases, prevalence of GDM including 95% confidence intervals, and diagnostic criteria.

2.2.3.3.2 Results of Literature Search

231 articles were identified from the database and websites search, and one paper was found through hand-search. After screening and assessing for eligibility, 15 articles which met inclusion criteria were included in the final analysis (Dang & Nguyen, 2011; P. T. H. Le & Ngo, 2014; T. T. Le & Dinh, 2008; T. X. Le, Lam, & Nguyen, 2014; Ngo, 2005; C. T. K. Nguyen, Tran, & Do, 2001; H. T. Nguyen & Ngo, 2012; H. V. Nguyen & Ngo, 2014; N. H. Nguyen & Nguyen, 2010; T. T. Nguyen, 2015; M. T. Pham & Nguyen, 2012; P. K. Pham & Ngo, 2011; To & Ngo, 2009; T. S. Tran et al., 2013; Vu, Nguyen, & Nguyen, 2008) (Figure 1).

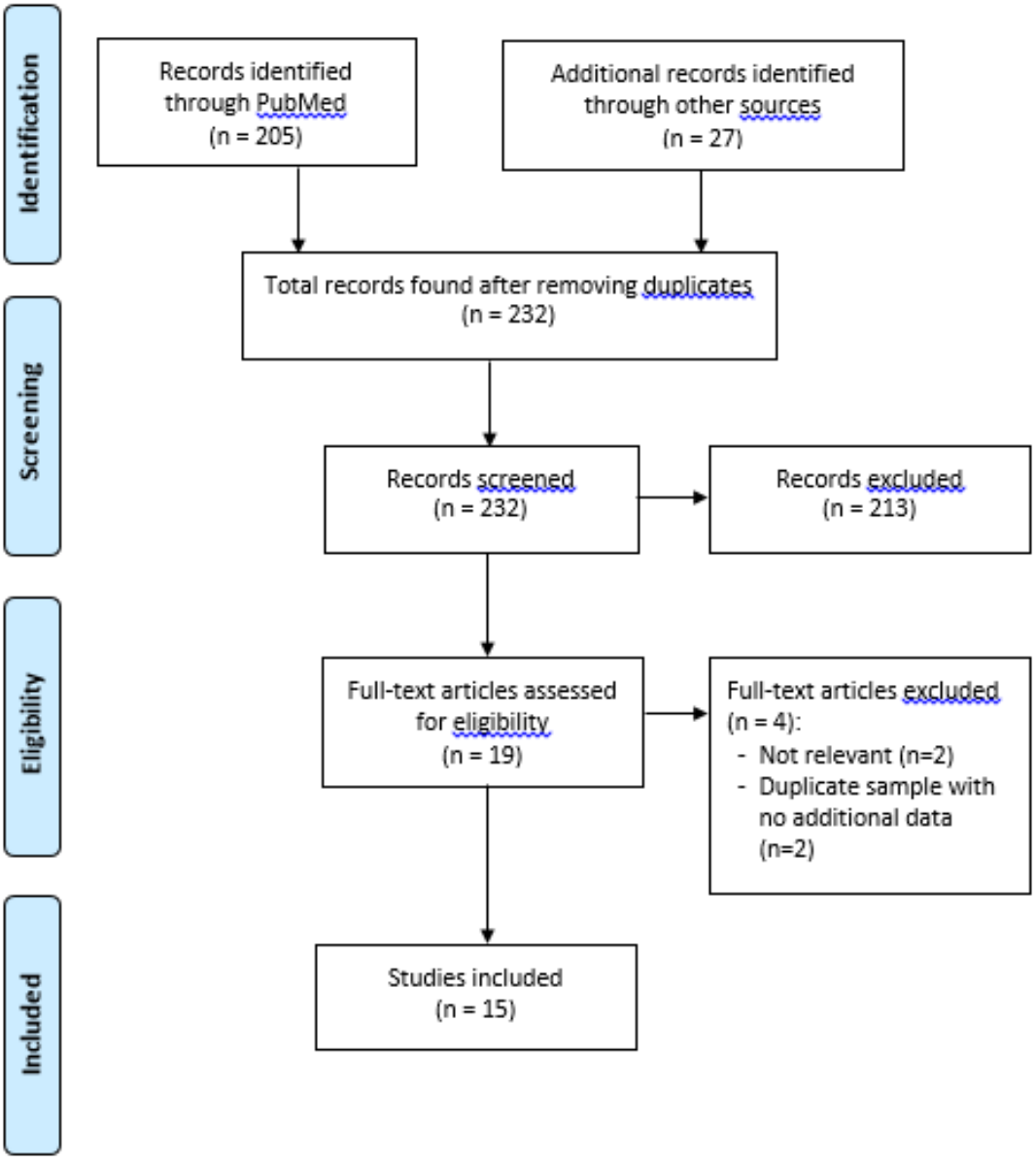

Figure 1. Flow diagram of study selection

The prevalence of GDM in Vietnam ranged significantly, from 3.6% to 30.6% due to various factors (Table 1). The first issue was that different criteria were used to diagnose GDM. The ADA criteria using a 75-g, 2-h oral glucose tolerance test (OGTT) with ≥2 abnormal values were mainly applied, while few papers used other diagnostic criteria. A study by Tran et al. showed that the estimates of GDM using the ADA, IADPSG, Australasian Diabetes in Pregnancy Society (ADIPS), and WHO criteria were 5.9%, 20.4%, 20.8%, and 24.3%, respectively (T. S. Tran et al., 2013). Another matter was small sample size. Several studies just had few participants (Dang & Nguyen, 2011; T. T. Le & Dinh, 2008; C. T. K. Nguyen et al., 2001; N. H. Nguyen & Nguyen, 2010). Screening approach also affected substantially the magnitude of GDM prevalence. A study by Dang et al. in pregnant women with high-risk factors of GDM reported that the prevalence of GDM was 30.6% (Dang & Nguyen, 2011). Therefore, caution is needed in interpreting the estimates of GDM prevalence.

Table 1. Prevalence data for gestational diabetes mellitus in Vietnam

No.	First author	Journal	Year publica-tion	Timing at OGTT (weeks)	Sample size	Prevalence (95% CI)	Diagnostic criteria used
1	Nguyen, C. T. K.	Journal of Practical Medicine	2001	24-28	196	3.6 (1.5-7.2)	NDDG, 100g OGTT (at least 2 criteria): Fasting glucose ≥105 mg/dL, 1h-OGTT ≥190 mg/dL, 2h-OGTT ≥165 mg/dL, 3h-OGTT ≥145 mg/dL
					196	5.6 (2.8-9.8)	Carpenter-Coustan, 100g OGTT (at least 2 criteria): Fasting glucose ≥95 mg/dL, 1h-OGTT ≥180 mg/dL, 2h-OGTT ≥155 mg/dL, 3h-OGTT ≥140 mg/dL
2	Ngo, P. T. K.	Ho Chi Minh City Medicine Journal	2005	24-32	808	4.0 (2.7-5.6)	ADA 2002 (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
3	Vu, N. B.	Vietnam Journal of Medicine and Pharmacy	2008	24-28	415	8.0 (5.5-11.0)	ADA 1998, 75g OGTT (at least 2 criteria): Fasting glucose ≥5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L

No.	First author	Journal	Year publica-tion	Timing at OGTT (weeks)	Sample size	Prevalence (95% CI)	Diagnostic criteria used
4	Le, T. T.	Journal of Practical Medicine	2008	24-28	316	3.2 (1.5-5.7)	Not obvious
5	To, N. T. M.	Ho Chi Minh City Medicine Journal	2009	24-28	720	10.7 (8.5-13.2)	ADA 2002 (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
6	Nguyen, N. H.	Journal of Practical Medicine	2010	24-28	106	9.4 (4.6-16.7)	ADA 1998, 75g OGTT (at least 2 criteria): Fasting glucose ≥5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
7	Dang, N. T. M.	Journal of Practical Medicine	2011	≤ 28	160	30.6 (23.6-38.4)	ADA 1998, 75g OGTT (at least 2 criteria): Fasting glucose ≥5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
8	Pham, P. K.	Ho Chi Minh City Medicine Journal	2011	24-32	761	3.7 (2.5-5.3)	ADA-100g OGTT (at least 2 criteria): Fasting glucose ≥ 95 mg/dL, 1h-OGTT ≥180 mg/dL, 2h-OGTT ≥155 mg/dL; 3h-OGTT ≥140 mg/dL
9	Nguyen, H. T.	Ho Chi Minh City Medicine Journal	2012	24-28	749	4.0 (2.7-5.7)	ADA 2007-75g (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
10	Pham, M. T.	Journal of Practical Medicine	2012	≥24	1707	30.3 (28.2-32.5)	IADPSG 2010 (at least 1 criterion): Fasting glucose ≥5.1 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.5 mmol/L
11	Tran, T. S.	Diabetes Care	2013	24-32	2772	5.9 (5.1-6.9)	ADA 2010 (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
					2772	20.4 (18.9-21.9)	IADPSG 2010 (at least 1 criteria): Fasting glucose ≥ 5.1 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.5 mmol/L
					2772	20.8 (19.3-22.4)	ADIPS 1998 (at least 1 criteria): Fasting glucose ≥ 5.5 mmol/L, 2h-OGTT ≥8.0 mmol/L
					2772	24.3 (22.7-26.0)	WHO 1999 (at least 1 criteria): Fasting glucose ≥ 7.0 mmol/L, 2h-OGTT ≥11.1 mmol/L

No.	First author	Journal	Year publica-tion	Timing at OGTT (weeks)	Sample size	Prevalence (95% CI)	Diagnostic criteria used
12	Nguyen, H. V.	Vietnam Journal of Preventive Medicine	2014	22-32	298	30.2 (25.0-35.8)	ADA 2011 (at least 1 criterion): Fasting glucose ≥5.1 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.5 mmol/L
13	Le, P. T. H.	Ho Chi Minh City Medicine Journal	2014	24-28	443	3.6 (2.1-5.8)	ADA 2010-75g (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
14	Le, T. X.	Ho Chi Minh City Medicine Journal	2014	3rd trimester	1123	10.2 (8.5-12.1)	ADA 2010-75g (at least 2 criteria): Fasting glucose ≥ 5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L
					1123	26.2 (23.6-28.9)	ADA 2011 (at least 1 criterion): Fasting glucose ≥5.1 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.5 mmol/L
15	Nguyen, T. T.	Vietnam Journal of Preventive Medicine	2015	24-28	846	3.9 (2.7-5.4)	ADA 1998, 75g OGTT (at least 2 criteria): Fasting glucose ≥5.3 mmol/L, 1h-OGTT ≥10.0 mmol/L, 2h-OGTT ≥8.6 mmol/L

ADA: American Diabetes Association; ADIPS: Australasia Diabetes in Pregnancy Society; CI: Confidence interval; IADPSG: International Association of Diabetes and Pregnancy Study Groups; OGTT: Oral glucose tolerance test; NDDG: National Diabetes Data Group; WHO: World Health Organization

2.2.4 Pathophysiology of gestational diabetes mellitus

As with the pathogenesis of type 2 diabetes, GDM is characterised by insulin resistance and impaired insulin secretion, and has been associated with environmental factors such as overweight and obesity, poor diet, and physical inactivity (Kohei, 2010; Mirghani Dirar & Doupis, 2017), and hereditary components (Kiani, Naz, Sayehmiri, Sayehmiri, & Zali, 2017; Moosazadeh et al., 2017). Insulin, which is a 51-amino acid polypeptide hormone, is secreted by β-cells of pancreas (Brange & Langkjoer, 1993). During pregnancy, the secretion of insulin in a healthy women increases two to fourfold to maintain normal glucose levels (Catalano, Huston, Amini, & Kalhan, 1999). The status of insulin during pregnancy is affected by multiple factors such as β-cell dysfunction and insulin resistance which act together to cause GDM.

2.2.4.1 β-cell dysfunction

The main function of β-cells is to store and secrete insulin which has effects on blood glucose concentration. β-cell dysfunction is defined when β-cells release insufficient insulin or lose the ability to adequately sense blood glucose concentration. β-cell dysfunction is related GDM and is exacerbated by insulin resistance (Kaaja & Ronnemaa, 2008). Compared with non GDM women, women with GDM reduced 67% of pancreatic β-cell function (Xiang et al., 1999). This dysfunction may be due to an autoimmune process (Singh & Rastogi, 2008) or a genetic defect (Moleda, Fronczyk, Safranow, & Majkowska, 2015).

2.2.4.2 Insulin resistance

Adipocytokines, which are produced by the adipose tissue, include pro- and anti-inflammatory mediators such as adiponectin, leptin, resistin, visfatin, tumour necrosis factor-α (TNF-α), interleukin-6. During pregnancy, these factors can affect glucose tolerance by adjusting the secretion and receptor signalling of insulin. This may cause the development of insulin resistance (Abell, De Courten, Boyle, & Teede, 2015). Particularly, a decreased level of adiponectin is associated with the risk of GDM (M. A. Williams et al., 2004) due to the reduction in insulin sensitivity and anti-inflammatory capability (Bao et al., 2015). In contrast, increased levels of TNF-α are associated with insulin resistance (Hotamisligil et al., 1996; Kirwan, Krishnan, Weaver, Del Aguila, & Evans, 2001). TNF-α appears to interfere with insulin receptor signalling and β-cell function that have effects on hyperglycaemia (Abell et al., 2015; Briana & Malamitsi-Puchner, 2009). Interleukin-6, which is an inflammatory marker, involves in the regulation of glucose homeostasis and metabolism through effects on skeletal muscle cells, adipocytes, hepatocytes, and pancreatic β-cells (Kristiansen & Mandrup-Poulsen, 2005). High interleukin-6 secretion during pregnancy might aggravate insulin resistance and take part in the pathogenesis of GDM (Richardson & Carpenter, 2007). Leptin has an effect on the regulation of whole blood glucose homeostasis (Al-Daghri, Bartlett, Jones, & Kumar, 2002; Ceddia, Koistinen, Zierath, & Sweeney, 2002). Patients with GDM had higher levels of leptin compared with normal glycaemic pregnant women (Ategbo et al., 2006; D. Chen, Xia, Xu, & Dong, 2010; Qiu, Williams, Vadachkoria, Frederick, & Luthy, 2004; J. Xu et al., 2014).

Adipocyte Fatty Acid-Binding Protein, which is a member of fatty acid-binding protein multigene family, has been found to be associated with GDM risk (Kralisch et al., 2009; Y. Y. Li, Xiao, Li, Huangfu, & Mao, 2015; Y. Zhang et al., 2016). Similarly, two recent systematic review and meta-analysis studies showed that pregnant women with GDM had increased circulating retinol-binding protein-4 concentrations compared with normal controls (Hu, Liu, Huang, & Tan, 2016; Huang et al., 2015). Resistin, a 114-amino acid polypeptide hormone, may play a critical role in regulating insulin sensitivity (Kusminski, McTernan, & Kumar, 2005; Steppan et al., 2001). Some studies found that resistin was significantly increased in women with GDM compared with normal counterparts (Briana & Malamitsi-Puchner, 2009; D. Chen et al., 2007; Kuzmicki et al., 2009) while other studies showed no difference (Lappas, Yee, Permezel, & Rice, 2005; L. P. Lowe et al., 2010). Visfatin is known to have a critical role in glucose homeostatis by exerting hypoglycaemic effect through enhancing glucose utilisation in peripheral tissues and decreasing glucose release from liver cells (Hong et al., 2007). It has been demonstrated that visfatin levels were elevated in pregnant women with GDM compared with healthy controls (Ferreira, Rezende, Vaikousi, Akolekar, & Nicolaides, 2011; Gok et al., 2011; Krzyzanowska et al., 2006).

Endothelial function and angiogenic growth factors have been shown to be altered in women with GDM (Mordwinkin et al., 2013; Savvidou et al., 2010). Compared with healthy counterparts, pregnant women with GDM had increased endothelial nitric oxide synthase expression, increased concentrations of soluble adhesion molecules, decreased superoxide dismutase expression, and decreased total endothelial progenitor cells (Mordwinkin et al., 2013). These alterations were observed in foetuses of mothers with GDM which may be associated with an elevated risk of T2DM and cardiovascular diseases (CVD) postpartum (Mordwinkin et al., 2013). Savvidou et al. reported that GDM women had a significantly increased level of tissue plasminogen activator reflecting endothelial activation (Savvidou et al., 2010).

Pregnancy itself is characterised by progressive insulin resistance and altered inflammation compared with non-pregnant women. Excessive inflammation has been

linked with a number of adverse perinatal outcomes including GDM (Christian & Porter, 2014). Obesity is recognised as a case of chronic inflammation in which inflammatory markers including pro-inflammatory cytokines are excessively secreted. These markers affect post-receptor insulin signalling leading to elevated insulin resistance (Shoelson, Herrero, & Naaz, 2007). Inflammatory cytokines have been found to be elevated in overweight and obese pregnant women (Christian & Porter, 2014; Friis et al., 2013; Retnakaran et al., 2003).

The increasing levels of pregnancy-associated hormones such as estrogen, progesterone, cortisol, and human placental lactogen have a vital role in the insulin resistance and the decrease in insulin sensitivity during pregnancy (Ahmed & Shalayel, 1999; Barbour et al., 2002; Hornnes, 1985; Polderman, Gooren, Asscheman, Bakker, & Heine, 1994; Ryan & Enns, 1988). Estrogen and progesterone are the critical hormones that affect β-cell function in early pregnancy and insulin resistance especially in late pregnancy (Polderman et al., 1994; Ryan & Enns, 1988). An increment of cortisol concentration during pregnancy plays a main hormone that results in the reduction of glucose tolerance in normal pregnancy (Ahmed & Shalayel, 1999; Hornnes, 1985). Human placental lactogen, a single polypeptide chain held together by disulphide bonds, has a metabolic role in mobilising lipids and free fatty acids. It has been acting as a main contributory factor in human insulin resistance (Handwerger & Freemark, 2000).

2.2.5 Risk and protective factors of gestational diabetes mellitus

2.2.5.1 Non-modifiable factors

2.2.5.1.1 Age

Maternal age is an established risk factor for gestational diabetes mellitus. A large number of studies have demonstrated that advanced maternal age is associated with an increased risk of GDM (Cypryk et al., 2008; Di Cianni et al., 2003; Keshavarz et al., 2005; Lao, Ho, Chan, & Leung, 2006; Lean, Derricott, Jones, & Heazell, 2017; Wagaarachchi, Fernando, Premachadra, & Fernando, 2001). Maternal age ≥25 years

is considered to increase risk of GDM and was suggested to use as the cut-off for GDM screening by the ADA (American Diabetes Association., 2004). More advanced maternal age more risk of GDM is and maternal age of ≥35 years is considered as high risk of GDM development (Wagaarachchi et al., 2001). Lao et al found that GDM risk rose significantly from 2.59 at 25-29 years to 10.85 at 35-39 years. It even rosed up to 15.90 at the age group of ≥40 years (Lao et al., 2006). In addition, advanced maternal age has been linked with adverse pregnancy outcomes. A recent review and meta-analysis of 74 observational studies showed that advanced maternal age increased the risks of stillbirth, foetal growth restriction, neonatal death, and neonatal intensive care unit admissions (Lean et al., 2017). Studies in Vietnam also found that advanced maternal age was positively associated with an increased risk of GDM (H. T. Nguyen & Ngo, 2012; N. H. Nguyen & Nguyen, 2010; T. T. Nguyen, 2015; To & Ngo, 2009). For instance, Nguyen et al. reported that women aged ≥25 years had approximately 10 times increased risk of GDM compared with those <25 years (N. H. Nguyen & Nguyen, 2010). Similarly, To et al. found that women aged ≥25 years had much higher prevalence of GDM than their counterparts <25 years (94.8% versus 5.2%) (To & Ngo, 2009).

2.2.5.1.2 Ethnicity

Ethnicity has been recognised as a risk factor for GDM development (Yue et al., 1996). Overall, women from South or East Asia, Pacific Islands, Indigenous Australians, Hispanic, African, and Native American are at high-risk groups for GDM (Berkowitz et al., 1992; Dornhorst et al., 1992; Kjos & Buchanan, 1999; Metzger & Coustan, 1998). Pu et al conducted a study of over 24,000 pregnant women with nine racial/ethnic groups in the United States. He found that the prevalence of GDM was significantly higher among Asian subgroups such as Asian Indian (19.3%), Filipino (19.0%), Chinese (15.3%) and among Hispanics (13.3%) compared with non-Hispanic whites (7.0%) (Pu et al., 2015). This similar trend was reported in the other studies (Bardenheier et al., 2015; Chang, Hurwitz, Miyamura, Kaneshiro, & Sentell, 2015; S. Y. Kim et al., 2013; McDonald, Karahalios, Le, & Said, 2015; Tsai, Roberson, & Dye, 2013; Wong, Lin, & Russell, 2017; Yeung et al., 2017). In Australia, a review and meta-analysis of 25 studies on GDM prevalence among Indigenous women showed

that Indigenous women had higher risk of GDM compared with non-Indigenous women (Chamberlain et al., 2015).

There is a great variation in GDM prevalence among ethnic groups between countries in one region. Among Asian women, South-Asian women (Indian, Sri Lankan, Pakistani, and Bangladeshi) tend to have higher prevalence of GDM than South-East Asian women (Filipino, Thai, Malaysian, Cambodian, Laotian, and Vietnamese) and East-Asian women (Chinese, Taiwanese, South Korean, and Japanese) (Pu et al., 2015; Savitz, Janevic, Engel, Kaufman, & Herring, 2008). Women from South Asia seem to have the highest risk of GDM (Pu et al., 2015; Savitz et al., 2008). These results are likely to be affected by genetics (Mirghani Dirar & Doupis, 2017; Yuen, Wong, & Simmons, 2018). Interestingly, foreign-born pregnant women had a higher risk of developing GDM compared with women of that ethnicity but were born in western countries (S. Y. Kim et al., 2013; Savitz et al., 2008). This could be partly explained by the effects of socioeconomic status, lifestyle, and acculturation.

Vietnamese women are known to have high risk of developing GDM. Pu et al. reported that the prevalence of GDM in Vietnamese women living in the United States was 18.8% while these proportions in Chinese, Hispanic, Korean, Japanese, and non-Hispanic white women were 15.3%, 13.3%, 12.9%, 9.7%, and 7.0%, respectively (Pu et al., 2015). Another study in Australia also indicated that Vietnam-born mothers had the higher risk of GDM compared with Australian-born mothers (Henry, Beischer, Sheedy, & Walstab, 1993).

2.2.5.1.3 Family history of diabetes and genetic factors

A family history of diabetes is considered as one of the strongest risk factors for GDM development (Bhat et al., 2010; Hossein-Nezhad, Maghbooli, Vassigh, & Larijani, 2007; Kautzky-Willer et al., 2008; Shirazian et al., 2009). Yang at al. reported that women with a family history of diabetes had about twofold greater risk of GDM than in women without (H. Yang et al., 2009). Similarly, Cianni et al. found that the

prevalence of GDM in women with and without a history of diabetes was 14.5% and 7.3%, respectively (Di Cianni et al., 2003). Erem et al. demonstrated that Turkish women with a history of diabetes had 4.5 times increased risk of GDM compared with those without (Erem, Kuzu, Deger, & Can, 2015). Three recent review studies also highlighted that a family history of diabetes was linked to an elevated risk for GDM development (Farahvar et al., 2018; Kiani et al., 2017; Moosazadeh et al., 2017). A study by Hirst et al. among Vietnamese pregnant women found a high prevalence of GDM in the group with a family history of diabetes (J. E. Hirst, Tran, Do, Morris, & Jeffery, 2012).

The magnitude of GDM risk in women with a family history of diabetes varies with the degree of relationship. Williams et al. found that the odds of GDM were increased twofold by maternal diabetes history only, 2.3-fold by parental diabetes history only, 3.8-fold by both maternal and paternal diabetes history, and 8.4-fold by sibling diabetes history (M. A. Williams, Qiu, Dempsey, & Luthy, 2003). Similarly, Rhee et al. conducted a study in Korean women and reported that the risk of developing GDM in women with diabetes history of parent only, sibling only, and parental and sibling together was 1.80, 5.21, and 6.51 compared with those without, respectively (Rhee, Kim, Woo, Kim, & Kim, 2010). These results have emphasised the role of genetics in susceptibility toward the development of GDM.

To date, eight genes which associate with GDM development have been identified using genome-wide association analysis. They include CDK5 regulatory subunit associated protein 1 like 1 (CDKAL1), melatonin receptor 1B (MTNR1B), glucokinase (GCK), insulin-like growth factor 2 mRNA binding protein 2 (IGF2BP2), insulin receptor substrate 1 (IRS1), potassium voltage-gated channel subfamily J member 11 (KCNJ11), potassium voltage-gated channel subfamily Q member 1 (KCNQ1), and transcription factor 7 like 2 (TCF7L2) (W. L. Lowe, Jr., Scholtens, Sandler, & Hayes, 2016; Petry et al., 2017; Yuen et al., 2018). Of these, CDKAL1 and MTNR1B had strong association with GDM in studies of Korean, Han Chinese, and Mexican women (Huerta-Chagoya et al., 2015; Kwak et al., 2012; C. Li et al., 2013;

Mei et al., 2015). Various genes, especially TCF7L2, are also known to be associated with the risk of type 2 diabetes (Ali, 2013).

2.2.5.1.4 Previous history of gestational diabetes mellitus

Previous GDM increases the likelihood of recurrence of this disease in future pregnancies. Teh et al. conducted a study of nearly 2900 Australian women and indicated that previous history of GDM was the strongest independent risk factor for developing GDM with an odds ratio of 10.7 (Teh et al., 2011). Cheung et al. examined over 2000 Asian women in Australia and found that a history of GDM was a significant risk factor of GDM with an odds ratio of 14.5 for the whole group (Cheung, Wasmer, & Al-Ali, 2001). Hirst et al. reported that Vietnamese pregnant women who had previous GDM were at increased risk for developing GDM (J. E. Hirst et al., 2012). Similarly, a large number of epidemiological studies have been consistently reported history of previous GDM as one of independent predictors of developing GDM (Aydin et al., 2018; Ben-Haroush, Yogev, & Hod, 2004; McGuire, Rauh, Mueller, & Hickock, 1996; Shahbazian et al., 2016).

2.2.5.1.5 Macrosomia in previous pregnancy

Previous macrosomia is one of the risk factors for developing GDM in subsequent pregnancies. A study of McGuire et al. in 1996 reported that women with a history of previous macrosomia were at increased risk for the development of GDM (McGuire et al., 1996). Another study conducted by Cheung at al. showed that women who had a macrosomic infant in the prior birth had 2.5 times increased odds for GDM compared to controls (Cheung et al., 2001). This association has been also observed in Vietnamese women (J. E. Hirst et al., 2012).

2.2.5.1.6 Previous history of adverse pregnancy outcomes

Previous history of adverse pregnancy outcomes such as abortion, stillbirth, neonatal death, and congenital malformations have been suggested to be associated with the

development of GDM. Aydin et al. conducted a nationwide multicentre prospective study in Turkey and found that history of abortion or foetal anomaly was significantly associated with GDM (Aydin et al., 2018). Chung et al. reported that women who had a previous stillbirth or foetal malformation had higher risk of GDM than their counterparts without (Cheung et al., 2001). Hirst et al. also demonstrated that Vietnamese women with a prior stillbirth were more likely to develop GDM (J. E. Hirst et al., 2012).

2.2.5.1.7 Hypertensive disorders

Hypertensive disorders of pregnancy can be classified into four categories including chronic hypertension, gestational hypertension, preeclampsia, and chronic hypertension with superimposed preeclampsia (National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy., 2000). Gestational hypertension is defined as hypertension that occurs after 20 weeks gestation and returns to normal within 12 weeks postpartum. Preeclampsia is defined as gestational hypertension with proteinuria. Hypertensive disorders of pregnancy complicate approximately 5-10% of pregnancies and 2-8% of pregnant women are affected by preeclampsia (Duley, 2009; Roberts, Algert, Morris, Ford, & Henderson-Smart, 2005; Roberts et al., 2011). Women with hypertensive disorders, especially preeclampsia, are at increased risk of developing GDM (Ben-Haroush et al., 2004; C. Zhang & Ning, 2011). Lee et al. found that women with preeclampsia in the first pregnancy had 1.2 times increased odds for GDM in the second pregnancy (95% CI, 1.1-1.3) compared to their counterparts without a previous history of preeclampsia (J. Lee et al., 2017). Cheung at al. reported that the risk of GDM was 3.4 times higher in women with previous pregnancy induced hypertension compared with controls (Cheung et al., 2001).

2.2.5.1.8 Polycystic ovarian syndrome

Polycystic ovarian syndrome (PCOS) is a heterogeneous condition characterised by hyperandrogenism, polycystic ovaries, and oligo- or anovulation. It is estimated that

5-10% of women have PCOS (Goodarzi & Azziz, 2006) and 50% of women with PCOS present insulin resistance (Glintborg et al., 2004). Many studies have been conducted comparing pregnancy outcomes in women with PCOS versus controls, of which GDM is the most common complication in pregnant women with PCOS. However, evidence of a link between PCOS and GDM risk is still conflicting (Toulis et al., 2009). In 2006, Boomsma et al. conducted the first meta-analysis of 15 studies with a total of 720 women with PCOS and 4505 controls (Boomsma et al., 2006). She found that GDM risk increased by approximately three times in women with PCOS. In 2011, Kjerulff et al. performed another meta-analysis of 23 studies involving 2544 women with PCOS and 89848 controls (Kjerulff, Sanchez-Ramos, & Duffy, 2011). The study showed that GDM was more than 2.8-fold higher in pregnant women with PCOS, compared with women without PCOS. Similarly, Quin et al. conducted the third meta-analysis of 27 studies including 4982 women with PCOS and 119692 controls (Qin et al., 2013). The author also reported a prevalence of GDM about 2.8 times higher in women with PCOS than in controls. It is noted that these studies did not adjust for BMI or other confounders and based on mainly retrospective or prospective studies with relatively small sample sizes. A recent review conducted by Palm et al. included 30 studies (10 prospective and 20 retrospective studies) with a total of 11263 women with PCOS and 1389161 controls (Palm et al., 2018). These studies showed an inconsistent association between PCOS and GDM. Moreover, the review revealed that the risk of GDM increased in PCOS patients who had higher BMI, higher age, Asian ethnicity, and fertility treatment. The most recent study conducted by Mustaniemi et al. among 1941 Finnish pregnant women reported that PCOS was not an independent risk for developing GDM after adjustment for pre-pregnancy BMI and age. Maternal obesity and advanced age were related to an elevated GDM risk in women with PCOS rather than to PCOS per se (Mustaniemi et al., 2018). Other studies also did not observe an elevated GDM risk in non-obese PCOS patients or when study participants were matched according to age and BMI (Haakova et al., 2003; Han et al., 2011; Turhan, Seckin, Aybar, & Inegol, 2003). Therefore, well-designed research is needed to clarify the association between PCOS and GDM. Meanwhile, pregnant women with PCOS should be early screened for GDM during pregnancy.

2.2.5.1.9 Other non-modifiable risk factors

Other non-modifiable risk factors for developing GDM such as low stature, parity, multiple pregnancy, and glycosuria have been investigated. Short stature was associated with a higher risk of GDM (Anastasiou et al., 1998; Branchtein et al., 2000; Jang, Min, Lee, Cho, & Metzger, 1998; Rudra, Sorensen, Leisenring, Dashow, & Williams, 2007). Women with higher parity had an increase in GDM risk, compared to the first pregnancy or those with only one childbirth (Berkowitz et al., 1992; Cheung et al., 2001; Egeland, Skjaerven, & Irgens, 2000). Multiple pregnancy may also increase the risk of GDM (Schwartz et al., 1999; Sivan et al., 2002). Glycosuria was observed to be prevalent in GDM women (Kiani et al., 2017; Solomon et al., 1997).

2.2.5.2 Modifiable factors

2.2.5.2.1 Body mass index and gestational weight gain during pregnancy

Overweight and obesity are on the rise worldwide with the prevalence of obesity has nearly tripled since 1975 including a large number of women of reproductive age (World Health Organization., 2018a). Being overweight or obese pre-pregnancy is considered as a significant risk factor for developing GDM (Baeten, Bukusi, & Lambe, 2001; Cypryk et al., 2008; Doherty, Magann, Francis, Morrison, & Newnham, 2006; Leung et al., 2008; Torloni et al., 2009). Chu et al. conducted a meta-analysis of 20 studies and found that women with overweight (25≤ BMI <30 kg/m^2), obesity (30≤ BMI <35 kg/m^2), and severe obesity (BMI >35 kg/m^2) had 2.14, 3.56, and 8.56 times increased risk of GDM compared with normal-weight pregnant women, respectively (Chu et al., 2007). Similarly, another meta-analysis of 70 studies conducted by Torloni et al. showed approximately twofold, threefold, and sixfold increases in the risk of GDM among overweight, moderately obese, and severely obese women compared with normal-weight women, respectively (Torloni et al., 2009). A study conducted in Vietnamese pregnant women by Hirst et al. also indicated that increase in BMI results in higher degrees of GDM (J. E. Hirst et al., 2012). In addition, a positive correlation between GDM and increased self-reported weight change from 18 years to just before pregnancy has been demonstrated (Rudra et al., 2007; Solomon et al., 1997). Solomon et al. reported that women who gained 10 kg of weight or more when they were 18

years to pregnancy had a threefold increase in GDM risk (Solomon et al., 1997). Rudra et al. revealed that women with a weight gain of 10.0-19.9 kg between the ages of 18 years to before pregnancy had 2.5 times increased risk of GDM (Rudra et al., 2007). Overweight and obese women are more prone to GDM than their healthy counterparts. This may be due to circulating inflammatory cytokines highly expressed in adipose tissues, while pro-inflammatory cytokines have reportedly been linked to GDM (Law & Zhang, 2017).

It is noted that women from Asia have GDM despite having normal or below range of BMI (M. Hedderson et al., 2012; Henry et al., 1993; Hunsberger, Rosenberg, & Donatelle, 2010; S. Y. Kim et al., 2013). A study conducted by Hunsberger et al. found that both low- and high-BMI Asian women had the greatest risk of GDM compared to women of any other ethnic groups (Hunsberger et al., 2010). Another study of Makgoba et al. also showed that GDM risk was significantly higher in South Asian women regardless of their BMI, compared with normal BMI White Europeans (Makgoba, Savvidou, & Steer, 2012). Asians are known to be at increased risk for developing GDM at a lower BMI than other ethnic groups as this population tend to have more intra-abdominal fat deposition or β-cell dysfunction, which can result in insulin resistance (Pi-Sunyer, 2004). This implies that pregnant Asian women should be screened for GDM regardless of their BMI levels.

Previous studies have demonstrated an association between gestational weight gain during pregnancy and GDM risk (Brunner et al., 2015; M. M. Hedderson, Gunderson, & Ferrara, 2010; Z. Liu, Ao, Yang, & Wang, 2014). Hedderson et al. found that higher GWG in the first trimester was positively correlated with an elevated risk of GDM, particularly in overweight and non-white women (M. M. Hedderson et al., 2010). Another study conducted by Liu et al. among Chinese women showed that high prevalence of GWG, especially early in pregnancy, was significantly associated with an increase in GDM risk (Z. Liu et al., 2014). Brunner et al. conducted a meta-analysis of eight studies and reported that excessive GWG prior to GDM testing increased GDM risk (Brunner et al., 2015). This association is biologically plausible as higher GWG can result in greater maternal fat deposition which might impair insulin

sensitivity (van Raaij, Peek, Vermaat-Miedema, Schonk, & Hautvast, 1988). The results of these studies have provided critical evidence and suggested that the risk of GDM could be reduced by avoiding excessive GWG. In 2009, the Institute of Medicine (IOM) issued new recommendations for the management GWG during pregnancy including specific guidelines for rate of weight gain by pre-pregnancy BMI (Institute of Medicine., 2009). However, the optimal weight gain during pregnancy for different ethnicity, age, or existing pregnancy complications to reduce GDM risk is still questionable.

2.2.5.2.2 Dietary factors

The relationship between dietary factors before and during pregnancy and GDM risk has been widely investigated. These factors may be a specific food (e.g. fast food, tea, coffee), macronutrients (e.g. carbohydrate, protein, fat), micronutrients (vitamins and minerals), or dietary patterns. The increased or decreased risk of GDM depends on the intake of particular types of foods.

Few studies have examined the associations between carbohydrate foods such as fibre, fruit, potato, beverage and GDM risk (Bao, Tobias, Hu, Chavarro, & Zhang, 2016; L. Chen et al., 2012; L. Chen, Hu, Yeung, Willett, & Zhang, 2009; Karamanos et al., 2014; C. Zhang, Liu, et al., 2006). Zhang et al. found that increased daily intake of total fibre, cereal or fruit fibre was associated with a significant decrease in GDM risk. The study also reported that high glycaemic load was linked with greater risk of GDM, especially when it combined with low cereal fibre diet (C. Zhang, Liu, et al., 2006). High intake of whole fruits before pregnancy was not associated with an elevated risk of GDM (L. Chen et al., 2012). The association between potato consumption and GDM is inconsistent. Bao et al. reported that higher intake of potatoes before pregnancy increased GDM risk and replacing two servings of potatoes per week with other vegetables, legumes, or whole grain foods could reduce the risk of GDM (Bao et al., 2016). In contrast, Karamanos et al. showed that less potatoes and cereals were consumed in women with GDM than non GDM women (Karamanos et al., 2014).

Higher consumption of sugar sweetened beverages before pregnancy, especially sugar sweetened cola, was associated with greater risk of GDM (L. Chen et al., 2009).

Higher intakes of animal fat and cholesterol before pregnancy were significantly associated with an increase in GDM risk (Bowers, Tobias, Yeung, Hu, & Zhang, 2012). A comparison between the highest and lowest quintile of animal fat and cholesterol intake showed an increase in GDM risk by approximately 90% and 55%, respectively. In addition, replacing 5% of energy from animal fat for energy from carbohydrates led to higher risk of GDM. However, a study by Baptise-Roberts et al. found no association between either total fat or cholesterol consumption and response to the glucose challenge test (Baptiste-Roberts, Ghosh, & Nicholson, 2011). No associations were recorded between total omega-3 or total omega-6 fatty acids and GDM risk (Bowers et al., 2012), while a lower n-6/n-3 ration and a higher consumption of n-3 fatty acid and polyunsaturated fats were observed in women with GDM compared to women without GDM (Radesky et al., 2008). Higher intake of olive oil was consumed in women with GDM but its association with GDM was not analysed (Karamanos et al., 2014). Two studies came to opposite results to whether high intake of egg increases GDM risk with one showing an elevated association (Qiu et al., 2011) and another showing no association (Bao, Bowers, Tobias, Hu, & Zhang, 2013).

Protein from animal and vegetable origin has a different role in the development of GDM. Higher intake of animal protein was associated with a 51% increased risk of GDM, while the risk of GDM was protective by around 30% with high consumption of vegetable protein (Bao et al., 2013). Another study found that a low carbohydrate dietary pattern with high protein and fat from animal origin before pregnancy increased GDM risk by 36%, whereas a low carbohydrate dietary pattern with high vegetable protein and fat was not associated with GDM risk (Bao, Bowers, et al., 2014). In addition, 51% of GDM risk could be reduced by replacing 5% energy of animal protein for vegetable protein (Bao et al., 2013). Among major dietary protein sources, a high red meat intake was associated with a greater risk of GDM (Bao et al., 2013; Schoenaker, Soedamah-Muthu, Callaway, & Mishra, 2015; C. Zhang, Schulze, et al., 2006) before pregnancy, but not in early pregnancy (Radesky et al., 2008). Similar

inconsistent findings were found for the association between processed meat intake before pregnancy and GDM with two studies showing a significantly increased risk (Bao et al., 2013; C. Zhang, Schulze, et al., 2006) and one study showing no association (Radesky et al., 2008).

The association between fast food consumption and GDM risk has been examined (Bao, Tobias, Olsen, & Zhang, 2014; Dominguez et al., 2014). Bao et al. found that women who consumed fast food ≥7 times per week before pregnancy had 2.18 times elevated risk of GDM compared to their counterparts with less than once per week (Bao, Tobias, et al., 2014). Another study by Dominguez et al. showed approximately twofold increase in GDM risk for the highest versus the lowest frequency intake of fast food (Dominguez et al., 2014). Women with higher intakes of fast food were typically younger, multiparous, current smokers, inactivity, and unhealthy diets (Bao, Tobias, et al., 2014; Dominguez et al., 2014).

Investigations on the associations of coffee and tea with GDM risk are limited. Adeney et al. found that moderate consumption of caffeinated coffee before pregnancy was associated with a 50% decreased risk of GDM (Adeney, Williams, Schiff, Qiu, & Sorensen, 2007). However, Hinkle et al. reported no associations between first trimester coffee intake and GDM risk (Hinkle et al., 2015). Decaffeinated coffee intake was not associated with reduction in GDM risk (Adeney et al., 2007). Increasing frequency of tea consumption suggested a potential protective effect against GDM, but non-significant association (Hinkle et al., 2015). Available data on the association between alcohol drinking and GDM is sparse. In addition, few Vietnamese pregnant women drink alcohol during pregnancy because of traditional culture.

Pre-pregnancy dietary patterns may affect the risk of developing GDM. Zhang et al. found that the Western dietary pattern was strong positive association with GDM risk, while the prudent dietary pattern was significantly and inversely associated with GDM (C. Zhang, Schulze, et al., 2006). The Western pattern was defined as a diet containing a high intake of red meat, processed meat, refined grain products, sweets, French fries,

and pizza, whereas the prudent dietary was characterised by a high consumption of fruit, green leafy vegetables, poultry, and fish (C. Zhang, 2010). The Mediterranean diet presented consistently protective dietary pattern against GDM risk with 15-38% decreased relative risk of GDM (Karamanos et al., 2014; Schoenaker et al., 2015; Schoenaker, Soedamah-Muthu, & Mishra, 2016; Tobias et al., 2012). The Mediterranean diet was characterised by a high intake of fruits, legume, vegetable, bread, cereal, fish, olive oil and a low or limited consumption of animal fat, meat, and eggs (Radd-Vagenas, Kouris-Blazos, Singh, & Flood, 2017). Pre-pregnancy adherence to a diet with high Alternate Healthy Eating Index 2010 score reduced 19-46% risk of GDM (Tobias et al., 2012; C. Zhang et al., 2014). This reduction rose up to 83% when additional lifestyle factors such as normal BMI, physically active, and non-smoker were taken into account (C. Zhang et al., 2014). A greater Dietary Approaches to Stop Hypertension diet compliance was associated with a 34% lower risk of GDM (Tobias et al., 2012), while a high Australian Recommended Food Score diet was not associated with GDM risk (Gresham, Collins, Mishra, Byles, & Hure, 2016).

Several dietary factors have been suggested to exert direct effects on GDM through some potential pathways (Bo et al., 2005; Javadian, Alimohamadi, Gharedaghi, & Hantoushzadeh, 2014). For instance, excessive iron supplementation during pregnancy has been found to increase the GDM risk, which may be due to elevated oxidative stress – a putative inducer of GDM (Javadian et al., 2014; Puntarulo, 2005). Other examples such as B vitamin deficiency and imbalance (e.g. folic acid, B2, B6, and B12) have been associated with GDM, probably explained by their essential role in the regulation of homocysteine homeostasis – a contributor to oxidative stress (Debreceni & Debreceni, 2014).

2.2.5.2.3 Cigarette smoking

Cigarette smoking is positively associated with insulin resistance, hyperinsulinism, and type 2 diabetes (Berlin, 2008; Perry et al., 1995; Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007), however, the association between tobacco and GDM remains controversial. Few studies reported an increased risk of GDM associated smoking (L.

J. England et al., 2004; Joffe et al., 1998; Solomon et al., 1997; X. Yang et al., 2002), whereas other studies did not find this association (Berkowitz et al., 1992; Campbell, Lynch, Esterman, & McDermott, 2012; Hosler, Nayak, & Radigan, 2011; Innes et al., 2002; Savvidou et al., 2010; Terry, Weiderpass, Ostenson, & Cnattingius, 2003). A meta-analysis of 12 studies conducted by Wendland et al. showed no association between smoking and GDM in smokers compared with non-smokers (Wendland, Pinto, Duncan, Belizan, & Schmidt, 2008). This association was not observed even when studies were limited to presenting adjusted analyses (four studies). Differences in study findings were likely due to variations in study design, study population, smoking measurement, GDM diagnosis, and the degree of adjustment for confounding factors. The underlying mechanism regarding the adverse effect of maternal smoking on GDM remains to be elucidated, though it may be ascribed to alterations in pro- and anti-angiogenic factors, immune-mediated events, and/or endothelial function (Moore Simas et al., 2014).

2.2.5.2.4 Physical activity

Physical activity has been known to play a critical role in the primary prevention of chronic diseases (Kruk, 2007) including type 2 diabetes (Sigal, Kenny, Wasserman, Castaneda-Sceppa, & White, 2006) and GDM (Tobias et al., 2011). A large number of studies on the associations between various types of PA before and/or during pregnancy and GDM risk have been conducted and provided different results (Aune et al., 2016; Russo, Nobles, Ertel, Chasan-Taber, & Whitcomb, 2015; Tobias et al., 2011; Yin, Li, Tao, Luo, & Liao, 2014). Tobias et al. conducted a meta-analysis of 8 epidemiological studies including seven pre-pregnancy and five early pregnancy studies with a total of 34929 women and 2855 total cases of GDM (Tobias et al., 2011). The results showed that higher levels of PA before pregnancy or in early pregnancy were significantly associated with a lower risk of GDM. However, a meta-analysis of six randomised controlled trials involving 947 participants performed by Yin et al. presented no significant difference in the risk of GDM between the intervention and the control groups (Yin et al., 2014). In contrast, Russo et al. conducted a meta-analysis of 10 randomised controlled trials with a total of 3401 women and indicated a significant lower risk of GDM among intervention group compared with control group

(Russo et al., 2015). Nevertheless, these meta-analyses did not report the association between the types of PA and GDM. It is noted that PA can be characterised by amount (e.g. total, time per day or week), intensity (e.g. sedentary, light, moderate, and vigorous), and domain (e.g. household/caregiving, occupational, sports/exercise, and commuting). Therefore, studies on the associations between these specific aspects of PA and GDM are critical to provide evidence for developing guidelines on GDM prevention.

Accumulative evidence has reported an inverse association between higher total PA before pregnancy and GDM risk. A meta-analysis of seven studies with a total of 34929 participants conducted by Tobias et al. found that women in the highest PA quantiles had a 55% lower risk of GDM compared with those in the lowest quantiles (Tobias et al., 2011). Another meta-analysis performed by Aune et al. reported that women with high total PA experienced a 38% reduced risk of GDM when compared with those women who had the low level (Aune et al., 2016). However, the inverse association between higher total PA during pregnancy and GDM risk was inconsistent. Two meta-analyses reported opposite conclusions to whether total PA during pregnancy reduces GDM risk with one showing an inverse association (Tobias et al., 2011) and another showing no association (Aune et al., 2016).

The association between combined PA before and during pregnancy and GDM risk has been examined (Dempsey et al., 2004; Oken et al., 2006). Oken et al. found that women who engaged in PA before and during pregnancy were likely to have a lower GDM risk compared to controls (Oken et al., 2006). Dempsey et al. reported that active women both before and during pregnancy experienced a 69% reduction in GDM risk even after adjusting for confounders compared to inactivity women (Dempsey et al., 2004). This pattern was also observed in a meta-analysis conducted by Aune et al. with a 59% reduction in GDM risk (Aune et al., 2016).

The associations between intensive levels of PA before and during pregnancy and GDM risk are conflicting. Two studies reported a decreased risk of GDM in women

who engaged in vigorous PA before pregnancy (Oken et al., 2006; C. Zhang, Solomon, Manson, & Hu, 2006), while one study found no association (Chasan-Taber et al., 2014). No associations between vigorous PA during pregnancy and GDM risk were observed in other studies (Chasan-Taber et al., 2014; Oken et al., 2006). These two studies also reported no associations between moderate-intensity activity both before and during pregnancy and risk of GDM (Chasan-Taber et al., 2014; Oken et al., 2006). However, Leng et al. showed a reduced risk of GDM in women with moderate-to-high PA during pregnancy (Leng et al., 2016).

Few studies have investigated the role of specific domains of PA in the development of GDM. Chasan-Taber et al. conducted two studies on Hispanic women and observed opposite results of the association between household/caregiving activity before pregnancy (Chasan-Taber et al., 2008; Chasan-Taber et al., 2014). These studies found no significant associations between GDM risk and occupational activity or sports/exercise before and during pregnancy. A meta-analysis of these studies conducted by Aune et al. showed no associations between occupational or household/caregiving activity before and during pregnancy and risk of GDM (Aune et al., 2016).

Evidence of the relationship between sedentary behaviours such as sitting time before and during pregnancy and GDM risk is limited. Oken et al. reported no association between television viewing before and during pregnancy and GDM (Oken et al., 2006). Padmapriya et al. found that total sitting time and television viewing during pregnancy were not associated with GDM (Padmapriya et al., 2017). In contrast, Leng et al. reported that long sitting at home (two or more hours per day) was significantly associated with an increased risk of GDM (Leng et al., 2016).

The mechanisms for PA effect on GDM risk have been partly elucidated. Firstly, PA can change the levels of adipokine profile such as adiponectin, resistin, leptin, and visfatin that may result in reduction in insulin resistance (Cao, 2014; Golbidi & Laher, 2013). Secondly, defects in the insulin signalling pathway can be compensated through

PA (Davenport, Mottola, McManus, & Gratton, 2008; de Barros, Lopes, Francisco, Sapienza, & Zugaib, 2010). Thirdly, increased PA may decline the inflammatory state, a contributory factor of insulin resistance, by controlling inflammation markers such as tumour necrosis factor alpha and interleukin 6 (Daniele et al., 2014; Hayashino et al., 2014). Finally, PA can increase the levels of antioxidant agents such as superoxide dismutase, catalase, and glutathione peroxidase which reduce oxidative stress, a pathogenesis of insulin resistance (Grissa et al., 2007; Kobe, Nakai, Koshino, & Araki, 2002).

2.2.5.2.5 Other modifiable risk factors

Other modifiable risk factors for developing GDM such as vitamin D deficiency and medications have been reported. A recent review by Zhang et al. involving 87 observational studies and 25 randomised controlled trials with a total of 58304 participants found that low blood vitamin D level during pregnancy was significantly related to an increase in GDM risk (Y. Zhang, Gong, Xue, Xiong, & Cheng, 2018). In addition, some medications might also affect glucose intolerance which increase GDM risk (Boden, Lundgren, Brandt, Reutfors, & Kieler, 2012; Fisher, Smith, Lagrandeur, & Lorenz, 1997).

In conclusion, various risk and protective factors of GDM have been identified. A healthy lifestyle that promotes protective factors and reduces risk factors might decrease the development of GDM.

2.2.6 Pregnancy outcomes associated with gestational diabetes mellitus

GDM not only raises the risk of adverse maternal and foetal outcomes during pregnancy, it also increases the risk for long-term complications in both mothers and their offspring. As the scope of this research limited to delivery, we mainly focused on short-term consequences of GDM.

2.2.6.1 Maternal morbidity

2.2.6.1.1 Maternal short-term consequences of GDM

Hypertensive disorders

Hypertensive disorders in pregnancy (HDP) is one of major causes of maternal and prenatal morbidity and mortality. It can be classified into three categories including chronic hypertension, gestational hypertension, and preeclampsia (M. A. Brown, Lindheimer, de Swiet, Van Assche, & Moutquin, 2001). GDM places mothers at increased risk for gestational hypertension and preeclampsia (Dodd, Crowther, Antoniou, Baghurst, & Robinson, 2007). Bryson et al. reported that GDM was related to elevated risk for gestational hypertension and preeclampsia even after adjustment for BMI, age, ethnicity, parity, and prenatal care. The study also indicated that Black women and women who received less prenatal care had a significantly increased risk of pregnancy-induced hypertension when compared to controls (Bryson, Ioannou, Rulyak, & Critchlow, 2003). Results of the HAPO study showed that the risk of preeclampsia in GDM women with the highest BMI increased by eight times compared to women with the lowest BMI (Metzger et al., 2008). GDM was also observed to be associated with an approximately 2.5-fold higher risk of HDP in Chinese women (Ye et al., 2014), 1.9-fold higher risk of gestational hypertension in Australian women (Jacobs et al., 2003), and 3.1- and 1.9-fold higher risk of preeclampsia in Swedish, Latin American and Caribbean women (Conde-Agudelo & Belizan, 2000; Ros, Cnattingius, & Lipworth, 1998). The development of hypertension in diabetic women may be explained by the impact of hyperinsulinemia on rising weight and renal sodium retention (Salzer, Tenenbaum-Gavish, & Hod, 2015). Hypertensive disorders may have long-term risk for developing hypertension, T2DM, MetS, and CVDs (Lykke et al., 2009).

Caesarean section

Caesarean section is common among women with GDM. The global prevalence of caesarean section was about 18.6% and it varied substantially across regions and countries (Betran et al., 2016). The HAPO study reported a significant association between caesarean section and maternal glucose levels (Metzger et al., 2008). A study

by Gorgal et al. found that the risk of non-elective caesarean section in women with GDM was increased 1.52-fold after adjustment for confounding factors such as maternal age, pre-pregnancy BMI, GWG, previous caesarean section, gestational age at delivery, and birthweight (Gorgal et al., 2012). Another study by Naylor et al. showed that caesarean section among women with treated GDM increased two-fold even they had lower prevalence of macrosomia compared to controls (Naylor, Sermer, Chen, & Sykora, 1996). This finding suggested that GDM itself might be an indicator for caesarean section. Farrar at al. conducted a systematic review and meta-analysis and concluded that caesarean section was positive associated with fasting and post-load glucose concentrations (Farrar et al., 2016). Caesarean section is a major surgical procedure so it can carry the risk of complications such as bleeding, infection, abdominal pain, hysterectomy, ureteral tract injury, vesical injury, placenta previa, neonatal respiratory morbidity, maternal and foetal mortality, and uterine rupture in subsequent pregnancies (Belizan, Cafferata, Althabe, & Buekens, 2006; C. Kim, 2010).

2.2.6.1.2 Maternal long-term consequences of GDM

Recurrence of GDM in subsequent pregnancies, T2DM, metabolic syndrome (MetS) and CVD are common maternal long-term consequences of GDM. Having a previous GDM is one of the major risk factors for the recurrence of GDM. The recurrence prevalence of GDM in women with a history of GDM ranged from 30% to 84% in subsequent pregnancies (Bottalico, 2007; L. England et al., 2015; C. Kim, Berger, & Chamany, 2007). GDM is one of the most predictive factors for developing T2DM postpartum. This association is largely supportive by numerous studies (Bellamy et al., 2009; C. Kim et al., 2002; Zhu & Zhang, 2016). A systematic review by Bellamy et al. involving 20 studies with a total of 675455 women and 10859 type 2 diabetic patients found that women with GDM had an approximately seven-fold increased risk of developing T2DM in the future compared with their counterparts with normoglycaemic pregnancy (Bellamy et al., 2009). The prevalence of progression from GDM to T2DM ranged substantially from 2.6% to 70% over a period between 6 weeks to 26 years after the index pregnancy (C. Kim et al., 2002). In addition, women with GDM have been associated with an increased postpartum risk of MetS and CVD.

MetS is considered as the concomitant risk factors including central obesity, insulin resistance, hypertension, and dyslipidemia (Balkau, Valensi, Eschwege, & Slama, 2007). A systematic review of 17 studies consisting of 5832 women and 1149 MetS events by Xu et al. found that the risk of MetS in women with previous GDM increased by almost four-fold, compared with their counterparts without a history of GDM (Y. Xu et al., 2014). The risk of CVD is high in women with prior GDM. Kessous et al. conducted a study of nearly 5000 women with a history of GDM over 10 year follow-up and reported that GDM was an independent risk factor for long-term cardiovascular morbidity such as non-invasive cardiac diagnostic procedures, simple cardiovascular events, and total cardiovascular hospitalisations (Kessous, Shoham-Vardi, Pariente, Sherf, & Sheiner, 2013). A nationwide population-based study by Goueslard et al. found that the risk of CVD was significantly higher in women with GDM history compared to controls after adjusting for confounder factors, particularly angina pectoris, myocardial infarction, ischemic stroke, and hypertensive disorders (Goueslard et al., 2016). A recent study conducted by McKenzie-Sampson et al. followed 67356 women with GDM and 1003311 women with GDM for up to 25.2 years after the index delivery. The results showed that GDM was associated with an elevated risk of CVD including ischemic heart disease, myocardial infarction, coronary angioplasty, and coronary artery bypass graft (McKenzie-Sampson et al., 2018).

The associations between GDM and other maternal long-term morbidities such as ophthalmic disease, renal disease, psychiatric disease, and malignancies have also been reported. A population-based study conducted by Beharier et al. showed that the incidence of ophthalmic morbidity (e.g. glaucoma, diabetic retinopathy, and retinal detachment) was significantly higher in women with GDM compared with non GDM women (Beharier et al., 2017). Another studies found that renal morbidity was higher in women with GDM compared to controls (Beharier et al., 2015; Bomback et al., 2010; Friedman et al., 1995). Women with a history of GDM had an increased risk of subsequent postpartum depression (Hinkle et al., 2016; Silverman et al., 2017). Furthermore, women with previous GDM had a significantly higher incidence of ovarian cancer, uterine cancer, and breast cancer (Fuchs et al., 2017) as well pancreatic cancer and hematologic malignancies (Sella et al., 2011).

2.2.6.2 Foetal/neonatal morbidity

2.2.6.2.1 Short-term consequences in offspring of mothers with GDM

Neonatal hypoglycaemia

The exposure to maternal hyperglycaemia causes foetal hyperinsulinaemia resulting in neonatal hypoglycaemia, which may be a complication of GDM (McIntyre et al., 2010). In the HAPO study, 2.1% of the infants experienced clinical hypoglycaemia. The study also found that there was a relationship between hypoglycaemia in the newborn and post OGTT maternal glucose. However, there was no such evidence for maternal fasting glucose levels (Metzger et al., 2008). It is noted that there were no significant differences in the occurrence of neonatal hypoglycaemia among women with treated GDM and untreated women (Crowther et al., 2005; Landon et al., 2009).

Hyperbilirubinemia

Hyperbilirubinemia is more common in women with GDM than those without GDM. Maternal hyperglycaemia and subsequent foetal hyperinsulinaemia may cause hyperbilirubinemia, which induce decreased oxygenation (C. Kim, 2010). Approximately 8.3% of the total participants in the HAPO study had hyperbilirubinemia. There was no association between hyperbilirubinemia with fasting glucose and its associations with post OGTT maternal glucose levels were mild (Metzger et al., 2008).

Macrosomia

Macrosomia is a common complication among GDM women with a prevalence range of 14% - 21% of these pregnancies (Crowther et al., 2005; Landon et al., 2009). Previous studies have demonstrated a continuous association between maternal glucose levels and foetal macrosomia even when the maternal glucose levels are mild hyperglycaemia (Landon et al., 2011; Metzger et al., 2008). Results of a recent systematic review and meta-analysis of 25 publications by Farrar et al. also showed that fasting and post OGTT maternal glucose levels (after 50g, 75g, and 100g loads) were positively associated with macrosomia (Farrar et al., 2016). Maternal

hyperglycaemia and following foetal hyperinsulinaemia may cause macrosomia (Pedersen, 1954). In turn, macrosomia in offspring of mothers with hyperglycaemia is associated with increased risk for developing obstetrical complications such as caesarean section, shoulder dystocia, postpartum haemorrhage, preterm birth, intrauterine death, fractured clavicle and humerus, and neonatal hypoglycaemia (Mohammadbeigi et al., 2013; Stotland, Caughey, Breed, & Escobar, 2004).

Respiratory distress syndrome

Respiratory complications in the neonate is one of the most common, serious, and potentially life-threatening perinatal complications related to GDM (Michael Weindling, 2009). The incidence of respiratory complications in offspring of mothers with GDM is high (34%) with a 4% - 6% incidence of respiratory distress syndrome. Mortier et al. reported that severe respiratory distress syndrome was significantly higher in neonates from mothers with GDM (20%) compared to controls (5.2%) (Mortier et al., 2017). A study by O'Sullivan et al. found that respiratory distress syndrome in neonates was significantly associated with GDM during pregnancy even after adjustment for confounding factors (E. P. O'Sullivan et al., 2011). In addition, GDM was also found to be an independent risk factor for transient tachypnoea of newborn (Fung et al., 2014). The foetal hyperinsulinaemia interfering with the impact of cortisol on surfactant synthesis may cause the occurrence of respiratory distress syndrome (Bourbon & Farrell, 1985).

Preterm birth

Preterm birth is characterised as newborns alive before completion of 37 weeks of gestation (World Health Organization., 2018b). It is one of the leading causes of infant mortality with an estimation of approximately 1 million deaths in 2015 (L. Liu et al., 2016). The prevalence of preterm birth ranges from 5% to 18% of babies born worldwide (World Health Organization., 2018b). GDM has been implicated as one of the risk factors for preterm birth (Billionnet et al., 2017; Metzger et al., 2008). Infants born preterm often have many complications such as respiratory distress syndrome, chronic lung disease, injury to the intestines, a compromised immune system, CVDs,

visual and hearing problems, and neurological insult (Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes., 2007). The prevalence of preterm birth in Vietnam was reported to vary between 5% and 11% (Giang, Bechtold-Dalla Pozza, Tran, & Ulrich, 2018; N. Nguyen, Savitz, & Thorp, 2004). These studies also highlighted some risk factors for preterm birth, however the role of GDM has not been investigated. A study by Hirst et al. at a tertiary maternal hospital in Ho Chi Minh city reported that women with GDM and borderline GDM were more likely to deliver preterm (J. E. Hirst et al., 2012).

Shoulder dystocia

Shoulder dystocia is an obstetrical emergency that occurs in 0.2% - 3% of the general obstetrical population (Nesbitt, Gilbert, & Herrchen, 1998; Tsur, Sergienko, Wiznitzer, Zlotnik, & Sheiner, 2012). It may cause temporary or permanent nerve palsies of the upper extremity, hypoxic neonatal injury, or neonatal death (Hope et al., 1998; Keller, Lopez-Zeno, Dooley, & Socol, 1991; Nesbitt et al., 1998). Women with GDM are at increased risk for shoulder dystocia because their large babies have more trouble passing through the pelvic outlet. In the HAPO study, shoulder dystocia related to increase in fasting glucose and post OGTT maternal glucose levels (Metzger et al., 2008). A recent systematic review and meta-analysis of 25 reports with a total of 207172 women showed that there were positive linear associations between all glucose concentrations and shoulder dystocia (Farrar et al., 2016).

Low birth weight

Low birth weight, a birth weight of less than 2,500 grams (World Health Organization., 2014), remains a public health problem in many countries for its short- and long-term consequences. Globally, about 20 million infants are born with low birth weight each year occurring largely in low- and middle-income countries (World Health Organization., 2014). On the one hand, low birth weight is one of the adverse pregnancy outcomes associated with GDM (Y. Chen et al., 2013). On the other hand, it is a predictor of subsequent GDM (Ogonowski, Miazgowski, Engel, & Celewicz, 2014; Pettitt & Jovanovic, 2007; Seghieri et al., 2002). In Vietnam, the prevalence of

low birth weight was approximately 5% (Graner et al., 2010), and it is still unknown whether GDM is associated with this newborn problem.

Large-for-gestational age

Large-for-gestational age (LGA) is defined as a born baby with a birth weight greater than the 90th percentile of birth weight in a reference population (Alexander, Himes, Kaufman, Mor, & Kogan, 1996). It is a common adverse pregnancy outcome related to GDM (Metzger et al., 2008). Some studies reported a positive association between hyperglycemia during pregnancy and LGA (Metzger et al., 2008; Wendland et al., 2012), while others did not find such an association (Koning et al., 2018; Luengmettakul, Sunsaneevithayakul, & Talungchit, 2015). In Vietnam there has been only one study that reported the incidence of LGA was 12.8%, and found a lack of significant association between GDM and LGA (J. E. Hirst et al., 2012).

Small-for-gestational age

Small-for-gestational age (SGA) is defined as a born baby with a birth weight less than the 10th percentile of birth weight in a reference population (Alexander et al., 1996). It has been linked to GDM (Wang, Kanguru, Hussein, Fitzmaurice, & Ritchie, 2013). A study of 1901 pregnant women in Western China found that women with GDM had a higher risk of SGA compared with their non-GDM counterparts (Mak et al., 2019). However no significant difference in SGA was found between GDM and non GDM mothers as evidenced from a previous Vietnamese cohort study, where the incidence of SGA was 7.8% (J. E. Hirst et al., 2012).

Other neonatal comorbidities

The associations between other neonatal comorbidities and GDM have been reported. Untreated GDM was related to increased risk of stillbirth by approximately four-fold (J. B. O'Sullivan, Charles, Mahan, & Dandrow, 1973). Neonatal hypocalcaemia has been observed in women with GDM but it is relatively infrequent and has little clinical importance (Cordero, Treuer, Landon, & Gabbe, 1998). GDM is also associated with

an elevated risk for major congenital malformations (Balsells, Garcia-Patterson, Gich, & Corcoy, 2012) and hypertrophic cardiomyopathy (Ullmo et al., 2007).

2.2.6.2.2 Long-term consequences in offspring of mothers with GDM

Cumulative evidence has suggested that GDM is associated with an increased risk of MetS and glucose intolerance in offspring. The prevalence of MetS was significantly higher in offspring born to women with GDM (Boney, Verma, Tucker, & Vohr, 2005; Tam et al., 2010). Offspring of pregnancies with GDM had approximately six times higher risk for developing impaired glucose tolerance, compared to controls (Holder et al., 2014). The risk for developing T2DM and pre-diabetes including impaired glucose intolerance or impaired fasting glucose increased by nearly eight times in offspring of mother with diet-treated GDM, compared to those from the background population (Clausen et al., 2008).

The increased risk of obesity in offspring of pregnancies with GDM has been wide investigated. The Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study reported that high birthweight and neonatal adiposity were positively associated with higher levels of maternal glucose intolerance (Hapo Study Cooperative Research Group., 2009). Particularly, Tam et al. found that the risk of childhood obesity in offspring of mothers with GDM increased by approximately 50%, even after adjustment for confounding factors including maternal BMI (Tam et al., 2017). A recent meta-analysis of 20 studies with a total of 26509 children highlighted that BMI z-score was higher in offspring of mothers with GDM (Kawasaki et al., 2018).

Children born to mothers with GDM are at risk of impaired neurodevelopmental outcome. Fraser et al. reported that offspring of diabetic mothers had lower cognitive ability despite adjustment for confounding factors (Fraser, Almqvist, Larsson, Langstrom, & Lawlor, 2014). Another study by Dionne et al. showed that infants of GDM mothers had significantly lower scores for expressive language compared to controls (Dionne, Boivin, Seguin, Perusse, & Tremblay, 2008). The association

between maternal GDM diagnosed at 26 weeks or earlier and the risk of developing autism spectrum disorders was found in a retrospective longitudinal cohort study involving 322323 singleton children by Xiang et al. even after adjustment for confounding factors (Xiang et al., 2015). A population-based cohort study with a total of 231271 participants by Nahum Sacks et al. indicated that GDM was an independent risk factor for long-term neuropsychiatric disease in the offspring (Nahum Sacks et al., 2016). In addition, a recent study suggested that children of mothers with GDM are at risk of paediatric ophthalmic morbidity (Walter, Tsumi, Wainstock, Spiegel, & Sheiner, 2018).

In conclusion, GDM is associated with adverse pregnancy outcomes for both mother and offspring in short- and long-term periods. Therefore, all pregnant women should be screened for GDM during pregnancy and actively managed in order to minimise the consequences of GDM.

2.2.7 Gestational diabetes mellitus screening and diagnosis

Early screening and diagnosis of GDM may improve outcomes for both mother and child through treatment and management. However, screening approaches and diagnostic criteria for GDM are still controversial on different international guidelines.

2.2.7.1 Screening

There is a great variety of screening for GDM in terms of indications (universal versus selective screening), timing (early versus mid-trimester screening), and type (one-step versus two-step screening).

Selective and universal are two common screening approaches for GDM. For selective screening, only women with high-risk factors for GDM such as age > 25 years; body mass index (BMI) > 25; ethnic background; family history of type 2 diabetes and a previous history of GDM; or previous adverse pregnancy outcomes are offered. In contrary, all women are offered to be screened for GDM in universal screening

approach. Ideally, universal approach should be used to identify all potential cases of GDM (Petrovic, 2014). Early detection and timely treatment of GDM could reduce the risk of adverse pregnancy outcomes (Donovan et al., 2013). Selective screening may be more cost-effective but many pregnant women with hyperglycaemia might be missed (Cosson et al., 2013; Ostlund & Hanson, 2003; Simmons & Moses, 2013). Therefore, the International Diabetes Federation (IDF) suggested that selective approach should only be considered in particular conditions with local cost-effectiveness (IDF Clinical Guidelines Task Force., 2009). Nevertheless, there is no consistency in GDM screening approaches across diabetes societies, countries and regions. Universal screening is recommended by the ADA in the United States (American Diabetes Association., 2011), CDA in Canada (Canadian Diabetes Association Clinical Practice Guidelines Expert et al., 2013), ADIPS in Australia (Nankervis et al., 2014), the Japan Diabetes Society (JDS) in Japan and the Brazilian Society of Diabetes (BSD) in Brazil (Agarwal, 2015), while the National Institute for Health and Care Excellence (NICE) (National Institute for Health and Care Excellence (NICE). 2015), the Scottish Intercollegiate Guidelines Network (SIGN) (Scottish Intercollegiate Guidelines Network., 2010), France, and Norway (Buckley et al., 2012; Cosson et al., 2014) support selective screening for women with risk factors.

It is crucial to decide when is the gold time to screen for GDM after identifying the population. Early screening for GDM at the first prenatal visit is recommended to women with high-risk factors such as obesity, advanced maternal age, previous GDM or macrosomic infant to identify overt diabetes. This screening is particularly important in the endemic areas of type 2 diabetes. For women who were negative or absent from early screening, they should be screened for GDM at 24 to 28 weeks of gestation. The timing of screening in practice might be various by local health practitioners. In Nigeria, GDM was screened at different stages of pregnancy regardless of the diagnostic criteria such as between 24 and 28 weeks of gestation (Anzaku & Musa, 2013), 24 weeks onwards (Olagbuji et al., 2015), to the third trimester (Olarinoye, Ohwovoriole, & Ajayi, 2004), or 4 to 40 weeks (Kuti et al., 2011). Similarly, the differences in timing of GDM screening were observed among countries in Europe (Buckley et al., 2012).

Using one-step or two-step approach for GDM screening is somewhat controversial. In one-step method, an oral 75-g glucose is given after taking a fasting venous blood sample. Plasma glucose values are measured at fasting and after 1 and 2 hours. GDM is defined if one or more values equal or exceed the thresholds. This approach is based on the results of HAPO study (Metzger et al., 2008) and is widely adopted by WHO (World Health Organization., 2013), IADPSG (International Association of Diabetes and Pregnancy Study Groups Consensus Panel. et al., 2010), and the International Federation of Gynecology and Obstetrics (FIGO) (Hod et al., 2015). In contrast, two-step approach includes two stages. Firstly, nonfasting women are given a glucose challenge test (GCT) using a 50-g oral glucose load. Venous glucose level is measured after one hour. Depending on the result of glucose test (≥130, 135, or 140 mg/dL), GCT is defined as positive. Secondly, women with positive screening test undergo a 100-g 3-h oral glucose tolerance test (OGTT). Venous glucose values are measured at fasting and after 1, 2, and 3 hours. Two or more abnormal values are required to diagnose GDM. This approach is mainly recommended by the American College of Obstetricians and Gynecologists (ACOG) (ACOG Committee on Obstetric Practice., 2011). Both one-step and two-step approaches were recommended by the ADA (American Diabetes Association., 2014) and the Diabetes Association of Nigeria (DAN) (Diabetes Association of Nigeria., 2013) to diagnose GDM. Although the consensus on using one- or two-step approach has not been achieved yet, it is likely that one-step approach was largely used due to its simplicity and accuracy (Rani & Begum, 2016).

2.2.7.2 Diagnosis

Diagnostic criteria for GDM have been developed and evolved over the past 50 years. However, it seems to be far to achieve the globally accepted diagnostic criteria.

The first diagnostic criteria for GDM were introduced by O'Sullivan and Mahan in 1964 (J. B. O'Sullivan & Mahan, 1964). His study included 752 pregnant women using a 100-g, 3-h oral glucose tolerance test (OGTT) at 24-28 weeks of gestation and the Somogyi-Nelson technique with four whole venous blood samples. The O'Sullivan

criteria were established to predict the development of diabetes in later life (not adverse pregnancy outcomes) based on two standard deviations above the mean. GDM was confirmed if at least two glucose values equalling or exceeding the thresholds (Table 2).

In 1979, the National Diabetes Data Group (NDDG) modified the O'Sullivan criteria as glucose levels were preferred to measure in plasma rather than in whole blood (National Diabetes Data Group., 1979). As a consequence, the thresholds of glucose for GDM diagnosis were added by approximately 15% to each glucose value (Table 2).

Carpenter and Coustan (C&C) further modified the O'Sullivan diagnostic criteria in 1982 (Carpenter & Coustan, 1982) based on a new glucose oxidase method which was used in the late 1970s to measure plasma glucose (Table 2). This technique replaced the Somogyi-Nelson method because it was not sensitive to a number of non-glucose substances. Lower glucose levels (about 5 mg/dL) were observed in glucose oxidase method compared with Somogyi-Nelson technique (Mager & Farese, 1965). It is noted that all O'Sullivan, NDDG, and C&C criteria were based on a 100-g, 3-h OGTT, following a 50-g glucose challenge test (GCT) with thresholds varied from 130 to 140 mg/dL.

In the 1980s, the World Health Organization proposed a 75-g, 2-h OGTT test using the same criteria for diagnosis of diabetes mellitus in non-pregnant adults to diagnose GDM (World Health Organization., 1985). Plasma glucose levels were measured at two time points including the fasting and 2-h later. 1-h and 3-h plasma glucose measurements were not recommended as in the 100-g, 3-h OGTT method. One or more abnormal values were sufficient to define GDM. In 1999, the WHO modified the fasting plasma glucose from 7.8 mmol/L to 7.0 mmol/L in order to make it in accordance with the recommendation of the American Diabetes Association (World Health Organization., 1999). In 2013, the WHO endorsed the IADPSG criteria (World Health Organization., 2013) (Table 2).

A limitation of the previous diagnostic criteria for GDM was that they were not developed through clinical pregnancy outcome-based studies. In addition, the diagnostic criteria in non-pregnant women were applied for pregnant population. To address these issues, the IADPSG organization was formed in 1998. A large prospective observational study namely the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study was conducted with the purpose of evaluating the associations between maternal glycaemic values (fasting, 1-h, and 2-h plasma glucose) and specific adverse pregnancy outcomes such as birthweight, cord blood serum C-peptide, primary caesarean delivery, neonatal hypoglycaemia, preterm delivery, shoulder dystocia, intensive neonatal care admission, hyperbilirubinemia, and preeclampsia (Hapo Study Cooperative Research Group., 2002). The study included over 25,000 pregnant women across 15 centres in 10 countries using a 75-g, 2-h OGTT test at 24-32 weeks of gestation. Based on the results of HAPO study (Metzger et al., 2008), the IADPSG recommended the new diagnostic criteria using a 75-g, 2-h OGTT with at least one abnormal values to diagnose GDM (International Association of Diabetes and Pregnancy Study Groups Consensus Panel. et al., 2010) (Table 2).

Table 2. Major diagnostic criteria for gestational diabetes mellitus

Criteria	Effective years	OGTT type (g)	Abnormal values (n)	Fasting (mg/dL)	1-h (mg/dL)	2-h (mg/dL)	3-h (mg/dL)
O'Sullivan and Mahan	Since 1964	100	≥2	90	165	145	125
NDDG	Since 1979	100	≥2	105	190	165	145
Carpenter and Coustan	Since 1982	100	≥2	95	180	155	140
WHO							
WHO 1985	1985-1998	75	≥1	140	-	140	-
WHO 1999	1999-2012	75	≥1	126	-	140	-
WHO 2013	2013-present	75	≥1	92-125	180	153-199	-
IADPSG	2010-present	75	≥1	92	180	153	-

IADPSG: International Association of Diabetes and Pregnancy Study Group; NDDG: National Diabetes Data Group; OGTT: Oral glucose tolerance test; WHO: World Health Organization

The adoption and use of diagnostic criteria for GDM depend on each diabetes society and country. The NDDG criteria was first recommended by the ADA before switching to the C&C criteria in 2000 (American Diabetes Association., 2000). In 2011, the ADA endorsed the IADPSG criteria (American Diabetes Association., 2011). However, in 2014 the ADA modified their guidelines to endorse either the one-step approach (the IADPSG criteria) or the two-step approach (NDDG or C&C criteria) (American Diabetes Association., 2014). In 1999, the WHO recommended the new criteria with only two measurements which were used in a number of countries (World Health Organization., 1999). In 2013, the WHO proposed its new criteria after reviewing current evidence on diagnostic criteria for hyperglycaemia in pregnancy, especially the results of HAPO study and the IADPSG criteria (World Health Organization., 2013). Accordingly, the WHO used the term hyperglycaemia which included both GDM and diabetes in pregnancy. The use of modified diagnostic criteria for GDM was observed in many countries and regions worldwide such as in America (American Diabetes Association., 2000, 2011, 2014), Canada (Canadian Diabetes Association Clinical Practice Guidelines Expert et al., 2013), Brazil (McIntyre, Colagiuri, Roglic, & Hod, 2015), Europe (C. J. Brown et al., 1996; National Institute for Health and Care Excellence (NICE). 2015), Australia (Hoffman, Nolan, Wilson, Oats, & Simmons, 1998; Martin, 1991; Nankervis et al., 2014), New Zealand (Ministry of Health., 2014), India (Seshiah et al., 2012), Japan (Kuzuya et al., 2002), and Nigeria (Diabetes Association of Nigeria., 2013) (Table 3). In Vietnam, the first national guidelines on GDM issued in 2018 by Ministry of Health adopted the 2013 WHO criteria (Vietnam Ministry of Health., 2018).

Table 3. Comparison of using diagnostic criteria for gestational diabetes mellitus worldwide

Area	Criteria	Effective years	OGTT type (g)	Abnormal values (n)	Fasting (mg/dL)	1-h (mg/dL)	2-h (mg/dL)	3-h (mg/dL)
Africa	DAN (endorsed C&C)	2013-present	100	≥2	95	180	155	140
			75	≥2	95	180	155	-
Asia	DIPSI (endorsed WHO 1985)	2006-present	75	≥1	-	-	140	-
	JSOG	1984-present	75	≥2	100	180	150	-
	Vietnam	2018-present	75	≥1	92-125	180	153-199	-

Area	Criteria	Effective years	OGTT type (g)	Abnormal values (n)	Fasting (mg/dL)	1-h (mg/dL)	2-h (mg/dL)	3-h (mg/dL)
Australasia	ADIPS							
	1991-2010	1991-2010	75	≥1	99	-	180	-
	Endorsed IADPSG	2011-2013	75	≥1	92	180	153	-
	Endorsed WHO 2013	2014-present	75	≥1	92-125	180	153-199	-
	NZSSD	2004-present	75	≥1	99	-	162	-
Europe	EASD	1996-present	75	≥1	108	-	162	-
	NICE	2015-present	75	≥1	101	-	140	-
North America	ADA							
	Endorsed NDDG	Before 2000 & 2014-present	100	≥2	105	190	165	145
	Endorsed C&C	2000-2010 & 2014-present	100	≥2	95	180	155	140
	Endorsed IADPSG	2011-present	75	≥1	92	180	153	-
	CDA	2013-present	75	≥1	95	190	162	-
South America	BSD	2014-present	75	≥1	92	180	153	-

ADA: American Diabetes Association; ADIPS: Australian Diabetes in Pregnancy Society; BSD: Brazilian Society of Diabetes; CDA: Canadian Diabetes Association; C&C: Carpenter and Coustan criteria; DAN: Diabetes Association of Nigeria; DIPSI: Diabetes in Pregnancy Study Group India; EASD: European Association for the Study of Diabetes; IADPSG: International Association of Diabetes and Pregnancy Study Group; JSOG: Japan Society of Obstetrics and Gynecology; NDDG: National Diabetes Data Group; NZSSD: New Zealand Society for the Study of Diabetes; NICE: National Institute for Health and Care Excellence; OGTT: Oral glucose tolerance test; WHO: World Health Organization

A great variation in the prevalence of GDM could be partly explained by the adoption of different diagnostic criteria. A study in California reported that the use of the C&C criteria led to an increase of 33-70% prevalence of GDM compared with the NDDG criteria (Ferrara, Hedderson, Quesenberry, & Selby, 2002). The prevalence of GDM further increased when using the IADPSG criteria with lower threshold values for diagnosis. Many studies showed that this prevalence grew up by two- to seven-folds compared with the previous diagnostic criteria (Agarwal et al., 2015; Duran et al., 2014; Huhn et al., 2017; T. S. Tran et al., 2013; Trujillo et al., 2015). This increase

resulted in two opposite opinions. In one hand, more pregnant women who were detected and managed GDM can improve their pregnancy outcomes through the effect of GDM treatment (Duran et al., 2014; Hartling et al., 2013; Power et al., 2013). On the other hand, increasing number of pregnant women diagnosed with GDM may cause a greater workload for health care system as well increase psychological stress for women (Chamberlain et al., 2013; Flack, Ross, Ho, & McElduff, 2010). In addition, the use of different diagnostic criteria made it difficult to evaluate the true burden of GDM as well hamper the comparison of GDM prevalence between and within countries. Therefore, a single global uniformity in diagnostic criteria for GDM is urgently needed.

2.2.8 Antenatal management of gestational diabetes mellitus

Previous studies have demonstrated that women with untreated GDM have higher rates of maternal and perinatal morbidity and mortality (Langer, Miodovnik, Reece, & Rosenn, 2010; Turok, Ratcliffe, & Baxley, 2003). In contrast, aggressive treatment of GDM has been associated with a significant reduce of these complications (Buchanan, Xiang, & Page, 2012; Crowther et al., 2005; Hartling et al., 2013; Landon et al., 2009). During pregnancy, women with GDM should be managed by a combination of medical nutrition therapy and weight management, physical activity, self-supervision of blood glucose, and pharmacological therapy when needed.

Medical nutrition therapy is the cornerstone of management of GDM during pregnancy. The goal is to provide adequate nutrition for the foetal and mother as well to achieve and maintain normal glycaemic regulation without ketosis and foetal compromise (C. Kim, 2010). A recent systematic review and meta-analysis of 18 randomised controlled trials by Yamamoto et al. found that dietary intervention was associated with lower levels of fasting and postprandial glucose as well decreased requirement for medication treatment (Yamamoto et al., 2018). Notably, a specific optimal caloric intake for women with GDM has not been identified yet and larger controlled randomised prospective studies are needed.

Monitoring weight changes during pregnancy has a vital role in attaining appropriateness of dietary therapy and maintaining an increase in weight following the guidelines. In 2009, the IOM released new guidelines for weight gain during pregnancy based on pre-pregnancy BMI (Institute of Medicine., 2009). Particularly, the guidelines suggested an increase in weight of 12.5-18 kg for underweight (< 18.5 kg/m^2), 11.5-16 kg for normal weight (18.5-24.9 kg/m^2), 7-11.5 kg for overweight (25.0-29.9 kg/m^2), and 5-9 kg for obese women (≥30 kg/m^2) during pregnancy. However, these recommendations are mainly for normal pregnancy and there is no specific suggestions for pregnant women with GDM.

Physical activity is linked with improved insulin sensitivity which can improve glucose tolerance (Mikines, Sonne, Farrell, Tronier, & Galbo, 1988). In addition, diet alone can fail to meet glucose targets up to 39% of women with GDM (Langer, Berkus, Brustman, Anyaegbunam, & Mazze, 1991). Thus, a combination between dietary therapy and PA is often suggested as an initial step for women with GDM. It is estimated that this strategy can attain blood glucose targets in 70-85% of women who were diagnosed with GDM by Carpenter-Coustan or NDDG criteria (American Diabetes Association., 2018). In addition, PA can help to avoid or reduce the use of insulin in women with GDM (de Barros et al., 2010; Horton, 1991). A review by Padayachee and Coombes suggested that GDM women should do both aerobic and resistance exercise at a moderate intensity with ≥3 times per week for 30-60 minutes each time (Padayachee & Coombes, 2015).

Women with GDM are encouraged to engage in glucose self-monitoring. This will help to know whether the glucose targets are achieved or an initially pharmacological therapy is needed (ACOG technical bulletin., 1995). The ADA recommended targets for women with GDM or diabetes are fasting <5.3 mmol/L, and/or one-hour postprandial <7.8 mmol/L, or two-hour postprandial <6.7 mmol/L (American Diabetes Association., 2018). A study conducted by Hawkins et al. indicated that frequent self-monitoring of blood glucose was related to decreased risk of adverse pregnancy outcomes (Hawkins et al., 2009).

Women with GDM who do not achieve the blood glucose targets with lifestyle intervention, should initiate pharmacological therapy. Insulin is considered as the first-line pharmacological strategy for GDM in the United States and Canada, whereas oral therapy is the preferred first-line treatment in the United Kingdom (American Diabetes Association., 2018; Feig et al., 2018; National Institute for Health and Care Excellence (NICE). 2015). Metformin and glibenclamide are usually used to treat GDM. A recent systematic review and meta-analysis of 11 trials compared metformin with insulin by Farrar et al. found that except for instrumental delivery, metformin was associated with a lower risk of most outcomes such as preeclampsia, pregnancy-induced hypertension, induction of labour, large for gestational age, macrosomia, admission to neonatal intensive care unit, and neonatal hypoglycaemia compared to insulin (Farrar et al., 2017). The safety and effectiveness of glibenclamide in treatment of GDM have been confirmed (Dhulkotia, Ola, Fraser, & Farrell, 2010; Langer, Conway, Berkus, Xenakis, & Gonzales, 2000). Nevertheless, results of a recent systematic review and meta-analysis by Farrar et al. consisting of nine trials compared glibenclamide with insulin and three trials compared glibenclamide with metformin found that glibenclamide is inferior to either insulin or metformin (Farrar et al., 2017). Therefore, glibenclamide should not be used for treating women with GDM if insulin or metformin is available.

2.2.9 Management during labour and postpartum

Management during labour and postpartum should be followed up after antenatal management of GDM.

2.2.9.1 Labour management

There is no consensus on the timing and mode of labour in women with GDM. GDM women should be monitored closely for excess foetal growth and induction of labour is generally recommended to avoid obstetric complications and late perinatal death related to foetal overgrowth (Witkop, Neale, Wilson, Bass, & Nicholson, 2009). Elective caesarean section is suggested if the estimated foetal weight >4.5 kg to prevent birth trauma (Bulletins, 2005). Insulin requirements during induced and spontaneous labour generally increase due to an increase in the physical work of

uterus. However, some women, especially who require treatment during pregnancy, may need continuous insulin during labour to manage hyperglycaemia and prevent ketosis (Jovanovic, 2004; C. Kim, 2010). The glucose levels in these women should be monitored continuously or at least every two hours between 72 and 126 mg/dL during labour (Blumer et al., 2013).

2.2.9.2 Postpartum management

2.2.9.2.1 Postpartum screening for diabetes

Most women reverse glycaemic levels to the pregestational status soon after labour. However, there are cases that remain hyperglycaemia that possibly represents undiagnosed T2DM during pregnancy (C. Kim, 2010). Therefore, GDM women should be checked blood glucose level until 72-hour following labour to determine their glucose status. If T2DM is confirmed, treatment will be considered based on individual basis. Otherwise, a 2-hour 75 g OGTT should be done between 6-12 weeks postpartum to identify glucose intolerance and T2DM (Blumer et al., 2013).

2.2.9.2.2 Breastfeeding

Women with GDM should be encouraged to breastfeed immediately after labour and for at least six months postpartum due to its benefits for both the mother and infant. Breastfeeding may encourage weight loss and prevent the development of metabolic syndrome and T2DM in the mother (Aune, Norat, Romundstad, & Vatten, 2014; Gunderson et al., 2010; Yasuhi et al., 2017). It can also reduce the risk of neonatal hypoglycaemia and offspring obesity (Cordero, Ramesh, Hillier, Giannone, & Nankervis, 2013; Yan, Liu, Zhu, Huang, & Wang, 2014). Longer duration and more intensive breastfeeding is linked with a lower risk of diabetes in the mother (Gunderson et al., 2015) as well obesity and diabetes in the offspring later in life (Al Mamun et al., 2015).

2.2.9.2.3 Contraception

Exclusive breastfeeding is linked with lactational amenorrhea, a highly effective contraception in the first six months postpartum (Labbok et al., 1997). Women who do not exclusively breastfeed should use other methods for contraception such as birth control pills, the ethinyl estradiol-etonorgestrel ring and patch (Teal & Ginosar, 2007).

2.2.9.2.4 Planning future pregnancies

Women with a history of GDM should plan future pregnancies in consultation with their health-care providers (Gaudier, Hauth, Poist, Corbett, & Cliver, 1992; MacNeill, Dodds, Hamilton, Armson, & VandenHof, 2001). They should be screened for diabetes before conception to confirm normoglycaemia at the time of conception or use treatment if needed. All women should take a folic acid supplement to decrease the risk of congenital anomalies and optimise pregnancy outcomes (Gaudier et al., 1992).

2.3 Nutritional status in Vietnam

Dietary intake during pregnancy has a vital role in the health of a mother and child. A suboptimal diet during pregnancy may affect short- and long-term pregnancy outcomes (Abu-Saad & Fraser, 2010; Fall, 2009). Pregnant women with a diet low in calories or poor in protein are at risk of delivering low birth weight babies (Lumey, 1992), whereas those adhering to a diet high in glycemic load are more prone to GDM (C. Zhang, Liu, et al., 2006). An inadequate intake of iron and zinc may lead to anaemia, preterm labour, low birth weight (Scholl & Hediger, 1994), congenital anomalies, and fetal development (King, 2000). A low calcium status may increase the risk of preeclampsia and maternal deaths (Hofmeyr, Lawrie, Atallah, Duley, & Torloni, 2014), and dietary folate deficiency can cause neural tube and congenital heart defects (De-Regil, Pena-Rosas, Fernandez-Gaxiola, & Rayco-Solon, 2015; van Beynum et al., 2010). A low intake of vitamin D is associated with an elevated risk of low birth weight, childhood adiposity, and poor foetal skeletal development (Crozier et al., 2012; Hewison & Adams, 2010; Miliku et al., 2016). Therefore, it is necessary

for women to have an optimal diet during pregnancy to prevent adverse outcomes for the mother and child.

Over-nutrition in pregnant women is common in high-income nations (Helms, Coulson, & Galvin, 2006; Schieve, Cogswell, & Scanlon, 1998) while under-nutrition during pregnancy is a prevailing problem in less developed countries (Darnton-Hill & Mkparu, 2015; S. E. Lee, Talegawkar, Merialdi, & Caulfield, 2013). Lee et al. conducted a review of dietary intakes of pregnant women in low- and middle-income countries and found that the mean intakes of macronutrients and most essential micronutrients such as iron, zinc, folate, and calcium were below the standard recommendations (S. E. Lee et al., 2013). Poor dietary intakes during pregnancy have been reported in some Asian countries such as India, China, and Thailand (Gao et al., 2013; Gautam, Taneja, Sharma, Gupta, & Ingle, 2008; Sukchan et al., 2010; J. M. Yang et al., 2017). In Vietnam, low intakes of macro- and micro-nutrients in adults and women of reproductive age remain concerning issues (Hoang, 2009; Laillou et al., 2012; National Institute of Nutrition., 2010; P. H. Nguyen et al., 2014; Tu et al., 2014). Results of a national nutrition survey reported that 20% and 70% of adults did not fulfil the national recommendations for energy and micronutrient consumption, respectively (Hoang, 2009). Although non-pregnant women are reported to commonly experience the deficiency of micronutrients such as zinc (67.0%), vitamin B12 (63.8%), folate (54.3%), vitamin B2 (40.4%), vitamin A (27.1%), and iron (24.8%) (Laillou et al., 2012; P. H. Nguyen et al., 2014), data on nutritional status during pregnancy is lacking. As such, studies on maternal dietary intakes in Vietnamese women are needed to understand the current status, develop appropriate interventions, and improve maternal and child health.

2.4 Summary

Gestational diabetes mellitus is increasing worldwide and it is recognised as a significant public health problem. GDM is associated with an increased risk of short- and long-term adverse health outcomes for both mother and offspring. Various risk factors for GDM have been identified such as maternal age, ethnicity, history of GDM,

family history of diabetes, pre-pregnancy BMI and gestational weight gain, dietary factors, and physical activity. The pathophysiology of GDM has been partly elucidated. Different methods for GDM screening and diagnosis have been developed and adopted. However, the prevalence of GDM ranges substantially due to the lack of global consensus on GDM screening and diagnosis, which makes it difficult to compare between or even within countries.

Several previous studies have reported a high prevalence of GDM among the Vietnamese women. These studies, however, have some shortcomings including small sample sizes, recruitment of participants from single hospitals or centres, or use of old criteria for GDM diagnosis. In addition, very few studies have followed up pregnancies until delivery, and investigated maternal lifestyle factors and foetal outcomes in relation to GDM. In particular, no study has evaluated the association between maternal physical activity and GDM, or assessed nutrient intakes during pregnancy. Given the lack of synthesized evidence on GDM in Eastern and Southeastern Asia and a paucity of longitudinal research exploring the relation of GDM to maternal characteristics and pregnancy outcomes, we performed a systematic review and meta-analysis of GDM in this sub-region and conducted a prospective cohort study on the relationship of maternal lifestyle and pregnancy outcomes with GDM in Vietnam.

Chapter 3. METHODOLOGY

3.1 Overview

This chapter presents the methodology used to achieve the study objectives. Detailed methods are described in 8 subsequent sections. Specifically, section 3.2 describes the study design. Section 3.3 gives information on the study settings. Section 3.4 defines participants and sample size calculation. Section 3.5 describes the procedure of data collection while study tools and outcome measurements are presented in section 3.6. Section 3.7 and section 3.8 discuss data management and statistical analysis, respectively. Finally, section 3.9 mentions some aspects of ethical considerations. Some materials described in this chapter have been published in the peer-reviewed journal article (C. L. Nguyen et al., 2017).

3.2 Study design

A multicentre hospital-based prospective cohort study was conducted among pregnant women at 24-28 weeks of gestation from three cities in Vietnam. It is part of a maternal and child health project in Vietnam, in which the relation of GDM to outcomes during pregnancy and at delivery was the central focus of the present research.

3.3 Study settings

The study was conducted in three cities of Vietnam namely Ha Noi, Hai Phong and Ho Chi Minh cities. Ha Noi is the capital of Vietnam located in the North whilst Ho Chi Minh City is the largest and most industrialised city in the South. Vietnam has a long coastline of 3,260 kilometres (Ministry of Foreign and Affairs., 2017), and the coastal city of Hai Phong was included in addition to the two metropolitan cities. For Ha Noi and Hai Phong city, one suburban district from each city was selected - Dong Anh and Vinh Bao district, respectively. Dong Anh has a mixture of industrial zones, traditional handicraft trade villages and agriculture with 23 communes and one town with a population of over 300,000 people covering an area of 182 km^2 (People's

committee of Dong Anh District., 2013). Vinh Bao is a coastal district with a total area of 180 km^2 comprising 29 communes and one town with over 180,000 people and the economy is based on agriculture (People's committee of Vinh Bao District., 2008). For Ho Chi Minh City, two typical urban districts (Tan Phu district and District 2) and one typical suburban district (Hoc Mon district) were chosen. Tan Phu (16.1 km^2) has 11 wards with a population of over 464.000 people while District 2 (49.7 km^2) consists of 11 wards and about 147.000 people. Hoc Mon (109.2 km^2) comprises one town and 11 communes with a population of approximately 422.000 people (Ho Chi Minh City Statistical Office., 2016). Each district has one district hospital that provides health cares for the majority of its citizens in the catchment areas. Moreover, some pregnant women from Tan Phu, Hoc Mon and District 2 may directly visit Hung Vuong hospital, a tertiary level, referral maternity hospital of Ho Chi Minh City, especially if their pregnancies have complicated health problems. Therefore, Hung Vuong hospital was also selected to capture participants from these three districts. A total of six hospitals participated in the study. Figure 2 shows the location of the cities and districts involved in the study.

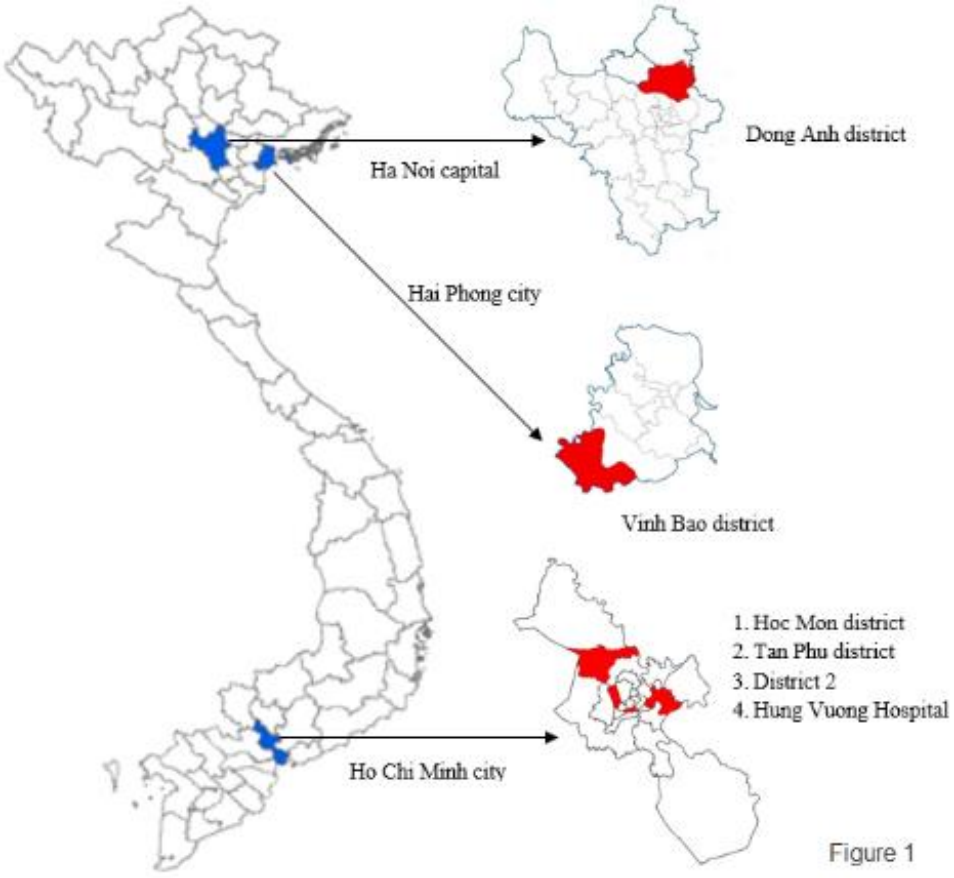

Figure 2. Location of the cohort study

3.4 Participants and sample size calculation

3.4.1 Selection criteria for participants

3.4.1.1 Inclusion criteria:

Participants were pregnant women who satisfied the following criteria:

1) Permanent residents in the study locations;
2) ≥18 years of age;
3) At 24-28 gestation weeks;
4) Singleton pregnancy;
5) Being able to read the information sheet and sign the consent form.

3.4.1.2 Exclusion criteria

Pregnant women who did not satisfy any of the aforementioned criteria were excluded from the study. They were also excluded if they had a serious pre-existing health conditions such as cancers, ischemic heart diseases, and following the advice from their medical doctors because such conditions might prevent them from ongoing participation in the study.

3.4.2 Sample size

As mentioned, this study is a part of a larger project. One of the main objectives of this project is to evaluate the impact of metabolic conditions during pregnancy (GDM) on the breastfeeding outcomes of mothers. An appropriate sample size was calculated based on the assumption that 20% of participants would have GDM diagnosed at 24-28 weeks of gestation (T. S. Tran et al., 2013), and that the rates of exclusive breastfeeding at three months postpartum among mothers with prior gestational hyperglycaemia and those without are 42% and 52%, respectively (Verd, de Sotto, Fernandez, & Gutierrez, 2016). A minimum sample size of 1,662 is required to attain

90% power to detect an expected odds ratio of 0.7 (Verd et al., 2016) between the two groups at 5% level of significance. Supposing a further 20% attrition, withdrawal or subsequent loss to follow up, 2000 pregnant women were targeted for recruitment. Based on the population of three cities (General Statistics Office., 2016), the subsample sizes assigned to Ha Noi, Hai Phong and Ho Chi Minh City were 900, 300, and 800, respectively. Participants were consecutively recruited from the three centres until their desired sampling quotas were reached.

3.5 Study procedure

3.5.1 Screening and recruitment

Recruitment began in August 2015 and ended in July 2016. During that period, all pregnant women from the participating hospitals were consecutively approached and invited to participate in the study if they met the eligible criteria. Participants were consecutively recruited from the three centres until their desired sampling quotas were reached.

3.5.2 Baseline interview

After enrolment, pregnant women who consented to participate in the study were interviewed face-to-face at 24-28 gestation weeks by trained personnel to obtain detailed information on demographic and personal characteristics, dietary intakes, and lifestyle habits including physical activity, cigarette smoking and alcohol drinking. Standard or validated questionnaires for Vietnamese adults were used to collect information.

3.5.3 Discharge interview

At the time of delivery, details including obstetric and neonatal outcomes (e.g. type of delivery, APGAR scores, problems/complications, intensive care treatment, and length of hospital stay) will be recorded. Infants will be weighed to the nearest 10 g

on an electronic scale immediately after birth. Length at birth will be measured on an infantometre. Other physical characteristics such as head, abdominal, and mid upper-arm circumference will be measured within 72 hours after birth to the nearest 0.1 cm using a standardized measuring tape.

The process of collecting data is illustrated in the Figure 3 below.

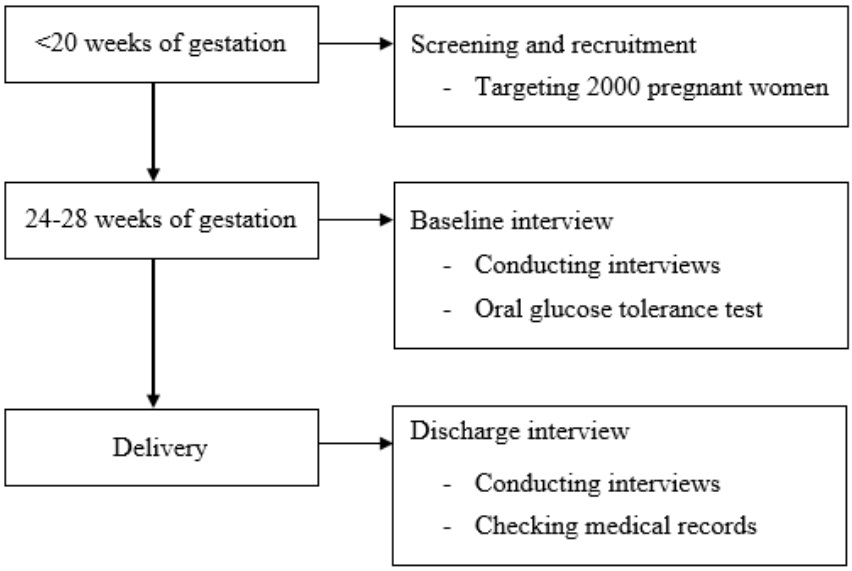

Figure 3. Flow chart of data collection

3.6 Questionnaire and exposure measurements

3.6.1 Description of variables and instruments

The major variables and instruments of the study are presented in the Table 4 below.

Table 4. Description of study variables and instruments

Variables	Instruments
Demographic characteristics: age, gender, education level, marital status, occupation, address, contact phone numbers; family medical history; health outcomes	Structured validated questionnaire

Variables	Instruments
Anthropometrics: height, weight, waist and hip circumferences; blood pressure Infant weight, length, abdominal, head and mid upper-arm circumferences	Portable stadiometer, tape measure, digital weight scale, infantometer, Omron M5-1 electronic sphygmomanometer
Habitual diet during pregnancy	Food Frequency Questionnaire (FFQ) for Vietnamese adults
Physical activity during pregnancy	Pregnancy physical activity questionnaire (PPAQ)
Cigarette smoking and alcohol drinking	WHO STEPS
Fasting glucose and 75-g oral glucose tolerance test	Medical records
Pregnancy outcomes such as stillbirth, preterm, APGAR, birthweight, mode of delivery	Medical records, measurement and data collection sheet

3.6.2 Dietary assessment

A validated and reliable food frequency questionnaire (FFQ) developed specifically for Vietnamese adults was used to determine food consumption and dietary intake of the women at 24-28 weeks gestation (Appendix C.3) (D. V. Tran, Hoang, Nguyen, & Lee, 2013). It consists of a list of 119 common food and beverage items which are organised into 18 groups: 1) alcohol; 2) coffee; 3) tea; 4) fruit juices and soft drinks; 5) soybean products; 6) vegetables; 7) fruits; 8) sweet desserts; 9) cereals; 10) red meat; 11) poultry; 12) offal; 13) fish & seafood; 14) eggs; 15) preserved food; 16) dairy products; 17) seasoning; and 18) supplement. For each food item, participants were asked to report the frequency (times per day, week, or month) and the quantity (number of standardised serves each time) since they became pregnant. Pictures (full size) of commonly used tableware were compiled and used during the interview to determine average portion sizes and average number of servings per meal. Photographs

of the types and amounts of food items such as a set of spoons, cups, and bowls were shown to the participants to aid portion size estimation.

3.6.3 Assessment of physical activity

A validated and reliable pregnancy physical activity questionnaire (PPAQ) for Vietnamese pregnant women was used to assess habitual PA during the past three months before the baseline interview at 24-28 weeks of gestation (Appendix C.3) (Ota et al., 2008). Results of the validated study indicated that the Vietnamese PPAQ was within acceptable reliability and validity. The PPAQ measures the duration, frequency, and intensity of physical activity during pregnancy. It is a semi-quantitative questionnaire that solicits the time spent participating in 32 activities under four domains, including household/caregiving (13 activities), occupational (5 activities), sports/exercise (8 activities), transportation (3 activities) and inactivity (3 sedentary activities). For each activity, respondents are asked to select a category with the nearest amount of time spent per day or per week. The possible duration ranged from 0 to 6 or more hours per day. An open-ended section is appended to allow listing of additional activities not covered.

3.6.4 Assessment of other lifestyle factors

Demographic characteristics include age, gender, level of education, marital status, occupation, resident address, and contact phone numbers. Such information was collected using a structured questionnaire via face-to-face interviews at baseline. Family medical history and health outcomes such as diabetes, previous GDM, prior macrosomia, previous stillbirth, hypertension before 20 weeks, previous history of preeclampsia, were recorded through personal interview at baseline. Information on cigarette smoking was acquired using WHO STEPS questions (World Health Organization., 2008).

Anthropometric assessment: Anthropometric measurements were made during the baseline and discharge interview. A digital scale was used to record weight to the

nearest 100 g. Height was measured using a stadiometer to the nearest 1 mm. Pre-pregnancy weight was retrieved from their medical records. Maternal BMI was calculated using weight and height recorded at baseline (kg/m^2).

Blood pressure: Blood pressure was measured by qualified nurses or physicians using an Omron M5-1 electronic sphygmomanometer. Participants were required to take a short rest, sitting, feet supported on a flat surface and arm supported at heart level. Two consecutive measurements were taken and a mean value was achieved.

3.6.5 Abstraction of clinical data

To determine maternal glucose-metabolic status, all pregnant women were required by the participating hospitals to undergo 75-gram oral glucose tolerance test between 24 and 28 weeks of gestation, by collecting three blood samples at fasting, 60 and 120 minutes. The confirmation of gestational diabetes mellitus was mainly based on the diagnostic criteria of WHO 2013 (World Health Organization., 2013). However, other international diagnostic criteria for GDM such as ADA, IADPSG, European Association for the Study of Diabetes (EASD), and National Institute of Health and Clinical Excellence (NICE) criteria were also used to compare pregnancy outcomes. Obstetric complications during pregnancy were extracted from medical records.

3.7 Data management

Data from the completed questionnaires were coded and entered into Epi-data in which logical errors, missing information, or incorrect coding could be automatically checked. Then, the data sets were transferred to Stata for cleaning and analysis. All variables were checked to detect missing data and outliers. All electronic data were securely stored in a personal computer and backed up at the network R: drive, password protected, and accessible by the chief investigators only. Data were de-identified prior to statistical analysis. Only aggregated data were reported. Hard copy of questionnaires of the collected data were kept in a locked filing cabinet in an office accessible to the investigators only.

3.8 Statistical analysis

Statistical analyses were mainly performed with the Stata version 12 (StataCorp LP, College Station, TX, USA) unless otherwise stated. Firstly, data were pooled and combined across study sites. After data screening and cleaning, summary statistics were applied to describe the profile of participants and to summarise the exposure and outcome variables. The results were presented as numbers and percentage for categorical variables, as mean and SD for normally distributed variables, and as median and percentile values for non-normally distributed variables. Group comparisons were undertaken using chi-square tests or Fisher's exact test for categorical variables, and either t-test/ANOVA or Mann-Whitney U test/Wilcoxon rank-sum test for continuous variables.

Further statistical analyses were performed according to the outcome variables (details are described in related peer-reviewed publications). For instance, fixed and random effects models were used to calculate the summary prevalence of GDM by similar or different diagnostic criteria. For foods that showed a statistically significant test statistic (F statistic) for an ANOVA (e.g., $P<0.05$), Tukey-Kramer test was performed to identify which specific groups had statistically significantly different means from one another. Logistic regressions were used to explore the associations between GDM and pregnancy outcomes. The association between PA and GDM was examined using multivariable logistic regression analyses. A two-sided p values <0.05 was considered statistically significant. Potential confounding factors were selected based on literature review. For instance, to assess the association between physical activity during pregnancy and GDM, possible confounders were maternal age, pre-pregnancy body mass index, blood pressure, passive smoking, and family history of diabetes (Aune et al., 2016; Currie, Woolcott, Fell, Armson, & Dodds, 2014; Dempsey et al., 2004). Another example is the investigation of the relationship between GDM and pregnancy outcomes where potential confounders included maternal age, education, pre-pregnancy body mass index, parity, passive smoking, alcohol drinking, previous GDM, history of previous pregnancy (e.g. macrosomia, stillbirth, preterm birth, cesarean section), family history of diabetes or hypertension, and sex of the infant (J. E. Hirst et al., 2012; Metzger et al., 2008).

3.9 Ethical considerations

The study protocol was approved by the Curtin University Human Research Ethics Committee (approval number: HR32/2015, Appendix D) and the Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number: No. 05/HPUMPRB/2015, Appendix D).

All participants were provided with verbal and written information on the study describing the purpose and their right (Appendix C.1). Written agreement was acquired from each consented participant (Appendix C.2). The participation of the subjects was completely voluntary. Participants could withdraw from the study at any time without prejudice. Each participant had a unique identity number known only to the investigators. All identifiable information of participants was coded and kept confidentially throughout the study and analysis. Aggregated data rather than individual data were reported for statistical and publication purposes. Electronic data were securely saved at Curtin University network drive while original questionnaires were stored at National Institute of Hygiene and Epidemiology, Vietnam. Data will be destroyed after seven years according to the Curtin University data safety and security policy.

Chapter 4. RESULTS AND DISCUSSIONS

4.1 Overview

This chapter presents results and discussions of the research including cohort profile (section 4.2), dietary intake (section 4.3), physical activity and GDM (section 4.4) which were published in international peer-reviewed journals. Section 4.5 presents the associations between GDM and pregnancy outcomes.

1. **Cong Luat Nguyen**, Phung T.H. Nguyen, Tan Khac Chu, et al. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794

   This paper addresses objective 2 (to investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index) and a part of objective 3 (to determine the prevalence of gestational diabetes mellitus).

2. **Cong Luat Nguyen**; Dong Van Hoang; Phung T.H. Nguyen, et al. 2018. Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam. *Nutrients*, 10(8), 1025. https://doi.org/10.3390/nu10081025

   This paper addresses objective 2 (to investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index)

3. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, et al. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol*, 55(9): 955-962. https://doi.org/10.1007/s00592-018-1174-3

This paper addresses objective 4 (to ascertain the association between maternal factors e.g. pre-pregnancy BMI, dietary intake, physical activity, cigarette smoking, alcohol drinking, gestational weight gain and gestational diabetes mellitus).

It is noted that a total of 2030 pregnant women were recruited at 24-28 weeks of gestation and 1909 (94.0%) of them were followed-up until delivery.

4.2 Characteristics of the sample

Related publication:

Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study

This paper addresses objective 2 (to investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index) and a part of objective 3 (to determine the prevalence of gestational diabetes mellitus).

Citation:

Nguyen CL, Nguyen PTH, Chu TK, et al. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794

Link to full text: https://bmjopen.bmj.com/content/7/9/e016794

BMJ Open

Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study

Cong Luat Nguyen,[1] Phung Thi Hoang Nguyen,[2] Tan Khac Chu,[3] Anh Vo Van Ha,[4] Ngoc Minh Pham,[5] Dat Van Duong,[6] Dung Van Do,[2] Hong Kim Tang,[4] Colin W Binns,[7] Andy H Lee[7]

To cite: Nguyen CL, Nguyen PTH, Chu TK, *et al*. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open* 2017;**7**:e016794. doi:10.1136/bmjopen-2017-016794

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2017-016794).

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ABSTRACT

Purpose To determine modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam.

Participants This prospective cohort study included pregnant women seeking prenatal care at six hospitals in three large cities in Vietnam. After enrolment, eligible participants who gave their consent to participate in the study were interviewed at 24–28 weeks' gestation. Glucose testing was conducted and blood pressure was measured during this period. Each participant will be assessed prospectively during their postnatal visits at delivery, 1, 3, 6, 12, 18 and 24 months, and will be followed up for 5 years.

Findings to date Of 2248 eligible pregnant women, 2030 were recruited (participation rate 90.3%) between August 2015 and July 2016. All participants completed the baseline assessment. Their mean (SD) age was 27.6 (5.3) years. The mean pre-pregnancy body mass index (BMI) was 20.2 (SD 2.6) kg/m^2, with nearly two-thirds of participants having a normal pre-pregnancy BMI (18.5 to <23.0 kg/m^2) and one-quarter being underweight (pre-pregnancy BMI <18.5 kg/m^2). Overweight or obese mothers (pre-pregnancy BMI ≥23.0 kg/m^2) accounted for 12.8%. No pregnant women reported smoking during their pregnancy while 13.4% of them had continued drinking. 22.8% of participants had hyperglycaemia. Their mean systolic blood pressure was 105.6 (SD 8.2) mm Hg, and diastolic blood pressure was 67.4 (SD 7.5) mm Hg.

Future plans The relationships of maternal lifestyle and nutritional status with the health outcomes of pregnancy, postpartum maternity and infants will be analysed. Meanwhile, participants will be closely tracked to minimise loss to follow-up.

Strengths and limitations of this study

- This is the first multicentre, prospective cohort study of maternal and child health in Vietnam, with a large sample size over a relatively long period of follow-up.
- The study investigates multiple modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam.
- All questionnaires used for data collection have been validated for Vietnamese people.
- Potentially high rates of loss to follow-up in more affluent settings.
- Lack of participants from rural and remote areas.

INTRODUCTION

Pregnancy and the first 2 years after giving birth are critical periods for mother and child health. Maternal lifestyle and dietary intake are known to be associated with metabolic disorders, such as gestational diabetes mellitus (GDM). These conditions increase the risk of adverse pregnancy and infant health outcomes.[1 2] In particular, overeating or sedentary behaviour during pregnancy has been positively associated with a risk of GDM.[3–6] Development of maternal GDM increases the risk of adverse health in mothers (gestational hypertension and pre-eclampsia, subsequent type 2 diabetes),[2] in infants (stillbirth, macrosomia, neonatal hypoglycaemia)[7] and in children (obesity, diabetes, hypertension and cardiovascular diseases).[8]

Vietnam is a middle-income country in Southeast Asia with a population of over 90 million.[9] It is undergoing epidemiological transition. A high burden of infectious diseases remains and the prevalence of chronic non-communicable diseases is increasing. The prevalence of overweight and obesity (BMI ≥23.0 kg/m^2) among Vietnamese adults has risen from 11.7% to 16.3% between 2000 and 2005.[10] The prevalence of GDM is reported to range from 6.1% to 20.3%, and women with GDM tend to deliver

preterm. Thus the newborns have a higher incidence of neonatal hypoglycaemia, and labour induction is more prevalent.[11] Although breastfeeding has significant benefits for infants and mothers,[12] many Vietnamese people underestimate its advantages. The rate of exclusive breastfeeding during the first 6 months of life is low and decreased from 25.0% in 2000 to 17.0% in 2011.[13] Notably, mothers with hyperglycaemia during pregnancy tend to have a high rate of exclusive breastfeeding cessation.[14]

Few prospective cohort studies of mothers and their infants have been conducted in Vietnam,[11 15–17] and the few which are underway are being carried out in single provinces with limited outcomes being investigated. Moreover, the available data on the relationship between maternal lifestyle, nutrition and adverse pregnancy, postpartum and child health outcomes are sparse. This research is the first multicentre prospective cohort study, representative of the Vietnamese population, which investigates broad aspects of modifiable maternal risk factors and their health consequences. The main objectives of this study are:

1. To investigate the lifestyle, nutritional and metabolic status of pregnant women in Vietnam, including physical activity, smoking, alcohol drinking, dietary intake, pre-pregnancy body mass index (BMI) and gestational weight gain.
2. To ascertain the impact of aforementioned maternal factors on (a) obstetric complications (eg, GDM, pre-eclampsia, pregnancy-induced hypertension); (b) pregnancy outcomes (eg, preterm delivery, caesarean section, low birth weight, macrosomia and postpartum haemorrhage) and (c) postpartum maternal and child health.
3. To examine the association between breastfeeding and (a) maternal metabolic conditions, including GDM; (b) postpartum maternal and infant health status.
4. To determine the relationship between antenatal and postnatal depressive symptoms and (a) pregnancy and birth outcomes; (b) breastfeeding intention and initiation; (c) the intensity and duration of breastfeeding; (d) infant care and adverse home events; (e) postpartum maternal and infant health status.

COHORT DESCRIPTION

Study settings

This ongoing prospective cohort study is conducted in three cities of Vietnam—namely, Ha Noi, Hai Phong and Ho Chi Minh cities. Ha Noi is the capital of Vietnam located in the north while Ho Chi Minh City is the largest and most industrialised city in the south. Hai Phong is a coastal city, located in the Red River delta. For Ha Noi and Hai Phong cities, one suburban district from each city was selected—the Dong Anh and Vinh Bao districts, respectively. Dong Anh has 23 communes and one town with a population of over 300 000 people.[18] Vinh Bao is a coastal district comprising 29 communes and one town with over 180 000 people.[19] For Ho Chi Minh City, two typical urban districts (Tan Phu district and District 2) and one typical suburban district (Hoc Mon district) were chosen. Tan Phu (16.1 km^2) has 11 wards with a population of over 464 000 people while District 2 (49.7 km^2) consists of 11 wards and about 147 000 people.[20] Hoc Mon (109.2 km^2) comprises one town and 11 communes with a population of approximately 422 000 people.[20] Each district has one district hospital that provides healthcare for the majority of its citizens in the catchment areas. Moreover, some pregnant women from Tan Phu, Hoc Mon and District 2 may directly visit Hung Vuong Hospital, a large provincial obstetric hospital, especially if their pregnancies have complications. Therefore, Hung Vuong Hospital was also selected to obtain details of participants from these three districts. A total of six hospitals participated in the study. Figure 1 shows the location of the centres and districts involved in the study.

Participants and eligibility criteria

Participants were pregnant women who satisfied the following criteria: (1) permanent residents in the study locations; (2) ≥18 years of age; (3) at 24–28 weeks' gestation; (4) singleton pregnancy; (5) not having a serious pre-existing health condition, such as cancer, ischaemic heart disease according to information from their medical doctors; (6) able to read the information sheet and sign the consent form.

Sample size

The sample size calculation was based on testing the hypothesis that mothers with gestational hyperglycaemia (primary exposure) have a lower rate of exclusive breastfeeding at 3 months post partum (primary outcome). Assuming that 20% of participants would have gestational hyperglycaemia diagnosed at 24–28 weeks of gestation,[21] and that the rates of exclusive breastfeeding at 3 months post partum among mothers with prior gestational hyperglycaemia and those without are 42% and 52%, respectively,[14] a minimum sample size of 1662 is required to attain 90% power to detect an expected OR of 0.7[14] between the two groups[22] at 5% level of significance. We assumed a further 20% attrition, owing to withdrawal or subsequent loss to follow-up, and thus 2000 pregnant women were targeted for recruitment. Based on the population of three centres,[23] the subsample sizes assigned to Ha Noi, Hai Phong and Ho Chi Minh City were 900, 300 and 800, respectively. Participants were consecutively recruited from the three centres until their desired sampling quotas were reached.

Data collection

Baseline and postpartum follow-ups of study participants are currently being implemented. The study procedure is summarised in figure 2.

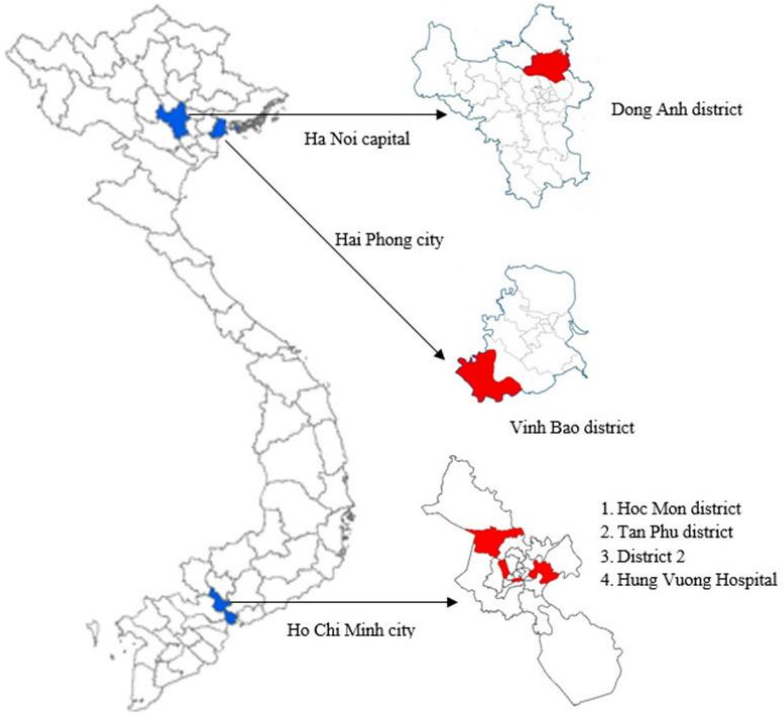

Figure 1 The location of study centres.

Recruitment

Recruitment began in August 2015 and ended in July 2016. During that period, all pregnant women from the participating hospitals were consecutively approached and invited to participate in the study if they met the eligible criteria. According to the Vietnam 2014 Multiple Indicator Cluster Survey, nearly 94% of the pregnant women delivered in hospitals.[24] Gestational age was determined using ultrasound during the first trimester and was available from medical records. A total of 2248 pregnant women who met the inclusion criteria were invited, 218 (9.7%) refused participation, and 2030 (90.3%) consented to take part in the study. No significant difference in mean age was found between participants and non-participants (p=0.991).

Baseline interview at 24–28 gestation weeks

After enrolment, pregnant women were interviewed face to face by trained personnel to obtain detailed information on demographic and personal characteristics, dietary intakes, lifestyle habits including physical activity, cigarette smoking and alcohol drinking, antenatal depressive symptoms and attitudes to breastfeeding. Standard or validated questionnaires for Vietnamese adults were used to collect information.

Dietary assessment

The Food Frequency Questionnaire for Vietnamese adults was applied to investigate habitual diet.[25] It consists of various food and beverage items grouped into categories, with frequencies and quantities consumed recorded in detail. The frequency recorded is either per day, per week, per month or never, with a standard portion or utensil defined for each food/beverage item listed.

Physical activity assessment

The Pregnancy Physical Activity Questionnaire (PPAQ) was used to examine physical activity.[26] The PPAQ measures the duration, frequency and intensity of physical activity during pregnancy. It is a semiquantitative questionnaire that asks about the time spent participating in 32 activities, including household/caregiving (13 activities), occupational (five activities), sports/exercise (eight activities), transportation (three activities) and inactivity (three sedentary activities). For each activity, respondents are asked to select a category with the closest amount of time spent per day or per week. The possible duration ranged from 0 to 6 or more hours a day. An open-ended section is appended to allow listing of additional activities not covered.

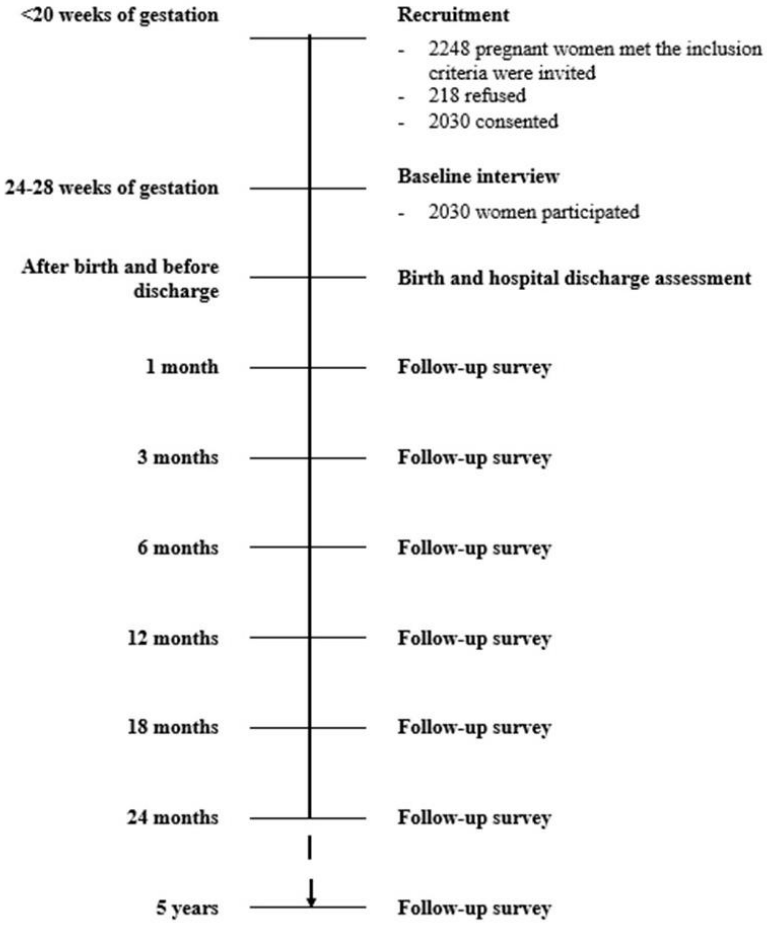

Figure 2 Recruitment and interview schedule planned.

Maternal depressive symptoms assessment

The Edinburgh Postnatal Depression Scale (EPDS) was used.[27] EPDS is a self-administered questionnaire widely used for research into antenatal and postnatal depressive symptoms to explore a woman's feelings within the past 7 days during the antenatal or postnatal period. It comprises 10 items rated on a four-point scale (from 0 to 3), reflecting the degree of agreement, with the total score ranging from 0 to 30.

Assessment of attitude to infant feeding

The Iowa Infant Feeding Attitude Scale was applied to study the breastfeeding attitudes of pregnant women.[28–30] It contains 17 items with a five-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). Approximately half the items are worded favourably towards breastfeeding and the remaining items favour formula feeding. Items favouring formula feeding are reverse-scored and a total score is computed by summing all items. Total attitude scores range from 17 to 85, with higher scores reflecting attitudes more positive towards breastfeeding. Total scores are grouped into three categories: positive towards breastfeeding (70–85), neutral (49–69) and positive towards formula feeding (17–48).

Assessment of smoking and alcohol drinking

Information on cigarette smoking and consumption of alcohol was acquired using WHO STEPS questions.[31]

Anthropometric assessment

Anthropometric measurements were made during the baseline interview. A digital scale was used to record weight to the nearest 100 g. Height was measured using a stadiometer to the nearest 1 mm. Data on pre-pregnancy weight, retrieved from medical records, were likely to be self-reported. Total gestational weight gain was estimated by subtracting the early first trimester weight from the last measured weight before delivery. Maternal BMI was

calculated using weight and height recorded at baseline (kg/m^2).

Clinical assessment

To determine maternal glucose-metabolic status, all pregnant women were required by the participating hospitals to undergo a 75 g oral glucose tolerance test between 24 and 28 weeks of gestation; three blood samples were collected at fasting, 60 and 120 min. Confirmation of gestational diabetes mellitus was based on the 2013 diagnostic criteria of the World Health Ogarnization.[32] To determine gestational hypertension, blood pressure was measured at the same time as the glucose tolerance test by qualified nurses or physicians using an Omron M5-1 electronic sphygmomanometer according to the WHO procedure. Participants were required to take a short rest (15 min), sitting, feet supported on a flat surface and arm supported at heart level. Two consecutive measurements were taken 3 min apart and a mean value was obtained. WHO diagnostic criteria for gestational hypertension were used.[1] Information on pre-eclampsia was obtained from medical records. Details of obstetric complications during pregnancy were extracted from medical records.

Birth and hospital discharge assessment

At the time of delivery, details including obstetric and neonatal outcomes (eg, type of delivery, Apgar scores, problems/complications, intensive care treatment and length of hospital stay) will be recorded. Infants will be weighed to the nearest 10 g on an electronic scale immediately after birth. Length at birth will be measured on an infantometre. Other physical characteristics, such as head, abdominal and mid upper-arm circumference, will be measured within 72 hours after birth to the nearest 0.1 cm using a standardised measuring tape.

Mothers will be asked about breastfeeding initiation, prelacteal feeds (if any) and breastfeeding self-efficacy at this time using a standardised breastfeeding questionnaire[15 33] and the Breastfeeding Self-Efficacy Scale (BSES).[30] The BSES is a 33-item, self-report instrument developed to measure breastfeeding confidence. The items are preceded by the phrase 'I can always' and anchored with a five-point Likert scale, where 1=not at all confident and 5=always confident. All items are presented positively, and scores are summed to produce a range from 33 to 165. A higher score indicates a stronger confidence in breastfeeding. They will be also interviewed about depressive symptoms using the EPDS.

Follow-up surveys

All mothers will be assessed during their postnatal visits at delivery, 1, 3, 6, 12, 18 and 24 months post partum. Detailed information on infant feeding practices, infant illnesses, anthropometrics, maternal depressive symptoms, maternal diet and physical activity, and other health problems of both mothers and infants will be sought at subsequent follow-ups of the cohort. The follow-up interviews will be conducted at community health centres or at the mother's home. A 48-hour food diary will be used to record the consumption of breast milk, formula, foods and beverages by the infants at 1, 3, and 6 months of age. Symptoms of illness of the child such as fever, infection and diarrhoea, and length of hospitalisation will also be documented in detail based on both self-report and/or medical records.

A follow-up study on these children up to 5 years of age is planned and subject to funding availability.

Statistical analysis

Data will be pooled and combined across study sites. After data screening and cleaning, descriptive statistics will be used to characterise study participants. Group comparisons will be undertaken using X^2 tests for categorical variables, and either t tests/analysis of variance or Mann-Whitney U tests for continuous variables. Independent variables include demographic factors, medical history and maternal lifestyle such as dietary intake, physical activity, smoking and alcohol drinking. The main dependent variables of interest are gestational diabetes status, pregnancy outcomes (eg, stillbirth, pre-eclampsia), delivery outcomes (eg, low birth weight, macrosomia, preterm birth, caesarean section), breastfeeding duration, depressive symptom scores, gestational weight gain and postpartum weight retention, infant growth and child health conditions.

Logistic or Poisson regression models will be fitted to investigate the relationships between selected exposures and binary or discrete outcomes measured at a single point in time. Mixed regression analyses with random effects will be undertaken to assess the association between plausible risk factors and the longitudinal outcomes, such as depressive symptom scores and infant weight, while accounting for the repeated measures and clustering of subjects within study sites (hospitals). Kaplan-Meier test and Cox regression will be performed to determine the effects of influencing factors on the breastfeeding duration. Crude and adjusted coefficients or OR estimates and associated 95% confidence intervals will be reported for regression analyses, and adjusted hazard ratios for survival random-effects models.

Potential confounding variables will be selected with reference to the literature and modelling strategies.[34 35] For instance, to assess the association between gestational diabetes and rates of exclusive breastfeeding, possible confounders might be parity, delivery type, birth weight,[14] in addition to demographic factors, energy intake, energy expenditure and other covariates. Effect modification will also be taken into account in the statistical modelling. All statistical analyses will be performed using the SPSS package version 22 (IBM, Armonk, New York, USA).

Ethics and dissemination

The project has been approved by the Curtin University human research ethics committee (HR32/2015) and the Hai Phong University of Medicine and Pharmacy human research ethics committee (No 05/HPUMPRB/2015).

All participants have been provided with verbal and written information on the study describing its purpose and their requirements. Each participant has a unique ID number with basic information, including name, address, and phone numbers of themselves and partners so that they can be followed up later. Participants could withdraw from the study at any time without prejudice. All identifiable information of participants has been coded and securely stored. Study results will be published in academic journals.

FINDINGS TO DATE

Baseline characteristics of participants are summarised in table 1.

The 2030 pregnant women had a mean age of 27.6 (SD 5.3) years (range 18–48 years). The majority (60.6%) of women were in the age group 25–35 years in all locations. Almost all of the subjects were married (99.3%). Manual work and farming were the main occupations (54.9%) of the participants, followed by office and technical staff (22.5%). More than 60% of the mothers had completed high school and over one-third of them had a degree from college or university. Women in Ha Noi had the highest level of advanced educational level (50.9%) while Ho Chi Minh City had the highest rate of low educational level (18.5%). A majority (61.8%) of the participants had a normal pre-pregnancy BMI (18.5 to <23 kg/m^2) and mean BMI was 20.2 kg/m^2 (SD 2.6). The prevalence of normal BMI was similar among the three centres. However, Ho Chi Minh City had a substantially higher rate of overweight and obesity (20.8%) while Hai Phong city had a higher rate of underweight (31.7%). About one-quarter of the pregnant women were underweight. This rate was similar to a study in Ha Nam (26%)[36] and in Nha Trang (26.1%).[16] No pregnant women smoked during pregnancy but more than one-half were exposed to passive smoking at home. The overall prevalence of alcohol consumption during pregnancy was 13.4% and the highest proportion of women consuming alcohol was found in Ha Noi with 18.0%.

Very few participants had a history of hypertension or pre-eclampsia in each site. During their last pregnancy, the rate of GDM was 1.4%, birth defects (1.8%), macrosomia (3.6%) or preterm delivery (6.3%). The reported rates of stillbirth, abortion and caesarean section were 10.4%, 17.9%, and 21.5%, respectively.

Analysis of the blood test of 2023 participants (excluding seven patients with diabetes before pregnancy) showed that the prevalence of hyperglycaemia was 22.8%, slightly lower than found in a previous cohort study in southern Vietnam.[21] The hyperglycaemia rate was highest in Ho Chi Minh City (31.0%), followed by Hai Phong (19.9%) and Ha Noi (16.4%). The mean systolic blood pressure in all centres was 105.6 (SD 8.2) mm Hg, and the mean diastolic blood pressure was 67.4 (SD 7.5) mm Hg.

Data on physical activity, dietary pattern, breastfeeding and antenatal depressive symptoms are currently being analysed and results will be presented in subsequent articles.

STRENGTHS AND LIMITATIONS

One major strength of this multicentre, prospective cohort study in Vietnam is its large number of patients, followed up over a relatively long period; it is conducted in two principal regions of Vietnam, thus representing the urban Vietnam population. The few previous prospective cohort studies undertaken in Vietnam were either conducted in a single province,[11 15–17 37] or their sample sizes were small[15 17] or their follow-up times were short.[11 17]

Another strength is that it investigates a variety of modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam. Unlike previous prospective studies in Vietnam,[11 17 37] this project examines lifestyle, nutritional and metabolic status of pregnant women, including physical activity, smoking, alcohol drinking, dietary intake, pre-pregnancy BMI, gestational weight gain, antenatal and postnatal depressive symptoms and breastfeeding. It will also ascertain the impact of maternal factors (eg, pre-pregnancy BMI, dietary intake, physical activity, gestational weight gain) on obstetric complications (eg, gestational diabetes mellitus, pre-eclampsia, pregnancy-induced hypertension), pregnancy outcomes (eg, preterm delivery, caesarean section, low birth weight, macrosomia and postpartum haemorrhage), postpartum health status (eg, postnatal depressive symptoms, morbidity) and child health and growth for at least 2 years.

The results of our study will provide new evidence on the impact of diet and physical activity on delivery and postpartum health outcomes in Vietnamese women, which can be compared with findings from other developing and developed countries. The research findings will provide significant information for the development of guidelines, policy planning and advocacy, and can be used to formulate appropriate intervention programmes to improve maternal and child health in Vietnam. In addition, all questionnaires used for data collection have been validated for the Vietnamese people, thereby increasing the accuracy of the information.

This study has several weaknesses. First, pregnant women were recruited from hospitals, which may present some selection bias. However, the participation rate was high (90.3%) and thus selection bias should be negligible. Second, recall errors and bias in the assessments of physical activity and dietary intake cannot be ruled out. Nevertheless, we minimise these impacts by using validated questionnaires and experienced interviewers. Third, although contact information of participants and their partners, such as addresses and mobile phone numbers have been recorded, a high rate of attrition in an industrialised city like Ho Chi Minh City is expected. This limitation is reduced by maintaining a regular good relationship with participants during the follow-up. Finally, although farming respondents are recruited from

Table 1 Baseline characteristics of participants

Variables	Ha Noi (n_1=905) n (%)	Hai Phong (n_2=298) n (%)	Ho Chi Minh (n_3=827) n (%)	Total (n=2030) n (%)
Age (years)				
<25, (n (%)	346 (38.2)	97 (32.6)	194 (23.5)	637 (31.4)
25–35, n (%)	499 (55.1)	178 (59.7)	553 (66.9)	1230 (60.6)
>35, n (%)	60 (6.6)	23 (7.7)	80 (9.7)	163 (8.0)
Mean (SD)	26.6 (5.0)	27.4 (5.4)	28.6 (5.3)	27.6 (5.3)
Marital status (married)	902 (99.7)	294 (98.7)	819 (99.0)	2015 (99.3)
Occupation				
Famers	194 (21.4)	44 (14.8)	58 (7.0)	296 (14.6)
Workers	303 (33.5)	139 (46.6)	376 (45.5)	818 (40.3)
Office and technical staff	226 (25.0)	44 (14.8)	186 (22.5)	456 (22.5)
Sales worker	35 (3.9)	10 (3.4)	74 (8.9)	119 (5.9)
Housewife/unemployed	147 (16.2)	61 (20.5)	133 (16.1)	341 (16.8)
Educational level				
Under secondary	15 (1.7)	3 (1.0)	153 (18.5)	171 (8.4)
Secondary	164 (18.1)	98 (32.9)	289 (34.9)	551 (27.1)
High school	265 (29.3)	88 (29.5)	172 (20.8)	525 (25.9)
College/university	461 (50.9)	109 (36.6)	213 (25.8)	783 (38.6)
Parity				
0	361 (39.9)	105 (35.2)	323 (39.1)	789 (38.9)
1	306 (33.8)	110 (36.9)	340 (41.1)	756 (37.2)
≥2	238 (26.3)	83 (27.9)	164 (19.8)	485 (23.9)
Body mass index (BMI) before pregnancy (kg/m^2)* (n=2010)				
Low (<18.5)	244 (27.0)	88 (31.7)	177 (21.4)	509 (25.3)
Normal (18.5 -<23.0)	587 (64.9)	178 (64.0)	478 (57.8)	1243 (61.8)
High (≥23.0)	74 (8.2)	12 (4.3)	172 (20.8)	258 (12.8)
Mean (SD)	19.8 (2.3)	19.5 (2.2)	20.8 (2.8)	20.2 (2.6)
History of previous pregnancy (n=1241)				
GDM	1 (0.2)	1 (0.5)	15 (3.0)	17 (1.4)
Hypertension	0 (0.0)	0 (0.0)	4 (0.8)	4 (0.3)
Pre-eclampsia	4 (0.7)	0 (0.0)	3 (0.6)	7 (0.6)
Preterm birth	43 (7.9)	8 (4.1)	27 (5.4)	78 (6.3)
Macrosomia	29 (5.3)	4 (2.1)	12 (2.4)	45 (3.6)
Birth defects	13 (2.4)	3 (1.6)	6 (1.2)	22 (1.8)
Caesarean section	135 (24.8)	18 (9.3)	114 (22.6)	267 (21.5)
Stillbirth	100 (11.1)	37 (12.4)	75 (9.1)	212 (10.4)
Abortion	207 (22.9)	46 (15.4)	110 (13.3)	363 (17.9)
History of participant's family				
Diabetes	38 (4.2)	6 (2.0)	84 (10.2)	128 (6.3)
Hypertension	74 (8.2)	36 (12.1)	197 (23.8)	307 (15.1)
Smoking and drinking during pregnancy				
Active smoking	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Passive smoking	481 (53.1)	150 (50.3)	439 (53.1)	1070 (52.7)
Drinking	163 (18.0)	29 (9.7)	80 (9.7)	272 (13.4)

Continued

Table 1 Continued

Variables	Ha Noi (n_1=905) n (%)	Hai Phong (n_2=298) n (%)	Ho Chi Minh (n_3=827) n (%)	Total (n=2030) n (%)
Blood glucose test (n=2023)				
Fasting (mean, SD)	4.4 (0.5)	4.4 (0.7)	4.5 (0.4)	4.5 (0.5)
1-Hour 75 g OGTT (mean, SD)	7.2 (1.8)	6.9 (1.6)	8.4 (1.8)	7.6 (1.9)
2-Hour 75 OGTT (mean, SD)	6.4 (1.5)	6.1 (1.3)	7.3 (1.5)	6.7 (1.6)
Hyperglycaemia†	148 (16.4)	59 (19.9)	255 (31.0)	462 (22.8)
Blood pressure				
Systolic, mm Hg (mean, SD)	105.0 (7.3)	107.0 (8.3)	105.8 (9.0)	105.6 (8.2)
Diastolic, mm Hg (mean, SD)	64.9 (6.4)	64.3 (6.1)	71.3 (7.3)	67.4 (7.5)
Pulse, bpm (mean, SD)	84.3 (9.3)	79.3 (6.0)	97.0 (9.9)	88.7 (11.5)

Results are shown as number (%) unless stated otherwise.
*BMI cut-off for Asian population was used.[38]
†Hyperglycaemia was classified by WHO 2013.[32]
GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

suburban districts, they may not represent rural women in the country.

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Collaborators There is room for future joint studies. This study will follow-up mothers and their babies until 2 years post partum. This duration can be extended to investigate the effects of maternal factors on the health problems of mothers and their children later in life. In addition, the study is currently performing in two regions (Red River Delta and Southeast), while Vietnam has six socioecological regions. It can be expanded into other regions to increase the sample size and representation. Therefore, the study welcomes all researchers who have the same objectives together with available funding. Study proposals must be submitted to the study research team for review and approval.

Contributors CLN, PTHN, TKC, and AWH participated in the study design and data collection. CLN wrote the draft and edited the manuscript. TKC performed the baseline analysis. NMP provided expert advice on the draft of the manuscript. DVDu, DVDo, HKT, AHL, and CWB were the study supervisors and involved in all aspects of the study. All the authors revised the article and approved the final version to be published.

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Competing interests None declared.

Patient consent Obtained.

Ethics approval The study was approved by the Curtin University human research ethics committee (approval number: HR32/2015) and the Hai Phong University of Medicine and Pharmacy human research ethics committee (approval number: 05/HPUMPRB/2015).

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Data sharing statement Researchers can access to the cohort data by sending us an applicationvia email () for discussion andapproval at the research team meeting.

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4.3 Dietary intake during pregnancy in Vietnam

Related publication:

Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam

This paper addresses objective 2 (to investigate the lifestyle and nutritional status of pregnant women in Vietnam, including physical activity, cigarette smoking, alcohol drinking, dietary intake, and pre-pregnancy body mass index)

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Article

Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam

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Abstract: Inadequate intake of nutrients during pregnancy has been associated with poor pregnancy and infant outcomes; however, evidence remains limited in low-resource settings in Asia. This paper assessed food, macronutrient, and micronutrient intakes among 1944 Vietnamese pregnant women. Dietary information was collected via an interviewer-administered food frequency questionnaire, and nutrient intakes were estimated using the Vietnamese food composition tables. The levels of nutrient intakes were evaluated against the Vietnamese recommended nutrient intakes (RNI) for pregnancy. The diet profiles were reported as means and percentages. The average daily food intakes across socio-demographic factors were compared using ANOVA, with adjustment for multiple comparisons by the Tukey–Kramer test. Rice, fruits, and vegetables were the main food sources consumed. The mean energy intake was 2004 kcal/day with 15.9%, 31.8%, and 52.2% of energy deriving from proteins, fats, and carbohydrates, respectively. Just over half of the women did not meet the RNI for total energy intake. The intakes of essential micronutrients including folate, calcium, iron, and zinc were below the RNI, and almost all pregnant women failed to meet the recommendations for these micronutrients. The associations of maternal age, education, and pre-pregnancy body mass index with nutrient intakes varied across the nutrient subgroups. Targeted programs are needed to improve nutrient intakes in Vietnamese pregnant women.

Keywords: dietary intake; food intake; nutrients; macronutrients; micronutrients; pregnancy; Vietnam

1. Introduction

Maternal diet during pregnancy plays a vital role in maternal and child health. Both undernutrition and overnutrition during pregnancy are associated with an increased risk of adverse pregnancy outcomes [1,2], obesity, and chronic disease in adult life [3,4]. While overnutrition

and obesity during pregnancy are common in developed countries [5,6], undernutrition among pregnant women including low intakes of macro- and micronutrients remains a challenge in developing nations [7,8]. A recent review indicated that the mean intakes of macronutrients and of the most essential micronutrients during pregnancy in low- and middle-income countries, including folate, iron, calcium, and zinc, were below the recommendations of the Food and Agriculture Organization of the United States and World Health Organization (WHO) [7]. Poor maternal nutrition has been documented in some Asian countries including China, India, Bangladesh, and Thailand [9–15].

Evidence suggests that inadequate intakes of macro- and micronutrients during pregnancy may cause adverse health outcomes in both mothers and their infants. Energy deficiencies and protein restriction are linked to low birth weight [16], while a high dietary glycemic load is associated with an increased risk of gestational diabetes mellitus [17]. A low vitamin D status may lead to low birth weight, increased childhood adiposity, or poor foetal skeletal development [18–20]. Folate deficiency during the periconceptional period is associated with an increased risk of neural tube defect [21] or congenital heart defects [22], and an inadequate calcium intake is known to elevate the risk of pre-eclampsia and maternal deaths [23]. Low intakes of important minerals such as iron and zinc have been associated with anaemia, low birth weight, preterm delivery [24], congenital anomalies, and fetal growth retardation [25]. As such, information about maternal diet during pregnancy would be useful for developing appropriate interventions to improve the health and well-being of mothers and children.

Although Vietnam has made significant progress in maternal nutrition, deficiencies of macro- and micronutrients in adults and women of reproductive age (WRA) are still a public health issue [26–30]. According to the most recent national nutrition survey in 2009, 20% and 70% of the Vietnamese adults did not meet the recommendations for energy and most micronutrients intakes, respectively [26]. The prevalence of inadequate intakes of most micronutrients among WRA was high, as shown for zinc (67%), vitamin B12 (63.8%), folate (54.3%), vitamin B2 (40.4%), vitamin A (27.1%), and iron (24.8%) [28,29]. Given that approximately 1.5 million babies are born every year in Vietnam [31], with nearly 12% of preterm births [32] and nearly 25% of children under five years of age being stunted [33], investigating the nutrition profiles of women during pregnancy is envisaged to uncover elements for future research and practice. However, to the best of our knowledge, there has been no study on maternal dietary intakes during pregnancy in Vietnam. The objective of this study was to assess the food, macronutrient, and micronutrient intakes of Vietnamese pregnant women.

2. Materials and Methods

2.1. Study Design and Population

This study used baseline data of a large prospective cohort study in Vietnam. The details of the study protocol have been published elsewhere [34]. Briefly, eligible pregnant women were recruited from six hospitals at prenatal care visits during early pregnancy in three metropolitan cities of Vietnam, namely, Ha Noi, Hai Phong, and Ho Chi Minh City. The participants were informed of the study purpose and procedure before they were asked for informed consent. During August 2015 and July 2016, the eligible participants were invited to attend a face-to-face interview at 24–28 weeks of gestation to provide information on their lifestyle, including dietary intake, physical activity, smoking, socio-demographics, and medical history.

2.2. Dietary Assessment

Information on dietary intakes was collected by trained interviewers using a modified version of the Food Frequency Questionnaire (FFQ) that had been validated for use in Vietnamese adults [35]. The FFQ includes a list of 119 common food and beverage items which are organized into 18 groups: (1) alcohol; (2) coffee; (3) tea; (4) fruit juices and soft drinks; (5) soybean products; (6) vegetables; (7) fruits; (8) sweet desserts; (9) cereals; (10) red meat; (11) poultry; (12) offal; (13) fish & seafood; (14) eggs; (15) preserved food; (16) dairy products; (17) seasoning; (18) supplement. For each food item, the participants were

asked to report the frequency (times per day, week, or month) and the quantity (number of standardized servings each time) since they became pregnant. Pictures (full size) of commonly used tableware were compiled and used during the interview to determine the average portion sizes and average number of servings per meal. Photographs of the types and amounts of food items, such as a set of spoons, cups, and bowls, were shown to the participants to aid portion size estimation.

The amounts of foods (e.g., meat, fruits, and vegetables) consumed were estimated using standardized portion sizes and converted into in grams per day. The daily intakes of macronutrients (carbohydrates, proteins, fats, and calories) and micronutrients (vitamins and minerals) were calculated using an ad-hoc computer algorithm, by referring to the Vietnamese food composition tables [36]. For calculating each nutrient intake for an individual, the consumption of a single food or food groups was multiplied by the corresponding average nutrient content; we then summed all the amounts from the previous calculations to achieve the total nutrient intake, as shown in the following equation: Intake (i) = c × cereal nutrient (i) + v × vegetable nutrient (i) + f × fruit nutrient (i) + s × soy nutrient (i) + m × meat nutrient (i) + sf × seafood nutrient (i) + e × egg nutrient + d × dairy nutrient + sw × sweet nutrient + b × beverage nutrient ('i' denotes each nutrient, and 'c', 'f', 's', 'm', 'sf', 'e', 'd', 'sw', and 'b' stand for intakes of cereals, vegetable, fruit, soy foods, red meat and poultry, fish and seafood, egg, dairy, sweet desserts, and fruit juice or soft drinks, respectively). Subgroup classifications of fruits and vegetables were presented according to the part of plant consumed [37]. The recommended nutrient intakes (RNI) from the latest National Guidelines on Nutrition for Pregnant Women and Breastfeeding Mothers were used as reference values [38]. We adopted the national recommendation of total energy intake for women with light physical activity during pregnancy because approximately 71% of the participants engaged in light physical activity. The bioavailability levels of iron and zinc were assumed on the basis of the national guidelines on recommended nutrient intakes (RNI) for pregnant women used as a standard reference [38]. A high bioavailability of iron was defined as the intake of vitamin C >75 mg/day (183.4 mg/day in our study), while a medium bioavailability of zinc was defined as a moderate intake of proteins from animals or fish. Intakes below the RNI were considered inadequate. Since most vitamin D is synthesized endogenously, the data from the food sources is presented, but no comments on adequacy can be made. The sources of folate in the diet vary considerably in bioactivity, and, while data are presented for protection against neural tube defects, supplementation with folic acid is recommended for all pregnant women [39].

2.3. Assessment of Other Variables

Socio-demographic characteristics, including age, marital status, occupation, education, parity, and medical history were collected through a structured interview. Age was divided into four groups: <25, 25–29, 30–34, and ≥35 years old. Education was categorized into three categories based on the highest grade level completed: less than high school, high school, and further than high school. Pre-pregnancy body mass index (BMI) was calculated by dividing the weight obtained from medical records by the squared height measured at the baseline interview and expressed in kg/m^2. Pre-pregnancy BMI was classified into three categories: underweight (<18.5 kg/m^2), normal (18.5 ≤ BMI < 23.0 kg/m^2), and overweight (≥23.0 kg/m^2) according to the BMI cutoff for the Asia population [40]. Smoking status (active and passive smoking) was elicited using the WHO STEPS questions [41]. Passive smoking was defined as exposure to tobacco smoke at home or workplaces.

2.4. Statistical Analyses

Women who had an implausible total energy intake (<500 or >3500 kcal per day) were excluded from statistical analyses [42]. Descriptive analyses were used to report the socio-demographic characteristics of the study sample. The total daily intakes of food groups, macronutrients, and micronutrients are presented as mean ± standard deviation (SD). Differences in nutrient intakes across categories of age group, education level, and pre-pregnancy BMI were examined using ANOVA tests. For foods that showed a statistically significant test statistic (*F* statistic) for ANOVA (e.g., $p < 0.05$),

we proceeded with the Tukey–Kramer test [43] to identify which specific groups had statistically significantly different means from one another. Energy and nutrient intakes were compared with the RNI for Vietnamese pregnant women to estimate the prevalence of adequate nutrient intakes [38]. The prevalence of adequacy for macronutrient intakes was determined as the proportion of participants with observed intakes that met, at a minimum, the following recommendations: 13–20% of energy from proteins, 20–30% of energy from total fat, and 55–65% of energy from carbohydrates. The corresponding data for micronutrients was defined as the prevalence of individuals with observed intakes that achieved the minimum or single values of the RNI [44]. In addition, energy-adjusted nutrient intakes were calculated using the density method (amount of nutrient intake per 1000 kcal of energy) [45]. All analyses were performed using the R Statistics software version 3.3.3 (R Foundation for Statistical Computing, Vienna, Austria) [46].

2.5. Ethics Approval

The study protocol was approved by the Human Research Ethics Committees of Curtin University in Australia (HR32/2015) and Hai Phong University of Medicine and Pharmacy in Vietnam (No. 05/HPUMPRB/2015). Written consent forms were obtained from all participants.

3. Results

3.1. Socio-Demographic Characteristics of the Study Participants

Of the 2248 eligible women approached, 2030 (90.3%) consented to participate in the study. Among them, 86 women were excluded from the study because of implausible total energy intakes, giving a final sample of 1944 women for analysis. The individual characteristics of these participants are presented in Table 1. The age ranged from 18 to 48 years, with a mean of 27.6 years of age (SD = 5.3). Nearly two-thirds of participants completed high school or higher education. The study sample had a mean pre-pregnancy BMI of 20.2 kg/m^2 (SD = 2.5), and the prevalence of underweight and overweight were 25.4% and 12.9%, respectively. No women smoked during pregnancy, but over half of them were exposed to passive smoking. Approximately one in eight women drank alcohol during pregnancy.

Table 1. Socio-demographic characteristics of the study participants.

Characteristic	*n*	%
Age (years)		
<25	611	31.4
25–29	673	34.6
30–34	450	23.2
≥35	210	10.8
Educational level		
Less than high school	697	35.9
High school	492	25.3
Further than high school	755	38.8
Parity		
0	768	39.5
1	708	36.4
≥2	468	24.1
Pre-pregnancy BMI (kg/m^2) [a]		
Underweight, <18.5 kg/m^2	494	25.4
Normal, 18.5≤BMI<23.0 kg/m^2	1199	61.7
Overweight, ≥23.0 kg/m^2	251	12.9
Smoking during pregnancy		
Active smoking	0	0.0
Passive smoking [b]	1017	52.3
Alcohol drinking during pregnancy [c]	256	13.2

BMI: Body mass index. [a] Based on cut-off for Asian population [40]. [b] Defined as any exposure to smoking at home or workplaces during pregnancy. [c] Defined as drinking any alcohol during pregnancy.

3.2. Food Intake

Table 2 summarizes the mean daily food intakes (g) among pregnant women. Overall, cereals were the most common foods (682.8 g/day), followed by fruits (315.0 g/day) and vegetables (240.7 g/day). Rice was the main food source of cereals (85.9%), while banana was the most commonly consumed fruit (63.4 g/day). Leafy vegetables, fruit-vegetables, roots and tubers were the main types of vegetables consumed (89.0%). The daily intakes of poultry, eggs, fish and seafood, red meat, and soy products were low, ranging from 17.6 to 54.8 g/day. Very low intakes of alcohol, coffee, and tea during pregnancy were reported.

Table 2. Average food intake by pregnant women in Vietnam, 2015–2016.

Food Group (g/day)	Mean ± SD
Cereals	682.8 ± 274.6
Bread	19.0 ± 22.4
Noodle	58.0 ± 48.1
Rice	586.6 ± 274.9
Vegetables	240.7 ± 179.1
Leafy vegetables	87.6 ± 76.4
Roots & tubers	48.2 ± 60.7
Flowers & stems	3.8 ± 8.8
Fruit-vegetables	78.4 ± 82.0
Pulses & sprouts	16.3 ± 27.4
Other vegetables	2.3 ± 7.4
Pickled vegetables	4.2 ± 12.1
Fruits	315.0 ± 235.9
Banana	63.4 ± 89.8
Mango	46.4 ± 63.4
Grapefruit and orange	45.9 ± 74.7
Watermelon	42.5 ± 70.5
Guava	38.6 ± 60.0
Papaya	28.6 ± 62.6
Apple and pear	16.4 ± 31.6
Grape	10.2 ± 26.2
Other fruits	23.0 ± 53.1
Soy products	54.8 ± 94.9
Red meat	46.4 ± 37.9
Poultry	17.6 ± 21.2
Fish & seafood	32.5 ± 36.6
Eggs	26.1 ± 29.0
Dairy	94.4 ± 155.1
Alcohol (grams ethanol/day) *	0.91 ± 1.54
Coffee (cup/day) *	0.37 ± 0.55
Tea (cup/day) *	0.95 ± 1.78
Sweet dessert	35.3 ± 43.2
Fruit juices & soft drinks (mL/day)	127.1 ± 160.7

* The data were obtained from the drinkers, noting that a small number of women drank alcohol (13.0%), coffee (21.9%), and tea (31.3%) during their pregnancy. Alcohol consumption was calculated only for mothers who consumed alcohol during pregnancy.

Table 3 shows the average daily intakes of foods and beverages together with multiple comparisons across age groups, educational levels, and pre-pregnancy BMI levels. In general, older women consumed more vegetables and fish and seafood than their younger counterparts, whilst young women consumed more cereals, fruits, red meat, poultry, eggs, sweet dessert, fruit juices and soft drinks than the older ones. There were statistically significant differences in the mean intakes of the aforementioned food items (except for fruits) between participants aged ≥35 years and those under 25 years of age ($p < 0.05$). The mean intakes of red meat, poultry, eggs, and fruit juices and soft drinks were significantly higher in more educated women, especially women with post-high school education. Overweight women ate soy products and fish and seafood more frequently but consumed less cereals, poultry, and eggs than those with a lower pre-pregnancy BMI. They had significantly lower mean intakes of cereals and poultry than pre-pregnancy underweight women. Meanwhile, their average intakes of soy products and fish and seafoods were significantly greater than those of underweight and normal-weight women before pregnancy, respectively.

Table 3. Food intake by age group, education level, and pre-pregnancy BMI level among pregnant women in Vietnam, 2015–2016.

Food Group (g/day)	Age (years)					Education Level				Pre-Pregnancy BMI (kg/m^2)			
	<25	25–29	30–34	≥35	*p*	Less than HS	High School	Post HS	*p*	<18.5	18.5 ≤ BMI < 23.0	≥23.0	*p*
Cereals	707.9	682.5	659.9 [a]	659.5 [a]	0.021	678.1	688.8	683.2	0.802	737.1	676.7 [a]	604.6 [a,b]	<0.001
Vegetables	226.2	241.1	244.2	274.5 [a]	0.009	242.9	242.9	237.4	0.804	238.8	244.5	226.7	0.347
Fruits	337.7	301.9 [a]	306.2	309.9	0.037	299.2	324.8	323.2	0.087	329.8	315.0	285.9 [a]	0.056
Soy products	51.3	55.4	59.3	53.8	0.595	52.5	59.4	54.0	0.441	46.6	56.4	63.8 [a]	0.042
Red meat	48.7	46.5	45.9	40.1 [a]	0.045	43.0	43.1	51.6 [a,b]	<0.001	49.6	45.6	43.8	0.076
Poultry	20.2	16.6 [a]	16.6 [a]	15.4 [a]	0.003	15.0	17.6	20.0 [a]	<0.001	19.6	17.4	14.8 [a]	0.012
Fish & seafood	27.4	34.8 [a]	34.7 [a]	35.1 [a]	0.001	34.4	28.1 [a]	33.5 [b]	0.008	34.0	30.9	37.0 [b]	0.028
Eggs	30.5	25.8 [a]	21.2 [a,b]	24.6 [a]	<0.001	19.9	29.0 [a]	29.9 [a]	<0.001	27.7	26.7 [a]	20.2 [b]	0.002
Dairy	86.0	102.7	98.8	83.1	0.158	100.5	84.8	95.1	0.224	87.0	95.6	103.2	0.369
Sweet dessert	40.7	34.4 [a]	32.3 [a]	29.4 [a]	0.001	36.6	35.5	34.1	0.528	38.4	34.2	34.7	0.190
Fruit juices & soft drinks (mL/day)	135.4	134.3	120.7	93.8 [a,b]	0.005	116.7	120.9	140.8 [a]	0.011	127.9	129.0	116.8	0.549

HS: High school; BMI: Body mass index, using cut-off for Asian population [40]. Data are means; superscript letters indicate a statistically significant difference ($p < 0.05$) according to the Tukey–Kramer test [43]. [a] Comparison between that group and "age < 25 years", "less than HS", and "pre-pregnancy BMI < 18.5" for age, education level, and pre-pregnancy BMI, respectively. [b] Comparison between that group and "age 25–29 years", "high school" and "pre-pregnancy normal BMI" for age, education level, and pre-pregnancy BMI, respectively.

3.3. Nutrient Intake

Table 4 presents the nutrient intakes among the participants, including energy, macronutrients, micronutrients, and comparisons with the RNI. The mean total energy intake was 2004 kcal/day (SD = 625), with 15.9%, 31.8%, and 52.2% of energy coming from proteins, fats, and carbohydrates, respectively. Overall, the energy intake met the national RNI, but only approximately half of the women achieved the recommendation. The mean intakes of proteins and fat were higher than the reference values, with the majority of women achieving the requirements.

The mean intakes of several micronutrients were above the RNI, whereas the intake levels of some important nutrients for optimal reproductive health, such as folate, calcium, iron, and zinc, were much lower than the RNI. Almost all participants did not meet the RNI for iron and calcium. Very few women had adequate intakes of folate (15.4%) and zinc (18.0%) before supplementation. The intake levels of different B vitamins not reaching the Vietnam RNI (not including folate) varied from 11.5% to 62.0%. The proportions with inadequate intakes of vitamin A and vitamin C were 41.3% and 27.7%, respectively. Most participants met the RNI for magnesium, selenium, phosphorus, and manganese.

Table 4. Daily energy and nutrient intakes of pregnant women in Vietnam, 2015–2016.

Energy and Nutrient (unit/day)	RNI			Our Study		
	Vietnam MOH	NIH 2016	WHO/FAO 2004	Observed Intakes [a]	Energy-Adjusted Intakes [a]	% Meeting Vietnam RNI [b]
Energy (kcal)	1980–2010	NA	NA	2004 ± 625	-	49.1
Percentage of energy from proteins (%)	13–20	10–35	NA	15.9	-	-
Percentage of energy from fat (%)	20–30	20–35	NA	31.8	-	-
Percentage of energy from carbohydrates (%)	55–65	45–65	NA	52.2	-	-
Protein (g)	70	71	NA	79.4 ± 25.0	40.0 ± 5.2	62.9
Fat (g)	52.5–64.5	NA	NA	70.9 ± 24.2	35.2 ± 4.2	-
Carbohydrate (g)	325–400	175	NA	261.6 ± 85.7	130.5 ± 11.8	-
Fiber (g)	28	28	NA	16.1 ± 6.7	8.1 ± 2.4	-
Vitamin A (µg) [c]	650–700	770	800	849.7 ± 500.1	431.6 ± 225.1	58.7
Vitamin C (mg)	110	85	55	183.4 ± 118.8	94.1 ± 56.4	72.3
Thiamin (mg)	1.2–1.3	1.4	1.4	1.4 ± 0.5	0.7 ± 0.2	65.0
Riboflavin (mg)	1.5	1.4	1.4	1.5 ± 0.6	0.8 ± 0.2	45.5
Niacin (mg)	18	18	18	26.6 ± 9.4	13.3 ± 2.3	83.2
Pantothenic acid (mg)	6	6	6	5.6 ± 1.9	2.9 ± 0.6	38.0
Pyridoxine (mg)	1.9	1.9	1.9	2.4 ± 0.9	1.2 ± 0.3	71.0
Folate (µg) [d]	600	600	600	440.8 ± 167.6	224.2 ± 62.1	15.4
Cobalamin (mg)	2.6	2.6	2.6	4.4 ± 1.7	2.2 ± 0.6	88.5
Vitamin D (µg)	15	15	5	2.3 ± 2.2	1.2 ± 1.1	-
Vitamin E (mg)	6.5	15	NA	4.2 ± 1.7	2.1 ± 0.7	9.1
Vitamin K (µg)	150	90	55	267.8 ± 229.5	137.0 ± 108.1	68.2
Calcium (mg)	1200	1000	1200	509.8 ± 263.5	260.2 ± 117.8	2.5
Phosphorus (mg)	700	700	NA	1322.6 ± 447.8	665.4 ± 113.7	94.1
Potassium (mg)	>3510	4700	NA	3038.4 ± 1186.9	1550.8 ± 471.9	29.6
Sodium (mg)	<2000	1500	NA	3312.7 ± 1273.7	1657.8 ± 375.3	12.2
Magnesium (mg)	40	350–360	220	289.1 ± 105.0	147.5 ± 39.3	100
Iron (mg) [e]	27.4	27	24.5	9.4 ± 3.4	4.8 ± 1.3	0.05
Zinc (mg) [f]	10	11	11–14	7.7 ± 2.9	3.9 ± 1.1	18.0
Copper (µg)	1000	1000	NA	1.0 ± 0.4	0.5 ± 0.2	0.0
Selenium (µg)	28	60	28–30	118.1 ± 43.0	60.0 ± 15.0	100
Manganese (mg)	2.0	2.0	NA	3.0 ± 1.1	1.5 ± 0.4	84.4

RNI: Recommended nutrient intakes; MOH: Ministry of Health; NIH: National Institutes of Health: WHO: World Health Organization; FAO: Food and Agriculture Organization of the United Nations; SD: Standard deviation; NA: Not available. [a] Data are presented as mean ± SD. Energy intakes were adjusted for the amount of nutrient intake per 1000 kcal of energy [45]. [b] Based on energy and nutrient intakes compared with the RNI for Vietnamese pregnant women [38]. [c] As retinol activity equivalents (RAEs). [d] As dietary folate equivalents (DFE). [e] Based on the assumption of high bioavailability of iron from the Vietnam diet (15%) [38]. [f] Based on the assumption of medium bioavailability of zinc from the Vietnam diet (30%) [38].

Associations between nutrient intakes and selected socio-demographic characteristics including maternal age, educational level, and pre-pregnancy BMI are shown in Supplementary Table S1. In brief, older women consumed less energy, macronutrients, B group vitamins, iron, and zinc than younger women. In contrast, educated women consumed more proteins, B group vitamins, iron, and zinc than their counterparts with a lower education level. Overweight women consumed less energy and lower levels of almost all macro- and micronutrients than women with a lower pre-pregnancy BMI.

4. Discussion

This is the first large-scale study to report a comprehensive profile of the diet of pregnant women in Vietnam. It found that rice, fruits, and vegetables were the major food sources of energy, with approximately half of the women meeting the RNI for total energy intake. The data also showed that almost all pregnant women did not meet the RNI for some essential micronutrients, including folate, calcium, iron, and zinc.

Our finding of rice being the main food source is consistent with previous studies among pregnant women in China, India, and Thailand [10,13,47]. Despite the lack of dietary information during pregnancy in Vietnam for a direct comparison, rice was also the staple food in 1985 and 2010 in Vietnam according to nationally representative nutrition surveys [27]. However, the amount of rice intake in our study was much higher than in prior research [10,13,27,47]. Variations in the intake levels of fruits and vegetables were found across countries. For example, women in our study consumed greater amounts of vegetables than those in China and Thailand [13,47] but had a lower intake of fruit compared with Chinese pregnant women [13]. Particularly, leafy vegetables and fruit-vegetables were the main vegetables consumed in our study. In addition, Vietnamese pregnant women consumed less soy products, poultry, and eggs than Chinese women [13]. The intake levels of animal-based foods were greater in higher-educated women and lower in younger and overweight women when compared to the respective lower groups. These findings are useful for developing guidelines for the population to achieve a balanced diet during pregnancy.

The mean energy intake of 2004 kcal/day in our study met the RNI for pregnant women with light physical activity but failed to attain the RNI for those with moderate physical activity [38]. This intake was similar to estimates from previous studies in low- and middle-income countries [7] and China [14,48], but much higher than the intakes determined in Thailand and India [12,49]. However, this calorie intake was lower than that of pregnant women in some Western countries such as the United States and Canada (2201 kcal/day), Europe (2197 kcal/day), and Australia and New Zealand (2212 kcal/day) [50]. The mean energy intake reported by our participants was higher than that of Vietnamese adults from the general nutrition survey 2009–2010 (1925 kcal/day per capita) [27], but lower than that of WRA (2196 kcal/day) [51]. Notably, half of the study participants did not meet the RNI for energy requirements during pregnancy. In addition, there was a large variation in energy intakes, which may be due to different dietary patterns between North and South Vietnam, seasonal food availability, and individual physical activity levels.

Our study found that protein, fat, and carbohydrate intakes accounted for 15.9%, 31.8%, and 52.2% of total energy, respectively, which are similar to the values determined for Chinese women [48] but are much higher than those obtained for Thai women [12]. No information on macronutrient intakes during pregnancy in Vietnam is available, but two studies conducted in adults and WRA reported that the protein intake was similar to that calculated in our study [27,51]. However, our participants consumed more fat and less carbohydrates than those in these studies. White rice was a major source of carbohydrates in the present study. As such, it may not be necessary for this population to achieve 55–65% of energy from carbohydrates, providing that the food sources are of high quality and supply a range of micronutrients with the carbohydrates. Further improvements in dietary diversity are needed to improve and balance the intakes of macronutrients.

The mean intakes of essential micronutrients for pregnant women, such as folate, vitamin D, calcium, iron, and zinc, were far below the RNI. The deficiency of these micronutrient intakes is prevalent in low- and middle-income countries [7,8,12,13,49] and it is not common in developed countries [52,53]. Our findings present the same problem of micronutrient deficiencies in pregnant women as the previous studies of Vietnamese adults and WRA [26–30]. This may be explained by a low intake of micronutrient-rich foods, such as eggs, fish, soy, and dairy products. In addition, our participants consumed foods that usually do not have high bioavailable iron and zinc. Such insufficient micronutrient intakes may influence foetal metabolism, organ growth, development, and function, and chronic diseases later in life [54]. It is noteworthy that the mean intakes of some

micronutrients such as vitamin A, vitamin C, vitamin K, thiamin, riboflavin, and pyridoxine achieved the RNI, but a large number of participants (27.7–54.7%) did not meet the recommendations still.

The association between dietary intakes and socio-economic status has been reported in previous studies in different countries and regions [12,14,29,51,55–58]. People of higher socio-economic status (education, occupation, or income) tend to have higher intakes of energy, macronutrients [14,51,57], and most micronutrients such as vitamin A, B12, C, D, and E, folate, calcium, iron, and zinc [14,29,55–58]. Our study also indicates that pregnant women with a higher educational level had significantly higher intakes of proteins, vitamin C, E, thiamin, niacin, pantothenic acid, pyridoxine, iron, zinc, selenium, magnesium, potassium, and phosphorus. It is conceivable that higher-educated women are more health-conscious during pregnancy and thus they may attempt to maintain a high-quality diet. Similarly, pregnant women aged <25 years had significantly higher levels of energy, macronutrients, B vitamins, iron, zinc, and selenium than older women. Moreover, consistent with studies in China and Germany [48,59], pregnant women with a higher pre-pregnancy BMI in our study had significantly lower intakes of energy, macronutrients, and most micronutrients than their counterparts in the lower BMI groups. Probably, overweight women tended to receive advice on the prevention of excessive gestational weight gain through diet control. Alternatively, a lower energy intake in women with pre-pregnancy overweight may be attributed to their lower physical activity levels compared to women without pre-pregnancy overweight and thus the need of less energy to achieve homeostasis. The difference in the average nutrient intakes across key demographic factors and maternal pre-pregnancy weight status is integral to planning interventions targeted at specific groups.

The strengths of the present study include a relatively large sample size from which the typical diet of pregnant women in Vietnam can be extrapolated. Additionally, the dietary intakes were comprehensively analyzed and reported, including food groups, energy, macronutrients, and micronutrients, based on an interviewer-administered food frequency questionnaire and food composition tables for local diet. However, the study has some limitations. The common drawbacks of the FFQ method in epidemiological studies include a recall bias, the selection of core foods, and the lack of information about the preparation methods, that may lead to imprecise estimates of nutrients [60,61]. In the Vietnamese context, there may also be a possible influence of seasonal variation in food sources that makes it difficult to correctly estimate the habitual nutrient intake of pregnant women. Another concern is that Vietnamese women normally share dishes with their family members, which may affect individual portion size estimates. We attempted to minimize these potential errors by asking a comprehensive item food list in Vietnam and conducting direct interviews using supportive materials such as standardized tableware sets and food portion images. Besides, we did not take into account dietary supplement data collected from our participants in the final analysis because it is beyond the scope of this study. Although our preliminary analyses showed that the supplementation rates of zinc, folic acid, multivitamin, iron, and calcium were 2.0%, 8.7%, 28.7%, 85.4%, and 86.0%, respectively (full data not presented for brevity), this is unlikely to have a significant impact on the results.

5. Conclusions

In conclusion, the present study indicates low dietary nutrient intakes among pregnant women in Vietnam. The prevalence of mothers failing to meet the national recommendations for essential micronutrient intakes was on average over 50%. Our report provides timely and important data to inform policy makers, researchers, and community stakeholders, so that appropriate nutrition interventions can be implemented to improve the diet quality and the overall health of Vietnamese women during pregnancy.

Supplementary Materials: The following are available online at http://www.mdpi.com/2072-6643/10/8/1025/s1, Table S1: Comparison of nutrient intakes by selected characteristics of pregnant women in Vietnam, 2015–2016.

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4.4 Physical activity during pregnancy and gestational diabetes mellitus

Related publication:

Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam

This paper addresses objective 4 (to ascertain the association between maternal factors e.g. pre-pregnancy BMI, dietary intake, physical activity, cigarette smoking, alcohol drinking, gestational weight gain and gestational diabetes mellitus).

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ORIGINAL ARTICLE

Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam

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Abstract

Aims To assess the association between physical activity (PA) during pregnancy and the prevalence of gestational diabetes mellitus (GDM) accounting for sitting time.

Methods The study used data from a cohort study of 2030 pregnant women in Vietnam. Women were recruited from six hospitals in Ha Noi, Hai Phong, and Ho Chi Minh City. Baseline measurements including PA and GDM were taken at 24–28 weeks of gestation. PA was assessed during the past 3 months before the interview using the interviewer-administered Pregnancy Physical Activity Questionnaire. GDM was diagnosed at 24–28 weeks of gestation using the 2013 World Health Organization criteria.

Results 1987 out of 2030 pregnant women were included in the final analysis, of which 432 had GDM (21.7%). Women undertaking the highest level (upper tertile) of PA during pregnancy appeared to have a lower risk of GDM [odds ratio (OR) 0.70, 95% confidence interval (CI) 0.53–0.94, P_{trend} 0.017] when compared to those at the lowest tertile of PA. Similarly, women with increased levels of moderate-intensive activity and household/caregiving activity during pregnancy were associated with reduced risks of GDM (OR 0.66, 95% CI 0.50–0.86, P_{trend} 0.002 and OR 0.72, 95% CI 0.55–0.95, P_{trend} 0.020, respectively). These apparent inverse associations were not attenuated by their sitting time. There were no significant associations between sitting time, light-intensity activity, vigorous-intensity activity, occupation, sports/exercise, commuting, or meeting exercise guidelines and GDM risk.

Conclusions High levels of PA, particularly moderate-intensity and household/caregiving activities during pregnancy were associated with a lower prevalence of GDM independent of sitting time.

Keywords Physical activity · Sitting time · Gestational diabetes · Pregnancy · Vietnam

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Introduction

Gestational diabetes mellitus (GDM), defined as any glucose intolerance with first diagnosis during pregnancy [1], is recognised as a significant public health problem for the mother [2] and infant [3]. According to the International Diabetes Federation in 2017, around 18.4 million live births were affected by GDM worldwide [4]. GDM is associated with increasing costs of care [5, 6], and has placed an economic burden on individuals and health care systems, particularly in low- and middle-income countries [7]. Our recent meta-analysis showed that the prevalence of GDM was approximately 10% in eastern and southeastern Asia [8]. Women with GDM tend to have an accelerated risk of adverse health outcomes for both mothers and their offspring such as gestational hypertension, preeclampsia, caesarean

section, macrosomia, and neonatal hypoglycaemia [9–12]. Particularly, GDM has been suggested to increase the risk of diabetes and cardiovascular disease later in life [13–15], while postpartum screening for diabetes is still lacking [16]. It is, therefore, important to develop appropriate measures for the prevention and management of GDM and subsequent complications.

Accumulating evidence has suggested that physical activity (PA) plays a major role in the primary prevention of chronic diseases [17] including type 2 diabetes [18] and GDM [19]. A meta-analysis of 25 interventional and cohort studies confirmed the inverse dose–response association between total PA before pregnancy and risk of GDM, despite the lack of such association for PA during pregnancy [20]. Similarly, GDM was inversely associated with vigorous PA before pregnancy, but unrelated to vigorous PA in early pregnancy [20]. The relationship between PA and GDM may differ according to the domains of PA, but available data remain scarce [20]. Indeed, previous studies on PA and GDM were mainly conducted in Western populations [21–28], even though Asian women have different PA patterns and risk profiles for GDM [29–31]. Evidence has been accumulated to suggest a detrimental effect of sedentary behaviour on type 2 diabetes [32, 33]; however, few studies have evaluated the relation of sedentary behaviour to GDM risk and their findings remain inconsistent [22, 30]. PA and sedentariness (e.g. sitting) are closely linked, but there has been no study that examined simultaneously the effects of PA and sitting time on GDM. Therefore, the present study aimed to address this scientific gap by investigating the association between PA during pregnancy and the prevalence of GDM in a large cohort of Vietnamese women, taking into consideration the potential mitigating effects of their sedentary behaviours.

Methods

Study design and participants

This study used baseline data that were collected as part of a prospective cohort study in Vietnam, details of which have been described elsewhere [34]. In brief, eligible pregnant women were selected from participating hospitals during their prenatal care visits in early pregnancy. Inclusion criteria were: (1) permanent resident of the study location; (2) ≥ 18 years of age; (3) at 24–28 weeks' gestation; (4) singleton pregnancy; (5) without serious pre-existing health conditions such as cancers and ischemic heart diseases, according to their medical doctor; (6) being able to read the information sheet and sign the consent form. Participants were informed of the study purpose and procedure before seeking their informed consent. They were invited to attend a baseline interview at 24–28 weeks of gestation to provide their lifestyle information including PA, smoking, alcohol drinking, demographics and medical history, before the determination of their GDM status. Interviews were conducted in Vietnamese by trained interviewers to minimise potential language and literacy barriers. Recruitment commenced in August 2015 and ended in July 2016. The study protocol was approved by the Human Research Ethics Committees of Curtin University (HR32/2015) and Hai Phong University of Medicine and Pharmacy (no. 05/HPUMPRB/2015).

Physical activity assessment

The Pregnancy Physical Activity Questionnaire (PPAQ), culturally modified and validated among Vietnamese pregnant women, was used to assess habitual PA during the past 3 months (i.e. 12–16 weeks' gestation) before the baseline interview at 24–28 weeks gestation [35]. The PPAQ measures the duration, frequency, and intensity of PA during pregnancy. It is a semi-quantitative questionnaire that solicits the time spent participating in 32 activities under four domains, namely, household/caregiving, occupation, sports/exercise, and commuting. In this study, each activity was calculated from its duration and intensity, and expressed in terms of Metabolic Equivalent Task (MET) hours per week, according to the PPAQ scoring mechanism [36] and the Compendium of Physical Activities [37]. PA was classified as light-intensity activity (1.5–< 3 METs), moderate-intensity activity (3–6 METs), and vigorous-intensity activity (> 6 METs) [38].

Sedentary behaviour was ascertained by measuring the number of hours spent sitting (at home/work or on the motorbike/car) per day during the same period of pregnancy. Specific sedentary activities included watching television, sitting in front of a computer, reading, talking, riding a car or bus, and sitting at work or class. Total sitting time was then defined as the sum of all sitting times at home, work and travel.

The American College of Obstetrics and Gynaecology (ACOG) recommends that healthy women during pregnancy should spend at least 150 min per week on moderate-intensity aerobic activity [39]. Therefore, PA was also dichotomised as "yes" or "no" on the basis of meeting this guideline if participants engaged in > 7.5 MET hours per week in sport/exercise activities of moderate-intensity or greater [39].

Gestational diabetes mellitus assessment

All participants were screened for GDM status between 24 and 28 weeks' gestation using the one-step 75-g oral glucose tolerance test (OGTT). Women were asked to fast overnight

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before undertaking the test in the next morning. A fasting blood sample was drawn before being instructed to drink 75-g glucose dissolved in 250 ml water within 5 min. Two additional blood samples were taken 1 and 2 h afterwards. Glucose levels were determined using the glucose oxidase method. GDM was diagnosed according to the 2013 criteria of the World Health Organisation (WHO) [40]. Women were confirmed with GDM if they met one or more of the following criteria: (1) fasting plasma glucose: 5.1–6.9 mmol/l; (2) 1-h plasma glucose after OGTT ≥ 10.0 mmol/l; (3) 2-h plasma glucose after OGTT: 8.5–11.0 mmol/l. Women who were diagnosed as diabetic in pregnancy (fasting plasma glucose ≥ 7.0 mmol/l- or 2-h plasma glucose after OGTT ≥ 11.1 mmol/l) were excluded from the analysis.

Assessment of covariates

Demographic information including age, marital status, occupation, education, parity, as well as history of previous pregnancy and diabetes, was collected during the baseline interview. Smoking status (active and passive smoking) and alcohol consumption were elicited using the WHO STEPS questions [41]. Passive smoking was defined as exposure to tobacco smoke at home and/or workplaces. Alcohol consumption included drinking any alcoholic beverage (e.g. beer, wine or liquor) during pregnancy. Height was measured using a stadiometer to the nearest 1 mm, whereas pre-pregnancy weight was obtained from medical records. Blood pressure was measured by trained nurses or physicians using an Omron M5-1 electronic sphygmomanometer.

Statistical analysis

In addition to descriptive statistics, baseline characteristics were compared between women with and without GDM using Pearson's Chi-square, two-sample *t* test or Wilcoxon rank-sum tests. Multivariable logistic regression analyses were performed to determine the association between PA and GDM prevalence. Total PA and PA levels by intensities and domains were categorised into tertiles, with the lowest tertile being the reference category. Both vigorous activity and meeting exercise guideline were dichotomised as binary variables in view of the small number of cases.

Results were presented as odds ratios (ORs) and corresponding 95% confidence intervals (CI). Established or plausible confounding factors from the literature [20, 21, 42], namely, maternal age, pre-pregnancy body mass index (BMI), blood pressure, passive smoking, and family history of diabetes, were selected for inclusion in the logistic regression models. Adjustment for sitting time was further made to examine its potential attenuation effect. Tests for linear trend across tertiles of PA were based on the corresponding medians. All statistical analyses were performed using the Stata package version 12.0 (StataCorp, College Station, USA).

Results

2030 out of 2248 (90.3%) pregnant women who met the inclusion criteria were recruited at the baseline survey. There was no significant difference in mean age between participants and non-participants. Among participants, 43 women were excluded due to history of diabetes before pregnancy ($n=7$), history of GDM during previous pregnancy ($n=17$), and diabetes in pregnancy ($n=19$). Of the total 1987 participants included in the final analysis, 432 women were subsequently diagnosed with GDM after administering the OGTT, giving a GDM prevalence of 21.7%.

Table 1 compares the characteristics of study participants with and without GDM. Women with GDM were significantly older, had a higher BMI and blood pressure, and more likely to have a family history of diabetes when compared to those without GDM. However, a lower proportion of them were exposed to passive smoking than their non-GDM counterparts.

Table 2 presents the intensity, duration and domains of PA by GDM status. Compared to non-GDM women, those with GDM were less physically active in terms of total PA (mean 116.6 vs. 125.0 MET hours per week) and had significantly lower levels in moderate-intensive activity (12.6 vs. 19.3 MET hours per week) as well as household/caregiving activity (46.2 vs. 49.7 MET hours per week). No differences in sitting time, light, vigorous, occupational, recreational, and commuting activities were found between the two groups. Very few participants engaged in vigorous activity (2.9%), and only one-fifth of the pregnant women met the recommended guideline for PA (17.4% for GDM and 21.5% for non-GDM groups).

Table 3 shows the results of regression analysis. In the crude models, higher levels of total PA, moderate-intensity activity, and household/caregiving activity were significantly associated with a reduced prevalence of GDM. These inverse associations remained significant after adjustment for age, BMI, blood pressure, passive smoking, and family history of diabetes. Moderate-intensity activity exhibited the largest reduction in GDM risk (highest vs. lowest tertile: OR 0.66, 95% CI 0.50–0.86, P_{trend} 0.002). The potential attenuation effect of sitting time was next examined. However, the observed inverse associations between GDM prevalence and total PA, moderate-intensity and household/caregiving activity persisted even after adjustment for sitting time. No apparent associations were evident for meeting the recommended PA guideline, light intensity, vigorous intensity,

Table 1 Characteristics of the study participants by gestational diabetes mellitus status

Variables	GDM	Non-GDM	*p* value[a]
Total, *n* (%)	432 (21.7)	1555 (78.3)	
Maternal age (years), mean (SD)	29.0 (5.3)	27.1 (5.2)	<0.001
Marital status, *n* (%)			
Single/divorced/separated/widowed	1 (0.2)	14 (0.9)	0.155
Married	431 (99.8)	1541 (99.1)	
Occupation, *n* (%)			
Farmers	63 (14.6)	229 (14.7)	0.143
Workers	176 (40.7)	621 (39.9)	
Office and technical staff	113 (26.2)	338 (21.7)	
Salesperson	21 (4.8)	94 (6.1)	
Housewife/unemployed	59 (13.7)	273 (17.6)	
Educational level, *n* (%)			
Primary school	162 (37.5)	539 (34.7)	0.539
High school	109 (25.2)	403 (25.9)	
College/university	161 (37.3)	613 (39.4)	
Pre-pregnancy body mass index (BMI)[b], *n* (%)			
Underweight (< 18.5 kg/m^2)	93 (21.5)	428 (27.5)	<0.001
Normal (18.5 to <23.0 kg/m^2)	254 (58.8)	965 (62.1)	
Overweight (≥ 23.0 kg/m^2)	85 (19.7)	162 (10.4)	
Mean (SD)	20.7 (2.8)	20.0 (2.4)	<0.001
Blood pressure, mean (SD)			
Systolic (mm Hg)	107.7 (8.3)	105.0 (8.0)	<0.001
Diastolic (mm Hg)	69.3 (8.0)	66.7 (7.1)	<0.001
Parity, *n* (%)			
0	165 (38.2)	614 (39.5)	0.742
1	166 (38.4)	566 (36.4)	
≥2	101 (23.4)	375 (24.1)	
Passive smoking, *n* (%)			
No	192 (44.4)	598 (38.5)	0.024
Yes	240 (55.6)	957 (61.5)	
Alcohol consumption, *n* (%)			
No	375 (86.8)	1344 (86.4)	0.840
Yes	57 (13.2)	211 (13.6)	
Family history of diabetes[c], *n* (%)			
No	392 (90.7)	1474 (94.8)	0.002
Yes	40 (9.3)	81 (5.2)	

GDM gestational diabetes mellitus, *SD* standard deviation

[a]Based on Chi-square or *t* test

[b]Classified according to World Health Organization's BMI guideline for Asian populations

[c]Diabetes in first-degree relatives

sports/exercise, occupational and commuting activities after controlling for the effects of confounding factors.

Discussion

In this prospective cohort of almost 2000 Vietnamese pregnant women, we found that total PA, moderate-intensity activity, and household/caregiving activity during early and mid-pregnancy were inversely associated with the prevalence of GDM, and the apparent reductions in GDM risk were not attenuated by their sitting time during pregnancy.

Our finding was somewhat different from four previous studies where total PA during pregnancy exhibited a non-significant reduction in GDM risk [22, 27, 42, 43], which could be attributed to differences in PA assessment, GDM diagnosis criteria and study sample size. Two of these studies used the Kaiser Physical Activity Survey [42, 43] measuring PA levels by a Likert scale (ranging from 1 to 5). One study used the Physical Activity Scale for the Elderly which comprises few questions about PA [22], while another study adopted the PPAQ [27], but its sample size was about half of ours. Moreover, unlike the 2013 WHO criteria, these studies applied the two-step approach of the American Diabetes Association criteria or the Society of Obstetricians and Gynaecologists of Canada guidelines to diagnose GDM, resulting in a smaller number of GDM cases for analysis [22, 27, 42, 43].

Few studies have investigated the role of PA in GDM aetiology by intensity level. Our observed inverse association between moderate-intensive activity during pregnancy and the GDM prevalence was consistent with other studies, which suggested that such activity might reduce the risk of abnormal glucose tolerance [22, 27] and GDM [30]. In contrast, investigations on specific domains of PA were limited. An earlier study reported that Hispanic women at the highest quartile of household/caregiving activity during mid-pregnancy experienced a significant GDM risk reduction relative to those at the lowest quartile [43], but a later study by the authors found no association for household/caregiving activity in both early and mid-pregnancy [27]. The disparity between their and our findings might be due to the different lifestyles and cultural practices. In particular, Asian pregnant women including Vietnamese women usually spend most time on household/caregiving activities rather than recreational activities [29, 44]. On the other hand, the lack of association between GDM and meeting PA guideline, light intensity, vigorous intensity, occupational, sports/exercise and commuting activities appeared to be consistent with previous studies [22, 27, 43].

The relation between sedentary behaviours such as sitting during pregnancy and GDM development has not been well-understood [22, 30, 31]. Similar to our results, two previous studies reported no association concerning

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Table 2 Physical activity during pregnancy by gestational diabetes mellitus status

Variable	All	GDM	Non-GDM	*p* value[a]
Total physical activity (MET-h/week), mean (SD)	123.2 (57.0)	116.6 (55.5)	125.0 (57.3)	0.006
By intensity				
Sitting (h/week)				
Median (IQR)	26.3 (21.0)	26.3 (21.0)	26.3 (22.8)	0.949
Light (MET-h/week)				
Median (IQR)	51.8 (47.1)	51.1 (46.9)	52.0 (46.9)	0.202
Moderate (MET-h/week)				
Median (IQR)	17.9 (33.2)	12.6 (26.6)	19.3 (35.7)	<0.001
Vigorous, *n* (%)				
No	1929 (97.1)	419 (97.0)	1510 (97.1)	0.900
Yes	58 (2.9)	13 (3.0)	45 (2.9)	
By domain				
Household/caregiving (MET-h/week)				
Median (IQR)	49.0 (52.1)	46.2 (45.4)	49.7 (53.4)	0.004
Occupational (MET-h/week)				
Median (IQR)	33.6 (45.1)	33.6 (45.1)	33.6 (45.1)	0.895
Sports/exercise (MET-h/week)				
Median (IQR)	5.6 (5.6)	2.8 (5.6)	5.6 (5.6)	0.070
Transportation (MET-h/week)				
Median (IQR)	7.9 (13.1)	7.0 (13.1)	7.9 (13.1)	0.256
Met exercise guideline[b], *n* (%)				
No	1577 (79.4)	357 (82.6)	1220 (78.5)	0.057
Yes	410 (20.6)	75 (17.4)	335 (21.5)	

GDM gestational diabetes mellitus, *SD* standard deviation, *MET* metabolic equivalent of task, *IQR* interquartile range

[a]Based on *t* test, Wilcoxon rank-sum test or Chi-square test

[b]Meeting American College of Obstetricians and Gynecologist guidelines of > 7.5 MET-h/week in sports/exercise activities of moderate-intensity or greater

sitting at work, reading, and watching television or videos [22, 31], but another study concluded that long sitting at home (two or more hours per day) can increase the risk of GDM [30]. Nevertheless, the simultaneous effect of physical and sedentary activities has never been examined in the literature. Our study provided the first finding that sitting time did not attenuate the inverse association between PA and the GDM risk.

With regard to possible mechanisms, it is known that the development of GDM is related to peripheral insulin resistance. During pregnancy, insulin secretion by a healthy woman generally increases 2–4-fold to maintain normal glucose levels. Women with GDM are unable to secrete enough insulin to compensate for the increased insulin resistance [45]. Increased PA levels can reduce the GDM risk in several ways. First, PA can compensate for defects in the insulin signalling pathway [46, 47]. Second, PA changes adipokine profile level including adiponectin, leptin, resistin, and visfatin that can lead to decreased insulin resistance [48, 49]. Third, PA reduces the inflammatory state, a contributory factor of insulin resistance, by controlling the secretion and activity of inflammation markers such as TNF-α and IL-6 [50, 51]. Fourth, PA can reduce oxidative stress, a pathogenesis of insulin resistance in GDM, by increasing the levels of antioxidant agents such as superoxide dismutase, catalase and glutathione peroxidase [52, 53].

The present study has several strengths and limitations. Our study with a large sample size enabled the first investigation of GDM and PA during pregnancy by intensity and domain in Southeast Asian women, taking into account their sitting time. However, unlike objective measures of PA, responses from the interviewer-administered PPAQ were based on self-report, and thus prone to potential errors and misclassification of the habitual PA levels during pregnancy, even we used the validated questionnaire for the Vietnamese population. Although PA levels were elicited prior to the confirmation of GDM status, timing of PA engagement assessed in our study may not be sufficient to affect the occurrence of GDM, the so-called "etiologically relevant time window" [54]. Moreover, pregnant women who reported being active in the early pregnancy are probably those who were already physically

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Table 3 Odds ratios of gestational diabetes mellitus by intensity and domain of physical activity during pregnancy

Variable	GDM		Crude		Adjusted[a]		Adjusted[b]	
	n	%	OR	95% CI	OR	95% CI	OR	95% CI
Total PA (MET-h/week)								
1st tertile	168	38.9	1.00		1.00		1.00	
2nd tertile	138	31.9	0.78	0.61–1.01	0.84	0.64–1.09	0.80	0.61–1.05
3rd tertile	126	29.2	0.70	0.54–0.91	0.74	0.57–0.97	0.70	0.53–0.94
P trend			0.007		0.031		0.017	
Sitting (h/week)								
1st tertile	154	35.6	1.00		1.00		1.00	
2nd tertile	155	35.9	1.17	0.90–1.50	1.22	0.94–1.58	1.22	0.83–1.79
3rd tertile	123	28.5	0.98	0.75–1.28	0.98	0.75–1.29	0.99	0.61–1.60
P trend			0.935		0.973		0.643	
Light (MET-h/week)								
1st tertile	157	36.3	1.00		1.00		1.00	
2nd tertile	139	32.2	0.86	0.66–1.11	0.89	0.68–1.16	0.88	0.67–1.15
3rd tertile	136	31.5	0.84	0.65–1.08	0.88	0.67–1.15	0.88	0.67–1.15
P trend			0.176		0.348		0.331	
Moderate (MET-h/week)								
1st tertile	195	45.1	1.00		1.00		1.00	
2nd tertile	122	28.3	0.72	0.55–0.93	0.78	0.60–1.02	0.78	0.60–1.02
3rd tertile	115	26.6	0.59	0.45–0.76	0.66	0.50–0.86	0.66	0.50–0.86
P trend			<0.001		0.002		0.002	
Vigorous (MET-h/week)								
No	419	97.0	1.00		1.00		1.00	
Yes	13	3.0	1.04	0.56–1.95	0.93	0.49–1.78	0.93	0.49–1.79
Household/caregiving (MET-h/week)								
1st tertile	165	38.2	1.00		1.00		1.00	
2nd tertile	145	33.6	0.87	0.67–1.12	0.90	0.69–1.17	0.90	0.69–1.17
3rd tertile	122	28.2	0.69	0.53–0.90	0.72	0.55–0.95	0.72	0.55–0.95
P trend			0.006		0.020		0.020	
Occupational (MET-h/week)								
1st tertile	142	32.9	1.00		1.00		1.00	
2nd tertile	150	34.7	1.07	0.82–1.39	1.04	0.80–1.36	1.03	0.76–1.41
3rd tertile	140	32.4	1.00	0.77–1.30	1.03	0.78–1.35	1.01	0.74–1.39
P trend			0.975		0.844		0.951	
Sports/exercise (MET-h/week)								
1st tertile	216	50.0	1.00		1.00		1.00	
2nd tertile	139	32.2	0.88	0.69–1.12	0.96	0.75–1.23	0.96	0.75–1.23
3rd tertile	77	17.8	0.75	0.56–1.00	0.79	0.58–1.06	0.79	0.58–1.06
P trend			0.048		0.139		0.144	
Transportation (MET-h/week)								
1st tertile	161	37.3	1.00		1.00		1.00	
2nd tertile	143	33.1	0.92	0.71–1.18	0.92	0.71–1.20	0.91	0.69–1.19
3rd tertile	128	29.6	0.87	0.67–1.14	0.88	0.67–1.16	0.87	0.66–1.15
P trend			0.311		0.369		0.330	
Met exercise guideline[c]								
No	357	82.6	1.00		1.00		1.00	
Yes	75	17.4	0.77	0.58–1.01	0.78	0.58–1.03	0.78	0.58–1.03

GDM gestational diabetes mellitus, *OR* odds ratio, *CI* confidence interval, *PA* physical activity, *MET* metabolic equivalent of task

[a]Adjusted for age, pre-pregnancy BMI, blood pressure, passive smoking, and family history of diabetes

[b]Additionally adjusted for sitting time

[c]Meeting American College of Obstetricians and Gynecologist guidelines of > 7.5 MET-h/week in sports/exercise activities of moderate-intensity or greater

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active before pregnancy which might have influenced the observed positive associations. Furthermore, despite controlling for established and plausible risk factors for GDM in the multivariable models, residual confounding by unmeasured factors could not be ruled out due to the nature of our observational study. Finally, it is possible that adoption of the single-step OGTT approach to determine GDM status might inflate the GDM prevalence or non-differential misclassification of the outcome. Consequently, the results may not reflect the true effect sizes of PA on the GDM risk.

Conclusions

This study suggests that an increased level of PA during pregnancy was inversely associated with the risk of GDM. Our findings have added the benefit of PA in prevention of GDM to the other healthy lifestyle activities that have been reported in the literature to be associated with lower rates of GDM. Moreover, our study may assist health leaders to develop guidelines or appropriate programmes in encouraging pregnant women to have an active lifestyle. Further studies assessing time, duration, and compliance of PA regimens may be needed to confirm the most appropriate guidelines for pregnant women.

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Author contributions CLN, TKC, PTHN, and AVVH designed the study and collected data. CLN drafted the manuscript. NMP assisted with data analysis. THD provided expert advice on the study design. DVD, NMP, AHL and CWB were the study supervisors and involved in all aspects of the study. All authors revised the article and approved the final version for publication.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Human and animal rights The study was approved by the Curtin University Human Research Ethics Committee (approval number: HR32/2015) and the Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number: 05/HPUM-PRB/2015).

Informed consent Informed consent was obtained from all individual participants included in the study.

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4.5 Gestational diabetes mellitus and pregnancy outcomes

This section presents the estimates of GDM prevalence according to different diagnostic criteria and their associations with pregnancy outcomes. The manuscript of these findings has been submitted to The Journal of Maternal-Fetal & Neonatal Medicine and is under review (Appendix E). Main results and discussions are summarised below.

4.5.1 Prevalence of gestational diabetes mellitus

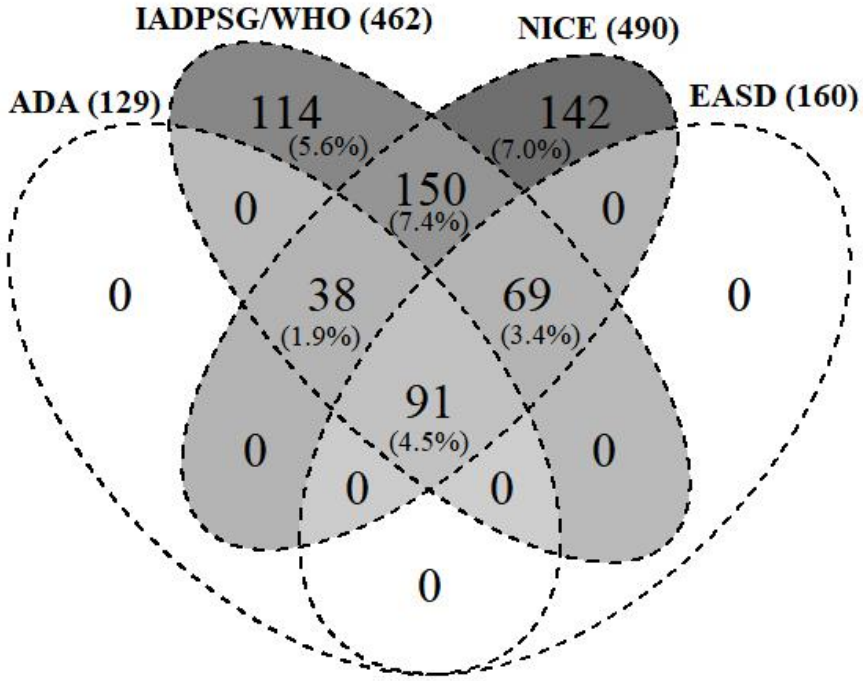

Figure 4. Venn diagram of GDM cases by five international diagnostic criteria for Vietnamese pregnant women, 2015-2016

ADA, American Diabetes Association; EASD, European Association for the Studies of Diabetes; IADPSG, International Association of Diabetes and Pregnancy Study Groups; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization

The NICE criteria gave the highest GDM prevalence of 24.2% (490/2023), followed by the IADPSG/WHO criteria at 22.8% (462/2023). The EASD and ADA criteria resulted in low prevalence, 7.9% (160/2023) and 6.4% (129/2023), respectively.

Figure 4 illustrates the overlap in GDM classification with respect to these five criteria. Overall, the number of women with GDM ranged from 91 (4.5%) by all five criteria to 604 (29.9%) by any criteria. All women diagnosed as GDM according to ADA or EASD were also confirmed by the IADPSG/WHO or the NICE criteria. There were 348 women (17.2%) diagnosed to be GDM when using either the IADPSG/WHO or the NICE criteria. Therefore, 114 (5.6%) and 142 (7.0%) women with GDM were identified respectively by the IADPSG and the NICE criteria only.

4.5.2 Pregnancy outcomes

Table 5 compares the maternal and neonatal outcomes between the NGT and GDM groups. Higher prevalence of caesarean section was evident among women meeting the ADA, EASD, and IADPSG/WHO criteria, but not for those with GDM under NICE. Women diagnosed with GDM according to the ADA and EASD criteria were more likely to experience preeclampsia than women without the condition, though the prevalence was rather low (less than 2%). No significant differences were observed for postpartum haemorrhage between the NGT and GDM groups.

Infants of mothers with GDM by ADA, EASD and NICE criteria were more likely to be macrosomic when compared to those born in the NGT group. Moreover, GDM diagnosis based on the ADA and EASD criteria led to significantly higher prevalence of LGA for infants of mothers with the condition, but not the case when IADPSG/WHO or NICE was used for diagnosis. There were no differences in other neonatal outcomes between NGT and the four GDM groups.

Multivariate logistic regression analysis showed no difference in risk of caesarean section after adjustment for confounding factors. Nevertheless, women with GDM defined according to the EASD criteria had a significantly higher risk of giving birth to macrosomic infants (adjusted odds ratio (OR) 4.35, 95% confidence interval (CI): 1.49–12.72), though there was suggestive evidence for association based on the ADA criteria (adjusted OR 3.18, 95% CI: 0.97–10.39). The results also confirmed that

babies born to mothers with GDM were more likely to be LGA in terms of the ADA criteria (adjusted OR 2.10, 95% CI: 1.10 to 4.02) or the EASD criteria (adjusted OR 2.15, 95% CI: 1.16 to 3.98), when compared to their counterparts in the normal group.

Table 5. Pregnancy outcomes by GDM status, Vietnam, 2015-2016

Pregnancy outcomes	NGT (n=1344)	GDM			
		ADA (n=115)	EASD (n=142)	IADPSG/WHO (n=425)	NICE (n=449)
Maternal:					
Preeclampsia, n (%)	2 (0.2)	2 (1.7)*	2 (1.4)*	3 (0.7)	3 (0.7)
Caesarean section, n (%)	493 (36.5)	54 (46.6)*	66 (46.2)*	184 (43.2)*	186 (41.3)
Postpartum haemorrhage (>500 ml), n (%)	13 (1.0)	2 (1.7)	4 (2.8)	6 (1.4)	5 (1.1)
Gestational age at birth (weeks), median (IQR)	39.0 (1.6)	39.0 (1.7)	39.0 (1.7)	39.0 (1.7)	39.0 (1.7)
Neonatal:					
Birthweight (g), mean ± SD	3138.6 ± 395.0	3177.2 ± 488.1	3167.2 ± 452.2	3152.3 ± 440.3	3149.2 ± 432.8
Macrosomia, n (%)[a]	13 (1.0)	4 (3.5)*	5 (3.5)**	9 (2.1)	10 (2.2)*
Low birthweight, n (%)[b]	53 (3.9)	7 (6.1)	6 (4.2)	20 (4.7)	22 (4.9)
LGA, n (%)[c]	70 (5.7)	14 (12.8)**	15 (11.3)*	30 (7.8)	30 (7.3)
SGA, n (%)[d]	108 (8.5)	6 (5.9)	9 (7.1)	41 (10.4)	40 (9.6)
Stillbirth, n (%)[e]	7 (0.5)	1 (0.9)	1 (0.7)	1 (0.2)	1 (0.2)
Preterm labour, n (%)[f]	66 (4.9)	15 (12.9)	11 (7.7)	26 (6.1)	31 (6.9)
Jaundice, n (%)	120 (8.9)	15 (13.0)	18 (12.7)	47 (11.1)	51 (11.4)
Admission to NICU, n (%)	37 (2.8)	5 (4.4)	6 (4.2)	15 (3.5)	17 (3.8)
Length of hospital stay (days), median (IQR)	3.0 (3.0)	4.0 (2.0)	4.0 (2.0)	3.0 (2.0)	3.0 (2.0)

*p<0.05, **p<0.01 compared to NGT group
[a] >4000 g
[b] <2500 g
[c] Birthweight >90th population percentile for gestational age
[d] Birthweight <10th population percentile for gestational age
[e] Baby born with no signs of life at ≥ 28 weeks of gestation
[f] <37 weeks of gestational age at delivery

ADA, American Diabetes Association; EASD, European Association for the Studies of Diabetes; GDM, Gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; IQR, Interquartile range; LGA, Large-for-gestational age; NGT, Normal glucose tolerance; NICE, National Institute for Health and Care Excellence; NICU, Neonatal Intensive Care Unit; SD, Standard deviation; SGA, Small-for- gestational age

Table 6. Crude and adjusted ORs of pregnancy outcomes associated with GDM according to four international diagnostic criteria in 1899 Vietnamese pregnancies, 2015-2016

Pregnancy outcomes	ADA		EASD		IADPSG		NICE	
	Crude (OR, 95% CI)	Adjusted* (OR, 95% CI)	Crude (OR, 95% CI)	Adjusted* (OR, 95% CI)	Crude (OR, 95% CI)	Adjusted* (OR, 95% CI)	Crude (OR, 95% CI)	Adjusted* (OR, 95% CI)
Preeclampsia	10.51 (1.74-63.52)	11.66 (1.76-77.14)	8.35 (1.38-50.40)	10.19 (1.58-65.80)	5.23 (0.87-31.42)	4.46 (0.88-33.95)	4.87 (0.81-29.24)	4.97 (0.80-30.68)
Preterm labour	3.07 (1.68-5.62)	2.25 (1.18-4.30)	1.57 (0.79-3.10)	1.20 (0.58-2.47)	1.33 (0.83-2.14)	1.04 (0.63-1.71)	1.63 (1.04-2.56)	1.33 (0.83-2.15)
Caesarean section	1.46 (1.00-2.13)	0.95 (0.59-1.51)	1.44 (1.02-2.03)	1.11 (0.73-1.68)	1.31 (1.05-1.63)	1.05 (0.81-1.37)	1.19 (0.96-1.47)	0.93 (0.72-1.21)
Macrosomia	3.18 (1.07-9.46)	3.18 (0.97-10.39)	3.34 (1.23-9.08)	4.35 (1.49-12.72)	2.10 (0.91-4.84)	2.01 (0.84-4.82)	2.34 (1.03-5.30)	2.16 (0.91-5.15)
Low birthweight	1.56 (0.70-3.48)	1.16 (0.49-2.72)	1.03 (0.44-2.42)	0.85 (0.35-2.08)	1.21 (0.72-2.03)	1.01 (0.58-1.75)	1.28 (0.77-2.13)	1.08 (0.63-1.84)
LGA	2.47 (1.35-4.49)	2.10 (1.10-4.02)	2.12 (1.19-3.78)	2.15 (1.16-3.98)	1.43 (0.92-2.21)	1.30 (0.82-2.06)	1.31 (0.84-2.03)	1.17 (0.74-1.87)
SGA	0.64 (0.28-1.48)	0.68 (0.29-1.62)	0.78 (0.39-1.56)	0.82 (0.40-1.67)	1.27 (0.87-1.84)	1.35 (0.92-1.99)	1.12 (0.77-1.64)	1.18 (0.80-1.75)
Jaundice	1.46 (0.83-2.57)	1.52 (0.84-2.75)	1.42 (0.84-2.39)	1.51 (0.88-2.60)	1.24 (0.88-1.77)	1.24 (0.86-1.79)	1.30 (0.92-1.83)	1.31 (0.92-1.87)
Admission to neonatology	1.58 (0.62-4.03)	1.15 (0.42-3.10)	1.54 (0.65-3.65)	1.35 (0.55-3.31)	1.31 (0.72-2.40)	1.09 (0.58-2.06)	1.46 (0.82-2.62)	1.27 (0.68-2.34)

ADA: American Diabetes Association; CI: Confidence interval; EASD: European Association for the Studies of Diabetes; GDM: Gestational diabetes mellitus; IADPSG: International Association of Diabetes and Pregnancy Study Groups; LGA: Large for gestational age; NICE: National Institute for Health and Care Excellence; OR: Odds ratio; PAF: Population attributable fraction; SGA: Small for gestational age.

* Adjusted through logistic regression for age, maternal education, pre-pregnancy body mass index, parity, passive smoking, alcohol drinking, previous GDM, history of macrosomia, history of stillbirth, history of preterm labour, history of caesarean section, family history of diabetes, family history of hypertension, and neonatal sex.

4.5.3 Discussion

This prospective cohort study highlights the considerable variations in the prevalence of GDM according to five international diagnostic criteria for GDM, from 6.4% (ADA) to 24.2% (NICE). Our results are consistent with previous studies in Vietnam (T. S. Tran et al., 2013) and other countries (Agarwal et al., 2015; Eades et al., 2017; Morikawa et al., 2010; Olagbuji et al., 2015; Sacks et al., 2012; Trujillo et al., 2015; Wong et al., 2017). A greater number of diagnosed cases may assist with clinical management and improve pregnancy outcomes (Crowther et al., 2005), however, it can affect women's mental health and lead to a higher burden on healthcare services (Visser & de Valk, 2013). Consequently, there is still a debate on the appropriateness of applying new criteria such as the IADPSG/WHO (Salmeen, 2016).

Our findings that the GDM groups experienced higher proportions of caesarean section, macrosomia and LGA are similar to previous studies (Hartling et al., 2014; T. S. Tran et al., 2013; Wendland et al., 2012). In particular, two systematic reviews concluded that women with GDM and their offspring had a greater risk of adverse outcomes including caesarean section, macrosomia, and LGA (Hartling et al., 2014; Wendland et al., 2012). Another study in Vietnam also reported higher prevalence of caesarean section and LGA in the GDM group (T. S. Tran et al., 2013). Elevated blood glucose levels among pregnant women are associated with neonatal fat deposition and foetal overgrowth (International Association of Diabetes and Pregnancy Study Groups Consensus Panel. et al., 2010), which contribute to macrosomia and caesarean section due to the larger size babies. Nevertheless, no differences in the prevalence of neonatal jaundice and admission to neonatal intensive care were observed in our cohort and the previous study in Vietnam (T. S. Tran et al., 2013).

The disparity between the various diagnostic criteria for GDM makes the evaluation and comparison of GDM prevalence difficult across nations and regions within a country. A universal diagnostic criteria for GDM is needed. Although the optimal glucose threshold to diagnose GDM remains unclear, women with the condition are associated with an increased risk of adverse pregnancy outcomes (Metzger et al.,

2008). Early detection and management of GDM will improve the well-being of mothers and their babies.

Chapter 5. CONCLUSIONS AND RECOMMENDATIONS

This chapter summarises the most important findings of the study. Strengths and limitations of the research are also described. Recommendations for future research and better clinic practice and health policies are taken from the findings of the study.

5.1 Conclusions

This study has addressed all five objectives as stated in chapter 1, section 1.4.2. Overall, there was a considerable variation in the prevalence of GDM in Eastern and Southeastern Asia. The prevalence of GDM in Vietnam ranged from 6.4% using the ADA criteria to 24.2% using the NICE criteria. Caesarean section was the most common outcome, while other maternal and neonatal outcomes accounted for smaller proportions. About half of pregnant women had lower total energy intake compared with the national dietary guidelines in Vietnam, and most of them had an inadequate intake of essential micronutrients such as folate, calcium, iron, and zinc. Women with higher levels of PA during pregnancy may have a lower risk of GDM. Main research findings are summarised below.

5.1.1 Prevalence of gestational diabetes mellitus in Eastern and Southeastern Asia (objective 1)

In the comprehensive review of the literature the overall prevalence of GDM in Eastern and Southeastern Asia was 10.1%. GDM prevalence varied considerably between countries in the region with the highest prevalence of 20.1% in Vietnam and the lowest prevalence of 6.1% in Japan and Thailand. Higher prevalence of GDM was observed in lower- and upper-middle income countries compared to high-incomes ones. There was a twofold increase in the prevalence of GDM between using two-step and one-step screening approach.

5.1.2 Maternal lifestyle during pregnancy (objective 2.1)

This study found that the mean energy intake was around 2000 kcal/day of which carbohydrates, fats, and proteins accounted for 52.2%, 31.8%, and 15.9% of the energy, respectively. The main food sources were rice, vegetables, and fruits. Approximately one in two women had lower total energy intake compared with the recommendations for Vietnamese pregnant women. Most of participants had a diet with deficiency in essential micronutrients such as iron, zinc, calcium, and folate.

Total physical activity during pregnancy was 123.2 MET-h/week. Women without GDM had higher levels of total PA, moderate-intensive activity, and household/caregiving activity compared to women with GDM. Few women (2.9%) involved in vigorous-intensity activity. Approximately one in five participants met the recommendations for PA during pregnancy.

No participants reported smoking during pregnancy, however, 52.7% of them were exposed to passive smoking. 13.4% of pregnant women drank alcohol on at least one time during pregnancy.

5.1.3 Prevalence of gestational diabetes mellitus and pregnancy outcomes (objective 2.2)

In this study the prevalence of GDM was 22.8% according to the 2013 WHO criteria. It ranged from 6.4% using the ADA criteria to 24.2% using the NICE criteria. 38.1% of participants gave birth by caesarean section method and few women had preeclampsia (0.3%) and postpartum haemorrhage (1.1%). The proportions of macrosomia, low birthweight, large-for gestational age, and small-for-gestational age were low, with 1.3%, 4.1%, 5.6%, and 8.3%, respectively. 5.2% of women were preterm whereas only 0.4% of participants were stillbirth.

5.1.4 Maternal lifestyle and gestational diabetes mellitus (objective 2.3)

It was found that PA during pregnancy may reduce the risk for developing GDM. Particularly, women with higher levels of total PA, moderate-intensity activity, and household/caregiving activity had lower risk of GDM, independent of sedentary behaviour. Our study did not observe the associations between other types of PA such as sitting time, light-intensity activity, vigorous-intensity activity, occupation, sports/exercise, commuting and GDM.

5.1.5 Gestational diabetes mellitus and pregnancy outcomes (objective 2.4)

Women with GDM using the ADA, EASD, and IADPSG/WHO criteria had significantly higher prevalence of caesarean section compared to those without GDM. However, these associations were not significant differences between the two groups after adjustment for confounding factors. Few women had preeclampsia and there were no significant differences in postpartum haemorrhage between women with and without GDM.

Women with GDM using the ADA, EASD and NICE criteria appeared to have a higher incidence of macrosomia than their counterparts without GDM. This association remained significant for the EASD criteria after adjustment for confounding factors. Women with GDM by the ADA and EASD were likely to give births with large-for-gestational age compared to controls. There were no differences in other neonatal outcomes between GDM and normal groups.

5.2 Study strengths and limitations

This study was a multicentre, prospective cohort study in Vietnam with a relatively large sample size followed up from pregnancy to delivery. Another strength of this study was that it assessed various modifiable maternal risk factors for adverse pregnancy outcomes. Particularly, PA was not only examined by total, but also by intensity and domain. Information on dietary intakes was collected based on a

comprehensive item food list in Vietnam. Our study is also the first prospective cohort study investigating the associations between maternal risk factors and pregnancy outcomes in Vietnam. In addition, the rate of loss to follow up in our study was relatively low, with only 5.6%. Finally, the first comprehensive literature review and meta-analysis of GDM prevalence in Eastern and Southeastern Asia region including Vietnam has been reported.

This study has several limitations that need to be considered when interpreting the study results. Firstly, participants were mainly recruited in urban and suburban areas and may not represent rural women in Vietnam. Thus, the extrapolation of the study findings to these areas should be undertaken with caution. Secondly, despite a high response rate of participation from the participated hospitals selection bias was not ruled out. Thirdly, data on maternal life style were obtained by self-reporting of participants which might present recall bias. We tried to minimise this error by using validated questionnaires for Vietnamese population and conducting direct interviews by experienced interviewers with supportive materials. Fourthly, the numbers of subjects who experienced several pregnancy outcomes including preeclampsia and stillbirth were small. This hampered our ability to assess the association between GDM and pregnancy outcomes. Fifthly, the nutritional profile of pregnant women was assessed, and respective results were published, despite the lack of consideration for the association between dietary intake and GDM. In addition, although various demographic and maternal lifestyle factors were controlled in the regression analyses, our findings may be influenced by residual confounding factors due to the nature of an observational study. Finally, results of a meta-analysis showed that the prevalence of GDM was substantially heterogeneous and not available in all countries belonging to the Eastern and Southeastern Asia.

5.3 Recommendations

5.3.1 Implications for health promotion programmes

Based on the findings of our study, some recommendations are suggested to improve maternal and child health outcomes as follows:

All pregnant women are encouraged to attend antenatal classes which should include information on dietary intake and physical activity during pregnancy in order to increase the rates of meeting standard requirements for both energy and activity during pregnancy.

All pregnant women are encouraged to undertake a GDM test during pregnancy to early detect their status as well have appropriate treatments to prevent adverse health outcomes for both mother and their offspring.

A national guidelines on diagnosis, treatment, and management of GDM should be disseminated to all hospitals and clinics for universal implementation. Appropriate nutrition and PA intervention programmes targeting pregnant women and women of reproductive age should be performed nationwide. Specifically, essential nutrients such as iron, zinc, folate, and calcium should be provided to meet the recommendations. Moderate-intensive activity, household/caregiving activity, and other types of PA should also be highlighted to meet the guidelines.

5.3.2 Implications for future research

Vietnam has six ecological regions with diverse characteristics, therefore the maternal lifestyle and GDM prevalence may differ between regions. In addition, the numbers of some pregnancy outcomes were not large enough to evaluate the associations between risk factors and outcomes. Thus, further cohort studies with larger sample size in different regions are needed, especially in rural and mountainous areas.

GDM is known to associate with long-term effects on maternal and child health postpartum. However, no study has examined this impact in Vietnam. There are needs for future studies to measure these effects.

As little was known about women and health workers' knowledge and practice on GDM, especially GDM management during and after pregnancy, future studies evaluating these aspects may help to develop appropriate intervention programmes.

The screening for GDM is not mandatory yet in Vietnam while the prevalence of GDM is relatively high compared to another countries. Therefore, the development of GDM risk score for Vietnamese women is needed to early screen and diagnose GDM. This would be an extremely useful tool in a resource-limited setting like Vietnam.

The use of smartphone apps to deliver health behaviour interventions is increasing rapidly as they have enormous advantages such as low cost, constant access, convenience for users, large reach, and timely feedback. In Vietnam, the rates of mobile phone ownership and mobile network are very high. Therefore, future research using mobile phone apps-based interventions against GDM would be helpful in improving maternal and child health in a resource-limited setting like Vietnam.

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Appendices

Appendix A Statement of contribution of others

20 January 2019

To Whom It May Concern:

I, Luat Cong Nguyen, contributed as the main person responsible for study design, data collection, data cleaning, data analysis, and writing up all presented as part of the thesis. Details of my publications as follows:

1. **Cong Luat Nguyen,** Phung T.H. Nguyen, Tan Khac Chu, et al. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID 7:e016794. doi: 10.113 6/bmj open-2017-016794
2. **Cong Luat Nguyen**, Ngoc Minh Pham, Colin W. Binns, Dat Van Duong, and Andy H. Lee. 2018. Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis. *Journal of Diabetes Research*, Article ID 6536974, 10 pages. https://doi.org/10.l 155/2018/6536974
3. **Cong Luat Nguyen**, Dong Van Hoang, Phung T.H. Nguyen, et al. 2018. Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam. *Nutrients,* 10(8),1025. https://doi.org/l 0.3390/nu 10081025
4. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, et al. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol,* 55(9): 955-962. https://doi.org/10.1007/s00592-018-l 174-3

Signature of Candidate: .....

I, as a Co-Author, endorse that this level of contribution by the candidate indicated above is appropriate.

Andy H. Lee .....

Colin W. Binns .....

Dat Van Duong .....

Ngoc Minh Pham .....

Phung Thi Hoang Nguyen .....

Anh Vo Van Ha .....

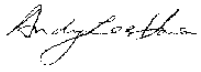
Tan Khac Chu .....

30 January 2019

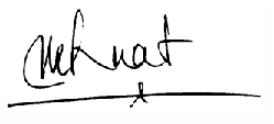
To Whom It May Concern

I, Prof. Andy H. Lee, contributed as a main supervisor of PhD candidate Luat Cong Nguyen. I had ongoing close involvement with the research including contribution to the study design, discussion of the findings and tentative papers, revising the manuscripts and giving comments to improve the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794
2. **Cong Luat Nguyen**, Ngoc Minh Pham, Colin W. Binns, Dat Van Duong, and Andy H. Lee. 2018. Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis. *Journal of Diabetes Research*, Article ID 6536974, 10 pages. https://doi.org/10.1155/2018/6536974
3. **Cong Luat Nguyen**; Dong Van Hoang; Phung Thi Hoang Nguyen, Anh Vo Van Ha, Tan Khac Chu, Ngoc Minh Pham, Andy H. Lee, Dat Van Duong, and Colin W. Binns. 2018. Low Dietary Intakes of Essential Nutrients during Pregnancy in Vietnam. *Nutrients*, 10(8), 1025. https://doi.org/10.3390/nu10081025
4. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Duong Van Dat, Thi Hong Duong, and Colin W. Binns. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol*, 55(9): 955-962. https://doi.org/10.1007/s00592-018-1174-3



Professor Andy H. Lee (Main supervisor)



Luat Cong Nguyen (PhD Candidate)

30 January 2019

To Whom It May Concern

I, Prof. Colin W. Binns, contributed as an associate supervisor of the PhD candidate Luat Cong Nguyen. I had ongoing close involvement with the research including contribution to the study design, discussion of the findings and tentative papers, revising the manuscripts and giving comments to improve the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID 7:e016794. doi: 10.1136/bmjopen-2017-016794
2. **Cong Luat Nguyen**, Ngoc Minh Pham, Colin W. Binns, Dat Van Duong, and Andy H. Lee. 2018. Prevalence of Gestational Diabetes Mellitus in Eastern and Southeastern Asia: A Systematic Review and Meta-Analysis. *Journal of Diabetes Research*, Article ID 6536974, 10 pages. https://doi.org/10.1155/2018/6536974
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4. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Dat Van Duong, Thi Hong Duong, and Colin W. Binns. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol*, 55(9): 955-962. https://doi.org/10.1007/s00592-018-1174-3

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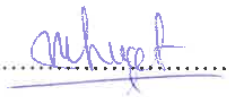
John Curtin Distinguished Professor Colin W. Binns (Associate supervisor)



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Luat Cong Nguyen (PhD Candidate)

23 January 2019

To Whom It May Concern

I, Dr. Dat Van Duong, contributed as an associate supervisor of the PhD candidate Luat Cong Nguyen. I had ongoing close involvement with the research including contribution to the study design, revising the manuscripts and giving comments to improve the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID 7:e016794. doi: 10.1136/bmjopen-2017-016794
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Dr. Dat Van Duong (Associate supervisor)

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Luat Cong Nguyen (PhD Candidate)

23 January 2019

To Whom It May Concern:

I, Dr. Ngoc Minh Pham, contributed as an associate supervisor of the PhD candidate Luat Cong Nguyen. I had ongoing close involvement with the research including contribution to the data analysis, revising the manuscripts and giving comments to improve the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

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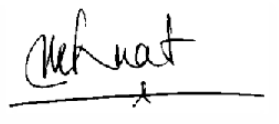
4. **Cong Luat Nguyen**, Ngoc Minh Pham, Andy H. Lee, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Dat Van Duong, Thi Hong Duong, and Colin W. Binns. 2018. Physical activity during pregnancy is associated with a lower prevalence of gestational diabetes mellitus in Vietnam. *Acta Diabetol*, 55(9): 955-962. https://doi.org/10.1007/s00592-018-1174-3

Dr. Ngoc Minh Pham (Associate supervisor)



Luat Cong Nguyen (PhD Candidate)

22 January 2019

To Whom It May Concern

I, Phung Thi Hoang Nguyen, provided advice on the study design and instruments, implemented data collection, and commended draft manuscripts of the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID 7:e016794. doi: 10.1136/bmjopen-2017-016794

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Phung Thi Hoang Nguyen (Co-author)

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Luat Cong Nguyen (PhD Candidate)

22 January 2019

To Whom It May Concern

I, Anh Vo Van Ha, provided advice on the study design and instruments, implemented data collection, and commended draft manuscripts of the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID 7:e016794. doi: 10.1136/bmjopen-2017-016794

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Anh Vo Van Ha (Co-author)

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Luat Cong Nguyen (PhD Candidate)

22 January 2019

To Whom It May Concern

I, Tan Khac Chu, provided advice on the study design and instruments, implemented data collection, and commended draft manuscripts of the following publications. Mr Luat Cong Nguyen was responsible for the study design and implementation, data collection, statistical analysis, interpreting the findings and drafting of manuscripts.

1. **Cong Luat Nguyen**, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha, Ngoc Minh Pham, Dat Van Duong, Dung Van Do, Hong Kim Tang, Colin W. Binns, Andy H. Lee. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794

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Tan Khac Chu (Co-author)

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Luat Cong Nguyen (PhD Candidate)

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1. **Cong Luat Nguyen**, Phung T.H. Nguyen, Tan Khac Chu, et al. 2017. Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study. *BMJ Open*, Article ID **7:**e016794. doi: 10.1136/bmjopen-2017-016794

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Appendix C Study instruments

C.1 Information letter (English version)

Project title: Maternal lifestyle and nutritional status in relation to pregnancy and child health outcomes: A multi-centre prospective cohort study in Vietnam

The School of Public Health at Curtin University is studying the associations among maternal lifestyle and nutritional status with pregnancy and child health outcomes in Vietnam. This research has been approved by the Curtin University Human Research Ethics Committee (No. HR32/2015) and the Hanoi University of Public Health Human Research Ethics Committee (No. 05/HPUMPRB).

We would like to invite you to participate in our study. There will be six interviews at antenatal, delivery, 1, 3, 6, and 12 months postpartum. It will take you 30-40 minutes for each interview to answer some questions related to your lifestyle, dietary intakes, attitude and practice in feeding and breastfeeding your new baby, antenatal and postnatal depression, and well-being postpartum. These questions are insensitive and there are no interventions in both you and your baby.

Your participation in this research is completely voluntary. You can refuse any specific question that you are uncertain or find it difficult to answer. You are totally free to withdraw from the study at any time without negative consequences. The information you provided will be kept strictly confidential, and your identity will remain anonymous. Only aggregated and de-identified data from all participants will be analysed and reported. Your participation has a vital role in supporting our study's success and improving maternal and child health in a resource-limited setting like Vietnam.

If you have any concern or questions about this study, please contact the following project staff:

- Professor Andy H. Lee, Main supervisor, Curtin University, on +61 8 92664180 or andy.lee@curtin.edu.au
- Luat Cong Nguyen, PhD candidate, Curtin University, on +84 912422277 or luatcong.nguyen@postgrad.curtin.edu.au

Thank you very much for your cooperation.

C.2 Consent form (English version)

Project title: Maternal lifestyle and nutritional status in relation to pregnancy and child health outcomes: A multi-centre prospective cohort study in Vietnam

(You are inviting to participate in this study. Please read the information document carefully and ask any questions you wish. Do not sign this informed consent form unless you fully understand the nature of the study and the commitment you may need to make over the next two years.)

I, …….……., have read and understood the Information letter given to me. I understand the purpose, participant's risks and rights, and requirements of the study. I fully understand that my participation is voluntary and I am free to withdraw from the study at any time without any negative consequences. I have also been given the opportunity to ask questions about the study. Data gained in this study may be published with de-identified personal information. Therefore, I agree to participate in the study.

Signature: _____ Date: _____/_____/_____

Full name of participant: _____

Signature of witness: _____ Date: _____/_____/_____

Full name of witness: _____

C.3 Baseline questionnaire (English version)

A. PARTICIPANT'S INDENTIFICATION AND BASIC INFORMATION

A1. Date of interview: _____/_____/_____(DD/MM/YYYY)

A2. Interviewer's name: _____

A3. Mother's name: _____

A4. Mother's address: _____

A5. Mother's phone number: _____

A6. Husband's name: _____

A7. Husband's phone number: _____

A8. Duration of pregnancy: _____ weeks

B. DEMOGRAPHIC INFORMATION

No.	Questions	Answers
B1.	What is your age (years)?	___/___/_____(DD/MM/YYYY) (_____ years)
B2.	What is your marital status?	1. Never married 2. Married 3. Widowed /Divorced/Separated
B3.	What is your main occupation? (Tick only one, don't read the list)	1. Farmer 2. Worker 3. Office staff 4. Housewife 5. Other (please specify): ……
B4.	What is your highest level of education you have completed?	1. No schooling 2. Primary school 3. Secondary school 4. High school 5. College or vocational school 6. University or higher
B5.	What is your husband's age (years)?	___/___/_____(DD/MM/YYYY) (_____ years)

No.	Questions	Answers
B6.	What is your husband's main occupation? (Tick only one, don't read the list)	1. Farmer 2. Worker 3. Office staff 4. Housewife 5. Other (please specify): ……
B7.	What is the highest level of education your husband completed?	1. No schooling 2. Primary school 3. Secondary school 4. High school 5. College or vocational school 6. University or higher
B8.	How many children have you given birth, including stillbirth?	Number: _____ Son: __ Daughter: ___ Stillborn: ____

C. ANTHROPOMETRICS

No.	Questions	Answers
C1.	Mother's height?	_ _ _ . _ cm
C2.	Mother's weight?	_ _ _ . _ kg
C3.	Mother's waist circumference?	_ _ _ . _ cm
C4.	Mother's hip circumference?	_ _ _ . _ cm
C5.	Mother's blood pressure and heart rate?	Measurement 1: – Systolic: _ _ _ . _ mmHg – Diastolic: _ _ _ . _ mmHg – Heart rate: _ _ _ beats/minute Measurement 2: – Systolic: _ _ _ . _ mmHg – Diastolic: _ _ _ . _ mmHg – Heart rate: _ _ _ beats/minute

D. MATERNAL HISTORY

No.	Questions	Answers
D1.	What was your weight before this pregnancy?	_ _ _ . _ kg
D2.	What was your weight at first antenatal visit?	_ _ _ . _ kg (at _ _ weeks of gestation)
D3.	What was the date of your last menstrual period (if remembered)	_____/_____/_____(DD/MM/YYYY)
D4.	What is the date you are expected to give birth (if known)?	_____/_____/_____(DD/MM/YYYY)
D5.	Do you have diabetes before this pregnancy?	1. No 2. Yes → 2a: Type I 2b: Type II 9. Unknown
D6.	Does anyone in your family such as your parents, brothers, sisters have type 2 diabetes?	1. No 2. Yes
D7.	Do you have hypertension before this pregnancy?	1. No 2. Yes → 2a: Systolic = _ _ _ . _ mmHg 2b: Diastolic = _ _ _ . _ mmHg 9. Unknown
D8.	Does anyone in your family such as your parents, brothers, sisters have hypertension?	1. No 2. Yes
D9.	Have you ever had gestational diabetes mellitus in your previous pregnancy?	1. No 2. Yes
D10.	Have you ever had stillbirth in your previous pregnancy?	1. No 2. Yes
D11.	Have you ever had preeclampsia in your previous pregnancy?	1. No 2. Yes

No.	Questions	Answers
D12.	Have you ever had preterm birth in your previous pregnancy?	1. No 2. Yes
D13.	Have you ever had macrosomia (>4000 g) in your previous pregnancy and childbirth?	1. No 2. Yes
D14.	Have you ever had congenital malformations in your previous pregnancy?	1. No 2. Yes
D15.	Have you ever had abortion in your previous pregnancy?	1. No 2. Yes
D16.	Have you ever had caesarean section in your previous pregnancy?	1. No 2. Yes
D17.	Do you have a history of polycystic ovary syndrome?	1. No 2. Yes
D18.	Do you have a history of renal disease?	1. No 2. Yes
D19.	Do you have a history of other chronic diseases?	1. No 2. Yes → Please specify: ……

E. PHYSICAL ACTIVITY (during pregnancy)

It is very important you tell us about yourself honestly. There are no right or wrong answers. We just want to know about the things you are doing during last month.

During last 3 months, when you are NOT at work, how much time do you usually spend:

E1. Preparing meals (cook, set table, wash dishes) None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E2. Dressing, bathing, feeding children while you are sitting None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6

E3. Dressing, bathing, feeding children while you are <u>standing</u> None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E4. Playing with children while you are <u>sitting or standing</u> None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E5. Playing with children while you are <u>walking or running</u> None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E6. Carrying children None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E7. Taking care of an old adult None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E8. Sitting and using a computer or writing, while <u>not</u> at work None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E9. Watching TV or a video None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hour per day.....3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6	E10. Sitting and reading, talking, or on the phone, while <u>not</u> at work None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6
E11. Playing with pets None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E12. Light cleaning (make beds, laundry, iron, put things away) None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E13. Shopping (for food, clothes, or other items) None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E14. Heavier cleaning (vacuum, mop, sweep, wash windows) None.....1 Less than 1/2 hour per week....2 1/2 to almost 1 hour per week..3 1 to almost 2 hours per week...4 2 to almost 3 hours per week...5 3 or more hours per week.....6

Going Places…

During last 3 months, how much time do you usually spend:

E15. Walking slowly to go to places (such as to the bus, work, visiting) Not for fun or exercise None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E16. Walking quickly to go to places (such as to the bus, work, visiting) Not for fun or exercise None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E17. Riding a bicycle to go places (such as the bus, work, or school) Not for fun or exercise None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E18. Driving or riding in a motorbike or bus None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6

For Fun or Exercise…

During last 3 months, how much time do you usually spend:

E19. Walking slowly for fun or exercise None.....1 Less than 1/2 hour per week.....2 1/2 to almost 1 hour per week..3 1 to almost 2 hours per week....4 2 to almost 3 hours per week....5 3 or more hours per week.....6	E20. Walking more quickly for fun or exercise None.....1 Less than 1/2 hour per week.....2 1/2 to almost 1 hour per week..3 1 to almost 2 hours per week....4 2 to almost 3 hours per week....5 3 or more hours per day.....6
E21. Walking quickly up hills for fun or exercise None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E22. Jogging None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E23. Prenatal exercise class None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	E24. Swimming None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6

E25. Dancing	E26.
None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	Name of Activity None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6
E27. Name of Activity None.....1 Less than 1/2 hour per day.....2 1/2 to almost 1 hour per day.....3 1 to almost 2 hours per day.....4 2 to almost 3 hours per day.....5 3 or more hours per day.....6	

Please fill out the next section if you work for wages, as a volunteer, or if you are a student. If you are a homemaker, out of work, or unable to work, you do not need to complete this last section.

At work…… During last 3 months, how much time do you usually spend:

E28. Sitting at working or in class	E29. Standing or slowly walking at work while carrying things (heavier than a 1 gallon milk jug)
None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6	None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6
E30. Standing or slowly walking at work not carrying anything None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6	E31. Walking quickly at work while carrying things (heavier than a 1 gallon milk jug) None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6
E32. Walking quickly at work not carrying anything None.....1 Less than 1/2 hour per day.....2 1/2 to almost 2 hours per day...3 2 to almost 4 hours per day.....4 4 to almost 6 hours per day.....5 6 or more hours per day.....6	

F. EXPOSURE TO CIGARETTE SMOKING

F1.	**Before** you became pregnant, did you smoke?	1 [ ] No *GO TO F4* 2 [ ] Yes	
F2.	How many years did you smoke or since what age?	_ _ years (or since _ _ years old)	
F3.	On average, how many of the following tobacco products did you smoke per day **before pregnancy**?	Manufactured cigarettes? Hand-roll cigarettes? Pipes full of tobacco? Cigars, cheroots or cigarillos? Number of water pipe sections? Any others? Specify……	……. per day ……. per day ……. per day ……. per day ……. per day ……. per day
F4.	**While** you are pregnant, do you smoke?	1 [ ] No *GO TO F6* 2 [ ] Yes	
F5.	On average, how many of the following tobacco products do you smoke per day **during pregnancy**?	Manufactured cigarettes? Hand-roll cigarettes? Pipes full of tobacco? Cigars, cheroots or cigarillos? Number of water pipe sections? Any others? Specify……	……. per day ……. per day ……. per day ……. per day ……. per day ……. per day
F6.	Did your relatives/people living with you smoke at home **before** you were pregnant?	1 [ ] No 2 [ ] Yes	
F7.	Are your relatives/people living with you smoking at home **while** you are pregnant?	1 [ ] No 2 [ ] Yes	
F8.	During the past 30 days, did someone smoke in closed areas in your workplace?	1 [ ] No 2 [ ] Yes	

G. FOOD FREQUENCY QUESTIONNAIRE

General dietary habit – *please recall your habit since you became pregnant*

No	Questions	Answer
G1.	Are you on a special diet listed below now?	0 [ ] No 1 [ ] Vegetarian 2 [ ] Low fat 3 [ ] Low salt 4 [ ] Other: ……
G2.	Do you have 3 meals per day regularly?	0 [ ] Regular 1 [ ] Often regular 2 [ ] Sometime regular 3 [ ] Almost irregular
G3.	Your eating habit *Eating breakfast:* 1 [ ]everyday 2 [ ]frequently 3 [ ]occasionally 4 [ ] never *Eating take-away food or eating out:* 1 [ ]everyday 2 [ ]frequently 3 [ ]occasionally 4 [ ] never *Eating snacks (Biscuits…):* 1 [ ]everyday 2 [ ]frequently 3 [ ]occasionally 4 [ ] never *Eating sweet food (candy, congee…*): 1 [ ]everyday 2 [ ]frequently 3 [ ]occasionally 4 [ ] never	
G4.	Did you or any of your family members feel your food was salty?	0 [ ] never 1 [ ] sometimes 2 [ ] usual
G5.	When you eat meat, did you trim off all the fat?	0 [ ] never 1 [ ] sometimes 2 [ ] usual
G6.	When you ate chicken, did you eat the skin	0 [ ] never 1 [ ] sometimes 2 [ ] usual
G7.	How often do you eat the following types of food? *(How many times per Month/Week/Day?)* *Fried food:* ..... times/[ ]**M** [ ]**W** [ ]**D** *Smoked food:* ..... times/[ ]**M** [ ]**W** [ ]**D** *Cured food:* ..... times/[ ]**M** [ ]**W** [ ]**D** *Grilled food:* ..... times/[ ]**M** [ ]**W** [ ]**D**	
G8.	How often do you use vegetable cooking oil?	..... times/[ ]**M** [ ]**W** [ ]**D**
G9.	How often do you use pork lard?	..... times/[ ]**M** [ ]**W** [ ]**D**
G10.	When you eat, how often do you use the following seasonings? *Fish sauce:* ..... times/[ ]**M** [ ]**W** [ ]**D** *Salt:* ..... times/[ ]**M** [ ]**W** [ ]**D**	

No	Questions	Answer
	Soybean sauce: *Tomato sauce:*	..... times/[ ]**M** [ ]**W** [ ]**D** ..... times/[ ]**M** [ ]**W** [ ]**D**
G11.	*Since you became pregnant, have you changed your diet habit*	1 [ ] No 2 [ ] Yes
G12.	*If yes, please specify:* *- How you have changed: ……* *- The reasons for this change: ……*	

Consumption of beverage: How often/what amount of/ how do you drink the following beverage? – Please tell us about your dietary habits since you became pregnant.

No	Beverage	Frequency Per **M**onth/**W**eek/**D**ay	Unit (PS: portion size)	Quantity/ each time (PS)	For how many months?
G13.	Beer	____times/[ ]**M** [ ]**W** [ ]**D**	*300ml cup* ***(A)***		
G14.	Home-made rice wine	____times/[ ]**M** [ ]**W** [ ]**D**	*30ml cup* ***(B)***		
G15.	Home-made herbal rice wine	____times/[ ]**M** [ ]**W** [ ]**D**	*30ml cup* ***(B)***		
G16.	Strong bottled liquor (≥ 39% alcohol; e.g. vodka)	____times/[ ]**M** [ ]**W** [ ]**D**	*30ml cup* ***(B)***		
G17.	Light bottled liquor (≤ 29% alcohol; e.g. small bottle vodka)	____times/[ ]**M** [ ]**W** [ ]**D**	*30ml cup* ***(B)***		
G18.	Red wine	____times/[ ]**M** [ ]**W** [ ]**D**	*100ml cup* ***(C)***		
G19.	White wine	____times/[ ]**M** [ ]**W** [ ]**D**	*100ml cup* ***(C)***		
G20.	Since you became pregnant, have you changed your drinking habit for any type of liquor above?			0 [ ] No 1 [ ] Yes	
If yes, please tell us the reasons for that change?					
G21.	Green tea (dried)	____times/[ ]**M** [ ]**W** [ ]**D**	*100ml cup* ***(D)***		
G22.	Green tea leave	____times/[ ]**M** [ ]**W** [ ]**D**	*200ml cup* ***(E)***		
G23.	Black tea	____times/[ ]**M** [ ]**W** [ ]**D**	*100ml cup* ***(D)***		
G24.	Oolong tea	____times/[ ]**M** [ ]**W** [ ]**D**	*100ml cup* ***(D)***		
G25.	Since you became pregnant, have you changed your drinking habit for any type of tea above?			0 [ ] No 1 [ ] Yes	
If yes, please tell us the reasons for that change?					

No	Beverage	Frequency Per **M**onth/**W**eek/**D**ay	Unit (PS: portion size)	Quantity/ each time (PS)	For how many months?
G26.	Black coffee	____times/[ ]**M** [ ]**W** [ ]**D**	*150ml cup* ***(F)***		
G27.	Instant coffee	____times/[ ]**M** [ ]**W** [ ]**D**	*Bag* *5gr spoon* ***(H)***	*……..bag* *…….spoon*	
G28.	Milk coffee	____times/[ ]**M** [ ]**W** [ ]**D**	*150ml cup* ***(G)***		
G29.	Since you became pregnant, have you changed your drinking habit for any type of coffee above?			0 [ ] No 1 [ ] Yes	
	If yes, please tell us the reasons for that change?				
G30.	Water	_____times/day	*250ml cup*	_____cup	
G31.	Soy milk	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G32.	Lemon juice	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G33.	Orange juice	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G34.	Coconut water	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G35.	Fruit shake juice	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G36.	*What type of fruits did you drink the most?*	1 [ ] mango 2 [ ] guava 3 [ ] water melon 4 [ ] avocado 5 [ ] custard apple	6 [ ] paw paw 7 [ ] Pineapple 8 [ ] sapodilla 9 [ ] Other:.....		
G37.	Soft drink (coke, pepsi…)	____times/[ ]**M** [ ]**W** [ ]**D**	*250ml cup*	_____cup	
G38.	*What type of soft drinks did you drink the most?*	1 [ ] Coca cola 2 [ ] Pepsi 3 [ ] Fanta	4 [ ] Nestea 5 [ ] Icetea 6 [ ] Other canned soft drink		
G39.	Did you add sugar into your drinks, such as tea, coffee or orange juice? *If yes, how many spoons (5g) did you add?*		0 [ ] No 1 [ ] Yes, …….spoons		

Consumption of soy bean products

How often do you eat soy bean products?

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal (0.5 PS, 1PS, 1.5PS)
G40.	Fried tofu	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**I**)	_____PS
G41.	Raw tofu	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**I**)	_____PS
G42.	Soybean curd with sweet syrup	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**J**)	_____PS

Consumption of vegetables and fruit

How often/what amount of/ how do you eat vegetables/fruit?

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G43.	Tomato	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G44.	Bean sprout	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G45.	Amaranth, Jute potherb	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G46.	Water spinach	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G47.	Mustard green, Chinese cabbage	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G48.	Malabar nightshade	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G49.	Crown-daisy	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G50.	Chinese leek	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G51.	Cabbage	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G52.	French bean	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G53.	Pumpkin	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G54.	Gourd	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G55.	Cucumber	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G56.	Broccoli	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G57.	Cauliflower	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G58.	Chinese yam	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G59.	Ash gourd, wax gourd	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G60.	Bitter melon	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**M**)	_____PS
G61.	Capsicum	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**N**)	_____PS
G62.	Carrot	____times/[ ]**M** [ ]**W** [ ]**D**	Whole (**O**)	_____PS
G63.	White potato	____times/[ ]**M** [ ]**W** [ ]**D**	Whole (**O**)	_____PS
G64.	Sweet potato	____times/[ ]**M** [ ]**W** [ ]**D**	Whole (**P**)	_____PS
G65.	Luffa	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**L**)	_____PS
G66.	Mushroom	____times/[ ]**M** [ ]**W** [ ]**D**	Gram	_____gr
G67.	Dragon fruit	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G68.	Banana	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G69.	Papaya	____times/[ ]**M** [ ]**W** [ ]**D**	Piece 20x4cm (**Q**)	_____PS
G70.	Pomelo	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**R**)	_____PS
G71.	Longan	____times/[ ]**M** [ ]**W** [ ]**D**	Kg	_____kg

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G72.	Orange	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G73.	Water melon	____times/[ ]**M** [ ]**W** [ ]**D**	Piece 100 gr (**S**)	_____PS
G74.	Pear	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G75.	Grape	____times/[ ]**M** [ ]**W** [ ]**D**	Kg	_____kg
G76.	Guava	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G77.	Apple	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G78.	Lychee	____times/[ ]**M** [ ]**W** [ ]**D**	Kg	_____kg
G79.	Mangoes	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G80.	Durian	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**T**)	_____PS

Consumption of sweet varieties - *How often/what amount of/ how do you eat sweet varieties?*

No	Food item	Frequency (per month/week/day)	Unit	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G81.	Sweet soup (made of glutinous rice and bean, corn…)	____times/[ ]**M** [ ]**W** [ ]**D**	250 ml cup (**U**)	_____PS
G82.	Please choose 3 types that you eat the most?		1 [ ] Glutinous soup with taro 2 [ ] Glutinous soup with corn 3 [ ] Glutinous soup with mung bean 4 [ ] Glutinous soup with black bean 5 [ ] Glutinous soup with white bean 6 [ ] Mix glutinous soup with bean 7 [ ] Other:.....	
G83.	Sweet cakes	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**V**)	_____PS
G84.	Biscuits	____times/[ ]**M** [ ]**W** [ ]**D**	Piece	_____PS

Consumption of bread and rice varieties - *How often/what amount of/ how do you eat the following items?*

No	Food item	Frequency (per month/week/day)	Unit	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G85.	French type bread (either plain or with meat)	___times/[ ]**M** [ ]**W** [ ]**D**	Load (**W**)	_____PS
G86.	Sliced bread (either plain or with meat)	___times/[ ]**M** [ ]**W** [ ]**D**	Slice	_____PS
G87.	Rice-based noodles	___times/[ ]**M** [ ]**W** [ ]**D**	Large bowl (**X**)	_____PS
G88.	Instant noodle	___times/[ ]**M** [ ]**W** [ ]**D**	Bag	_____PS

No	Food item	Frequency (per month/week/day)	Unit	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G89.	Plain rice (at home)	___times/[ ]**M** [ ]**W** [ ]**D**	Small bowl	_____PS
G90.	Rice comes in a serving (a plate of fried rice, broken rice…) when eating outside	___times/[ ]**M** [ ]**W** [ ]**D**	Plate	_____PS
G91.	Glutinous rice (either plain, with bean, or salted)	___times/[ ]**M** [ ]**W** [ ]**D**	Small bowl	_____PS
G92.	Rice porridge	___times/[ ]**M** [ ]**W** [ ]**D**	Large bowl (KK)	_____PS

Consumption of meat- *How often/what amount of/how do you eat?*

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G93.	Pork lean	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**Y**)	_____PS
G94.	Pork medium fat	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**Z**)	_____PS
G95.	Pork rib	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**AA**)	_____PS
G96.	Pork lower leg	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**BB**)	_____PS
G97.	Pork steak	____times/[ ]**M** [ ]**W** [ ]**D**	Piece 60g (**CC**)	_____PS
G98.	Beef	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl (**DD**)	_____PS
G99.	Chicken	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**EE**)	_____PS
G100.	Pigeon	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**FF**)	_____PS
G101.	Duck	____times/[ ]**M** [ ]**W** [ ]**D**	Small piece (**FF**)	_____PS
G102.	Pork heart	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G103.	Pork liver	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G104.	Pork kidney	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G105.	Poultry offal	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr

Consumption of fish, egg and milk- *How often/what amount of/how do you eat?*

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G106.	Sea fish (Mackerel, tuna...)	____times/[ ]**M** [ ]**W** [ ]**D**	Piece 70g (**GG**)	_____PS
G107.	*Please check two types of sea fish that you eat the most often?*		1 [ ] Mackerel 2 [ ] Tuna 3 [ ] Mullet 4 [ ] other, specify……	

No	Food item	Frequency (per month/week/day)	Unit (PS)	Quantity/meal? (½ PS, 1PS, 1.5PS...)
G108.	Fresh water fish (Tilapia...)	____times/[ ]**M** [ ]**W** [ ]**D**	Piece 50g (**HH**)	_____PS
G109.	*Please check two types of fresh water fish that you eat the most often?*		1 [ ] Tilapia 2 [ ] Snake-head 3 [ ] Carp 4 [ ] Chub 5 [ ] Other, specify……	
G110.	Shrimp	____times/[ ]**M** [ ]**W** [ ]**D**	Whole (**II**)	_____PS
G111.	Squid/octopus	____times/[ ]**M** [ ]**W** [ ]**D**	Piece (**JJ**)	_____PS
G112.	Sea shells	____times/[ ]**M** [ ]**W** [ ]**D**	Small bowl	_____PS
Egg				
G113.	Chicken egg	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
G114.	Duck egg	____times/[ ]**M** [ ]**W** [ ]**D**	Whole	_____PS
Preserved food				
G115.	Pickle vegetable & garlic	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G116.	Fermented soy product	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G117.	Salted fish	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
G118.	Preserved meat (sausage…)	____times/[ ]**M** [ ]**W** [ ]**D**	gram	_____gr
Milk				
G119.	Cow whole milk	____times/[ ]**M** [ ]**W** [ ]**D**	Cup 250ml	_____PS
G120.	Soya milk	____times/[ ]**M** [ ]**W** [ ]**D**	Cup 250ml	_____PS
G121.	Milk powder, whole	____times/[ ]**M** [ ]**W** [ ]**D**	5gr spoon (**H**)	_____PS
G122.	Yogurt	____times/[ ]**M** [ ]**W** [ ]**D**	Box	_____PS
G123.	Condensed milk	____times/[ ]**M** [ ]**W** [ ]**D**	ml (**C**)	_____PS

Dietary supplements - *How often/what amount of/how did you use?*

No.	Item	Frequency (per month/week/day)	Unit	Quantity /time (unit)	Years of use
G124.	Multivitamin	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G125.	Vitamin A	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G126.	Vitamin C	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G127.	Vitamin E	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G128.	Riboflavin (Vitamin B6)	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G129.	Vitamin D	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G130.	Acid Folic	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G131.	Calcium	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		

G132.	Selenium	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G133.	Iron	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G134.	Zinc	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G135.	Iodine	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G136.	DHA	____times/[ ]**M** [ ]**W** [ ]**D**	Tablet		
G137.	Fish oil	____times/[ ]**M** [ ]**W** [ ]**D**			
G138.	Ginseng	____times/[ ]**M** [ ]**W** [ ]**D**			
Other?					
G139.	Energy drink (eg. red bull)	____times/[ ]**M** [ ]**W** [ ]**D**			
G140.					
G141.					
G142.					
G143.					
G144.					
G145.					

THANK YOU VERY MUCH FOR YOUR PARTICIPATION!

C.4 Discharge questionnaire (English version)

A. PARTICIPANT'S IDENTIFICATION

A1. Date of interview: _____/_____/_____(DD/MM/YYYY)

A2. Interviewer's name: _____

A3. Mother's name: _____

A4. Mother's address: _____

A5. Mother's phone number: _____

A6. Husband's phone number: _____

B. INFORMATION ON PREGNANCY OUTCOMES

No.	Questions	Answers
B1.	When was your baby born?	_____/_____/_____(DD/MM/YYYY)
B2.	What is baby's gender?	4. Male 5. Female 6. Other (please specify): _____
B3.	How much did your baby weight at birth?	_____ gr
B4.	How length was your baby at birth?	_____ cm
B5.	How many gestational weeks were you when your baby was born?	_____ weeks _____ days
B6.	Which method did you give birth?	1. Vaginal delivery without forceps or suction 2. Vaginal delivery with forceps or suction 3. Caesarean section (please specify main reason: _____ _____
B7.	What were APGAR scores at 1 and 5 minutes?	1. APGAR score at 1 minute: _____ 2. APGAR score at 5 minutes: _____

No.	Questions	Answers
B8.	Did the baby stay at intensive care unit?	1. No 2. Yes (_____ days)
B9.	Did the baby have any health problems?	7. No 8. Yes (please specify): _____ _____
B10.	Did the mother have any health problems during this pregnancy?	1. No 2. Yes (please specify): _____ _____
B11.	Did the mother have any health problems during or after delivery?	1. No 2. Yes (please specify): _____ _____
B12.	How long did your baby stay at hospital after delivery?	_____ days

C. ANTHROPOMETRICS

No.	Questions	Answers
C6.	Mother's blood pressure and heart rate before delivery?	– Systolic: _ _ _ . _ mmHg – Diastolic: _ _ _ . _ mmHg – Heart rate: _ _ _ beats/minute
C7.	Mother's weight before delivery?	_ _ _ . _ kg
C8.	Mother's weight after delivery?	_ _ _ . _ kg
C9.	Baby's head circumference?	_ _ _ . _ cm
C10.	Baby's abdominal circumference?	_ _ _ . _ cm
C11.	Baby's mid upper-arm circumference?	_ _ _ . _ cm

THANK YOU VERY MUCH FOR YOUR PARTICIPATION!

Appendix D Ethics approval

MEMORANDUM

Curtin University

To:	Prof Andy H Lee
	Public Health
CC:	
From	Professor Peter O'Leary, Chair HREC
Subject	Ethics approval
	Approval number: HR32/2015
Date	16-Feb-15

Office of Research and Development
Human Research Ethics Office

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Office for the project: 4873

Maternal lifestyle and nutritional status in relation to pregnancy and child health outcomes: A multi-centre prospective cohort study in Vietnam.

Your application was reviewed by Human Research Ethics Committee at Curtin University at their meeting on the 9/12/2014

Thankyou for providing the additional information requested by the Human Research Ethics Committee. The information you provided was satisfactory and your proposal is now approved.

Please note the following conditions of approval:

1. Approval is granted for a period of four years from **17-Feb-15** to **17-Feb-19**
2. Research must be conducted as stated in the approved protocol.
3. Any amendments to the approved protocol must be approved by the Ethics Office.
4. An annual progress report must be submitted to the Ethics Office annually, on the anniversary of approval.
5. All adverse events must be reported to the Ethics Office.
6. A completion report must be submitted to the Ethics Office on completion of the project.
7. Data must be stored in accordance with WAUSDA and Curtin University policy.
8. The Ethics Office may conduct a randomly identified audit of a proportion of research projects approved by the HREC.

Should you have any queries about the consideration of your project please contact the Ethics Support Officer for your faculty, or the Ethics Office at hrec@curtin.edu.au or on 9266 2784. All human research ethics forms and guidelines are available on the ethics website.

Yours sincerely,

Professor Peter O'Leary
Chair, Human Research Ethics Committee

MINISTRY OF HEALTH
HAIPHONG UNIVERSITY OF MEDICINE AND PHARMACY

SOCIALIST REPUBLIC OF VIETNAM
Independence-Freedom-Happiness

No: 05 /HPUMPRB
Issue: Approval of HPUMPRB

CERTIFICATE OF APPROVAL

Basing on the Decision No. 580A/QD-YHP on June 22nd 2012 by The Rector of Haiphong Medical University on the foundation of the HPMU Review Board and secretariat for reviewing the ethical issues in Bio-medical researches;

Basing on the Decision No. 2153/2013/QĐ-TTg on November 11th 2013 by Prime Minister on rename of Haiphong Medical University to Haiphong University of Medicine and Pharmacy.

Basing on the Agreed Minutes (enclosured) of the Haiphong University of Medicine and Pharmacy Review Board (HPUMPRB) and the ratification and assessment committee on August 20th 2015.

HAIPHONG UNIVERSITY OF MEDICINE AND PHARMACY REVIEW BOARD (HPMURB) IN BIO-MEDICAL RESEARCH

approves the ethical issues of the following research proposal:

- Research title: ***Maternal lifestyle and nutritional status in relation to pregancy and child health outcomes: A multi-centre prospective cohort study in Viet Nam***
- Principal Investigators: ***Prof. AnDy Lee***
  Chu Khac Tan, MD
  Nguyen Cong Luat, MD
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TRƯỜNG ĐẠI HỌC Y DƯỢC HẢI PHÒNG

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Appendix E Manuscript on gestational diabetes mellitus and pregnancy outcomes

Prevalence and pregnancy outcomes of gestational diabetes mellitus: a prospective cohort study in Vietnam

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Conflict of Interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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Abstract

Background: Several diagnostic criteria for gestational diabetes mellitus (GDM) have been developed and used internationally. This study determined the prevalence of gestational diabetes mellitus (GDM) and pregnancy outcomes among Vietnamese women.

Methods: A prospective cohort study of 2030 women was undertaken in Vietnam between 2015 and 2016. Baseline interview and a single-step 75-g oral glucose tolerance test were conducted at 24-28 weeks of gestation. GDM was defined by five international diagnostic criteria: America Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), International Association of the Diabetes and Pregnancy Study Groups (IADPSG), National Institute of Health and Clinical Excellence (NICE), and World Health Organization (WHO). Maternal and neonatal outcomes were assessed using medical records. Besides descriptive statistics and univariate analyses, logistic regressions were performed to ascertain the associations between GDM and maternal and neonatal outcomes.

Results: The prevalence of GDM varied considerably by the diagnostic criteria: 6.4% (ADA), 7.9% (EASD), 22.8% (IADPSG/WHO), and 24.2% (NICE). Women with GDM according to EASD were more likely to have macrosomic infants (adjusted odds ratio (OR) 4.35, 95% CI: 1.49 to 12.72), despite no apparent increase in risk under other criteria. Babies born to mothers with GDM appeared to be large-for-gestational age by ADA criteria (adjusted OR 2.10, 95% CI: 1.10 to 4.02) or EASD criteria (adjusted OR 2.15, 95% CI: 1.16 to 3.98), when compared to their counterparts in the normal group. No significant differences in maternal and other neonatal outcomes were found between the normal and GDM groups.

Conclusions: A global guideline is needed for the diagnosis, prevention and management of GDM.

Keywords: Gestational diabetes, maternal outcome, neonatal outcome, pregnancy, Vietnam

Introduction

Gestational diabetes mellitus (GDM), defined as diabetes in the second and third trimester of pregnancy [1], is a common metabolic condition during pregnancy. Globally, over 18 million live births were affected by GDM in 2017 [2], and about one in ten pregnant women in East and Southeast Asia experienced GDM [3]. Women with GDM and their offspring tend to have higher risks of adverse health outcomes such as preeclampsia, preterm birth, cesarean section, macrosomia, neonatal hypoglycemia, type 2 diabetes and cardiovascular disease later in life [4-9].

The prevalence of GDM varies considerably between and within countries [10, 11]. In 2010, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) proposed a diagnostic criteria for GDM [12] based on findings from the Hyperglycemia and Adverse Pregnancy Outcomes study [6]. This IADPSG criteria was subsequently endorsed by the World Health Organization (WHO) [13]. Nevertheless, a consensus has not been reached internationally, with different criteria widely adopted, including the American Diabetes Association (ADA) [14], European Association for the Study of Diabetes (EASD) [15], and National Institute of Health and Clinical Excellence (NICE) [16]. Consequently, more or less pregnant women may be diagnosed and managed for the condition which will affect their health as well as maternal and neonatal outcomes [17]. A comparison between different criteria can assist in decision making and clinical management, yet previous studies seldom reported the results from applying several criteria simultaneously.

For Vietnamese women, information on GDM and its adverse maternal and neonatal health outcomes is still limited. A study conducted in a tertiary maternity hospital in Ho Chi Minh City reported the prevalence of GDM varying from 5.9% to 24.3% [18], while maternal and neonatal outcomes such as preeclampsia, cesarean section, large-for-gestational age and small-for-gestational age were similar between the GDM and non-GDM groups [19]. Due to the lack of national guidelines, hospitals in Vietnam currently use different criteria to diagnose GDM, making comparison of rates difficult across regions, nationally and over time. Therefore, the present prospective cohort study determined the prevalence of GDM

and related pregnancy outcomes using different international diagnostic criteria for GDM to provide insights on the problem.

Materials and methods

Study design and participants

A prospective cohort study was conducted in six hospitals across three metropolitan cities of Vietnam, namely, Ha Noi, Hai Phong, and Ho Chi Minh City. Pregnant women were recruited during their prenatal care visits. Eligibility criteria were: (1) permanent residency in the study locations; (2) ≥18 years of age; (3) at 24-28 weeks of gestation; (4) singleton pregnancy; (5) no serious pre-existing health condition such as cancer or ischemic heart disease; and (6) ability to read the information sheet and sign the consent form. Ethical approval was obtained from Curtin University (approval number HR32/2015) and Hai Phong University of Medicine and Pharmacy (approval number 05/HPUMPRB). Details of the study protocol have been published [20].

Consented participants were invited to attend a baseline interview at 24-28 weeks of gestation. Information on sociodemographic characteristics was collected, including age, marital status, education level, occupation, residency and parity. Their medical history, such as stillbirth, induced abortion, preterm birth, macrosomia (birthweight >4000g), previous GDM or preeclampsia, cesarean section, and family history of diabetes or hypertension, were also recorded. Smoking status (active and passive smoking) was obtained using the WHO STEPS questions. Passive smoking was defined as exposure to tobacco smoke at home or workplace. Drinking of alcoholic beverages (beer, wine or spirits) was documented via a validated food frequency questionnaire [21]. Height was measured at the baseline interview whereas pre-pregnancy weight was acquired from first visit medical records. Pre-pregnancy body mass index (BMI) was then calculated and classified according to BMI cutoffs for the Asian population [22].

All participants underwent a single-step 75g oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation except for 7 women with a history of diabetes. They were

instructed to fast overnight. Three blood samples were taken in the morning at fasting, 1-h and 2-h after drinking 75-g anhydrous glucose dissolved in 250 ml water within 5 minutes. Their glucose levels were determined using the glucose oxidase method [23].

GDM classification

All one-step methods using a 75-g 2-h OGTT were assessed, and chosen if they met two conditions: 1) currently advocated; and 2) commonly utilized and endorsed by international expert panels. As a result, five international diagnostic criteria were selected, namely, ADA 2014 [14], EASD 1996 [15], IADPSG 2010 [12], NICE 2015 [16], and WHO 2013 criteria [13]. The IADPSG and WHO criteria were almost identical and thus combined. On the basis of OGTT results, women were classified into:

- Group 1: Normal OGTT result by all five criteria, denoted as "NGT";
- Group 2: GDM according to ADA 2014 (at least two abnormal glucose values: fasting glucose ≥5.3 mmol/l; 1-h ≥10.0 mmol/l; 2-h ≥8.6 mmol/l), denoted as "ADA";
- Group 3: GDM according to EASD 1996 (fasting glucose ≥6.0 mmol/l or 2-h ≥9.0 mmol/l), denoted as "EASD";
- Group 4: GDM according to IADPSG 2010 and WHO 2013 criteria (fasting glucose ≥5.1 mmol/l or 1-h ≥10.0 mmol/l or 2-h ≥8.5 mmol/l), denoted as "IADPSG/WHO";
- Group 5: GDM according to NICE 2008 (fasting glucose ≥5.6 mmol/l or 2-h ≥7.8 mmol/l), denoted as "NICE".

Pregnancy outcomes

Participants were followed up after delivery to assess maternal and neonatal outcomes. Information was retrieved from hospital medical records. Maternal outcomes were preeclampsia (blood pressure >140/90 mmHg on at least two occasions and proteinuria >300 g in 24-h), cesarean section status, and postpartum hemorrhage (>500 ml of blood loss within 24-h). Neonatal outcomes included macrosomia (>4000 g), low birthweight (<2500 g), large-for-gestational age (LGA, defined as >90th birth centile), small-for-

gestational age (SGA, defined as <10th birth centile), preterm labor (<37 weeks of gestation), stillbirth (no signs of life at birth after 28 weeks of gestation), jaundice requiring phototherapy, admission to neonatal intensive care, and length of hospital stay. Birth centiles were calculated using the international new-born standards from the INTERGROWTH-21st Project [24].

Statistical analysis

In addition to descriptive statistics, groups were compared using two-sample *t* or Mann-Whitney *U* tests for continuous variables, and Pearson's Chi-square or Fisher's exact test for categorical variables. Logistic regressions were performed for maternal and neonatal outcomes, accounting for the effects of established or plausible confounding factors, including maternal age, education, pre-pregnancy BMI, parity, passive smoking, alcohol drinking, previous GDM, history of macrosomia, stillbirth, preterm birth, cesarean section, as well as family history of diabetes or hypertension, and infant sex [19]. All analyses were conducted using STATA version 12.0 (StataCorp, College Station, USA), with the exception of the Venn diagram produced using the R 3.5.0 software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Cohort follow-up and sample characteristics

Between August 2015 and July 2016, of the 2248 eligible women recruited, 2030 (90.3%) consented to be interviewed. There was no difference in mean age between participants and non-participants. Seven women were subsequently excluded due to their history of diabetes before pregnancy, leaving 2023 pregnant women who underwent OGTT at baseline. After delivery, complete information on birth and neonatal outcomes were available for 1909 mothers, with 114 dropouts due to termination of pregnancy (n=1), human immunodeficiency virus (n=2), or loss to follow-up (n=111). No significant differences were found in demographic characteristics between the dropouts and the remaining participants in the cohort.

Table 1 presents the characteristics of the final sample. The mean age was 27.6 years (SD 5.3). One quarter of the women were underweight while one in eight women was overweight. No women smoked during pregnancy but over half of them were exposed to passive smoking, and a small proportion (13.6%) consumed alcohol. Of the 1174 women who had a history of previous pregnancy, about a quarter reported abortion, and one-fifth experienced cesarean section.

Prevalence of gestational diabetes

The NICE criteria gave the highest GDM prevalence of 24.2% (490/2023), followed by the IADPSG/WHO criteria at 22.8% (462/2023). The EASD and ADA criteria resulted in low rates, 7.9% (160/2023) and 6.4% (129/2023), respectively. Figure 1 illustrates the overlap in GDM classification with respect to these five criteria. Overall, the number of women with GDM ranged from 91 (4.5%) by all five criteria to 604 (29.9%) by any criteria. All women diagnosed as GDM according to ADA or EASD were also confirmed by the IADPSG/WHO or the NICE criteria. There were 348 women (17.2%) diagnosed to be GDM when using either the IADPSG/WHO or the NICE criteria. Therefore, 114 (5.6%) and 142 (7.0%) women with GDM were identified respectively by the IADPSG and the NICE criteria only.

Pregnancy outcomes

Table 2 compares the maternal and neonatal outcomes between the NGT and GDM groups. Higher rates of cesarean section were evident among women meeting the ADA, EASD, and IADPSG/WHO criteria, but not for those with GDM under NICE. Women diagnosed with GDM according to the ADA and EASD criteria were more likely to experience preeclampsia than women without the condition, though the rates were rather low (less than 2%). No significant differences were observed for postpartum hemorrhage between the NGT and GDM groups.

Infants of mothers with GDM by ADA, EASD and NICE criteria were more likely to be macrosomic when compared to those born in the NGT group. Moreover, GDM diagnosis

based on the ADA and EASD criteria led to significantly higher rates of LGA for infants of mothers with the condition, but not the case when IADPSG/WHO or NICE was used for diagnosis. There were no differences in other neonatal outcomes between NGT and the four GDM groups.

Multivariate logistic regression analysis showed no difference in risk of cesarean section after adjustment for confounding factors. Nevertheless, women with GDM based on the EASD criteria had a significantly higher risk of giving birth to macrosomic infants (adjusted odds ratio (OR) 4.35, 95% confidence interval (CI): 1.49 to 12.72), but not using the ADA criteria (adjusted OR 3.18, 95% CI: 0.97 to 10.39). The results also confirmed that babies born to mothers with GDM were more likely to be LGA in terms of the ADA criteria (adjusted OR 2.10, 95% CI: 1.10 to 4.02) or the EASD criteria (adjusted OR 2.15, 95% CI: 1.16 to 3.98), when compared to their counterparts in the normal group.

Discussion

This prospective cohort study highlights the considerable variations in the prevalence of GDM according to five international diagnostic criteria for GDM, from 6.4% (ADA) to 24.2% (NICE). Our results are consistent with previous studies in Vietnam [18] and other countries [25-32]. A greater number of diagnosed cases may assist with clinical management and improve pregnancy outcomes [33], however, it can affect women's mental health and lead to a higher burden on healthcare services [34]. Consequently, there is still a debate on the appropriateness of applying new criteria such as the IADPSG/WHO [35].

Our findings that the GDM groups experienced higher proportions of cesarean section, macrosomia and LGA are similar to previous studies [17, 18, 36]. In particular, two systematic reviews concluded that women with GDM and their offspring had a greater risk of adverse outcomes including cesarean section, macrosomia, and LGA [17, 36]. Another study in Vietnam also reported higher rates of cesarean section and LGA in the GDM group [18]. Elevated blood glucose levels among pregnant women are associated with neonatal fat deposition and fetal overgrowth [12], which contribute to macrosomia and

cesarean section due to the larger size babies. Nevertheless, no differences in the rates of neonatal jaundice and admission to neonatal intensive care were observed in our cohort and the previous study in Vietnam [18].

A major strength of this study is the prospective study design to compare the five common international diagnostic criteria for GDM. Maternal and neonatal health outcomes were obtained from reliable medical records. The rate of follow-up for women and neonates was high (94.4% of women who underwent OGTT). However, several limitations should be considered. Firstly, information on diabetes before pregnancy was based on self-report data and not confirmed by pathology. Nevertheless, pregnant women in Vietnam were usually managed by hospital doctors and kept informed about their history of diseases. Secondly, despite the apparent differences, the small number of cases in some pregnancy outcomes may constrain our comparisons between normal and GDM groups. Thirdly, information on GDM treatment at the hospital was not collected which may affect the adverse outcomes for some mothers.

The disparity between the various diagnostic criteria for GDM makes the evaluation and comparison of GDM prevalence difficult across nations and regions within a country. A universal diagnostic criteria for GDM is needed. Although the optimal glucose threshold to diagnose GDM remains unclear, women with the condition are associated with an increased risk of adverse pregnancy outcomes [6]. Early detection and management of GDM will improve the wellbeing of mothers and their babies [37, 38].

Conclusion

This study demonstrated that using different diagnostic criteria would lead to substantial differences in the number of GDM cases and pregnancy outcomes. Until a consensual criterion is reached, the IADPSG/WHO criteria which tend to identify a larger number of GDM cases may be beneficial for Vietnam to prevent adverse health outcomes for both the mother and the infant.

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Author contributions

Luat Cong Nguyen, Phung Thi Hoang Nguyen, Tan Khac Chu, Anh Vo Van Ha designed and performed the study. Luat Cong Nguyen analyzed the data and wrote the manuscript. Andy H. Lee, Minh Ngoc Pham, Dat Van Duong, Hong Thi Duong, and Colin W. Binns provided review, editing, and supervision. All authors revised the manuscript and approved the final version for publication.

Ethical approval

The study was approved by the Curtin University Human Research Ethics Committee (approval number: HR32/2015) and the Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number: 05/HPUMPRB/2015).

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Table and figure legends

Table 1. Characteristics of participants (n=1909), Vietnam, 2015-2016

Table 2. Maternal and neonatal outcomes by GDM status, Vietnam, 2015-2016

Figure 1. Venn diagram of GDM cases by five international diagnostic criteria for Vietnamese pregnant women, 2015-2016

Table 1. Characteristics of participants (n=1909), Vietnam, 2015-2016

Variables	n (%)
Maternal age (years)	
<25	600 (31.4)
25-29	670 (35.1)
30-34	438 (23.0)
≥35	201 (10.5)
Mean ± SD	27.6 ± 5.3
Educational level	
Less than high school	660 (34.6)
High school	498 (26.1)
Beyond high school	751 (39.3)
Pre-pregnancy BMI[a]	
Underweight (<18.5 kg/m^2)	485 (25.4)
Normal (18.5 to <23.0 kg/m^2)	1187 (62.2)
Overweight (≥23.0 kg/m^2)	237 (12.4)
Mean ± SD (kg/m^2)	20.2 ± 2.5
Parity	
0	735 (38.5)
1	707 (37.0)
≥2	467 (24.5)
Passive smoking[b]	1007 (52.8)
Alcohol drinking[c]	260 (13.6)
Family history of diabetes[d]	113 (5.9)
History of previous pregnancy (n=1174)	
Abortion	286 (24.4)
Cesarean section	240 (20.4)
Stillbirth	182 (15.5)
Preterm birth	76 (6.5)
Macrosomia	40 (3.4)
Birth defects	22 (1.9)
GDM	12 (1.0)
Preeclampsia	6 (0.5)

[a] BMI classification for Asian populations [22].
[b] Exposure to tobacco combustion products at home or workplace during pregnancy
[c] Drinking alcohol such as beer or wine during pregnancy
[d] Related to first-degree relatives

Table 2. Maternal and neonatal outcomes by GDM status, Vietnam, 2015-2016

		GDM			
Pregnancy outcomes	**NGT** (n=1344)	ADA (n=115)	EASD (n=142)	IADPSG/WHO (n=425)	NICE (n=449)
Maternal:					
Preeclampsia, n (%)	2 (0.2)	2 (1.7)*	2 (1.4)*	3 (0.7)	3 (0.7)
Cesarean section, n (%)	493 (36.5)	54 (46.6)*	66 (46.2)*	184 (43.2)*	186 (41.3)
Postpartum hemorrhage (>500 ml), n (%)	13 (1.0)	2 (1.7)	4 (2.8)	6 (1.4)	5 (1.1)
Gestational age at birth (weeks), median (IQR)	39.0 (1.6)	39.0 (1.7)	39.0 (1.7)	39.0 (1.7)	39.0 (1.7)
Neonatal:					
Birthweight (g), mean ± SD	3138.6 ± 395.0	3177.2 ± 488.1	3167.2 ± 452.2	3152.3 ± 440.3	3149.2 ± 432.8
Macrosomia, n (%)[a]	13 (1.0)	4 (3.5)*	5 (3.5)**	9 (2.1)	10 (2.2)*
Low birthweight, n (%)[b]	53 (3.9)	7 (6.1)	6 (4.2)	20 (4.7)	22 (4.9)
LGA, n (%)[c]	70 (5.7)	14 (12.8)**	15 (11.3)*	30 (7.8)	30 (7.3)
SGA, n (%)[d]	108 (8.5)	6 (5.9)	9 (7.1)	41 (10.4)	40 (9.6)
Stillbirth, n (%)[e]	7 (0.5)	1 (0.9)	1 (0.7)	1 (0.2)	1 (0.2)
Preterm labor, n (%)[f]	66 (4.9)	15 (12.9)	11 (7.7)	26 (6.1)	31 (6.9)
Jaundice, n (%)	120 (8.9)	15 (13.0)	18 (12.7)	47 (11.1)	51 (11.4)
Admission to NICU, n (%)	37 (2.8)	5 (4.4)	6 (4.2)	15 (3.5)	17 (3.8)
Length of hospital stay (days), median (IQR)	3.0 (3.0)	4.0 (2.0)	4.0 (2.0)	3.0 (2.0)	3.0 (2.0)

*p<0.05, **p<0.01 compared to NGT group
[a] >4000 g
[b] <2500 g
[c] Birthweight >90th population percentile for gestational age
[d] Birthweight <10th population percentile for gestational age
[e] Baby born with no signs of life at ≥ 28 weeks of gestation
[f] <37 weeks of gestational age at delivery

ADA, American Diabetes Association; EASD, European Association for the Studies of Diabetes; GDM, Gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; IQR, Interquartile range; LGA, Large-for-gestational age; NGT, Normal glucose tolerance; NICE, National Institute for Health and Care Excellence; NICU, Neonatal Intensive Care Unit; SD, Standard deviation; SGA, Small-for- gestational age

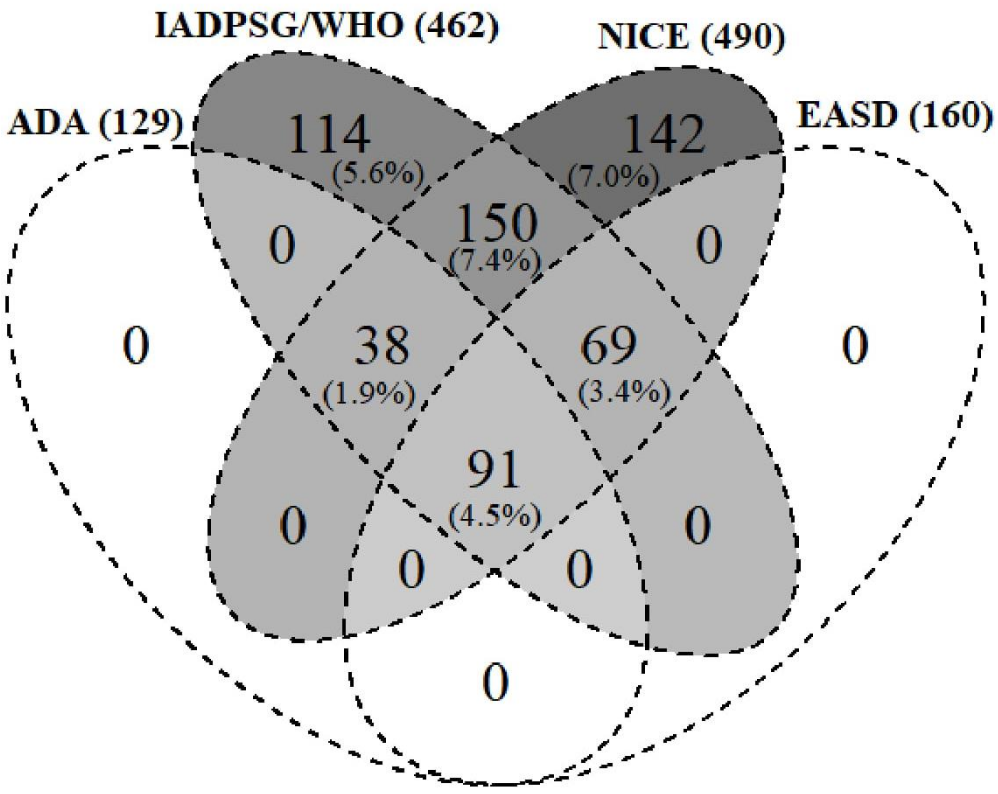

Figure 1. Venn diagram of GDM cases by five international diagnostic criteria for Vietnamese pregnant women, 2015-2016

ADA, American Diabetes Association; EASD, European Association for the Studies of Diabetes; IADPSG, International Association of Diabetes and Pregnancy Study Groups; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization

Appendix F Oral and poster presentation from the PhD project

Curtin University

Faculty of Health Sciences

CERTIFICATE OF PARTICIPATION

Presented to

Luat Cong Nguyen

School of Public Health

For presenting a poster at the

THE MARK LIVERIS RESEARCH STUDENT SEMINAR

28 September 2017

Professor Michael Berndt
Pro Vice-Chancellor
Faculty of Health Sciences

Curtin University

FACULTY OF HEALTH SCIENCES

CERTIFICATE OF PARTICIPATION

Presented to

Luat Cong Nguyen

School of Public Health

For presenting a paper at the

MARK LIVERIS RESEARCH STUDENT SEMINAR

27 September 2018

Professor Archie Clements
Pro Vice-Chancellor
Faculty of Health Sciences

27 September 2018

2018 Diabetes Canada/CSEM Professional Conference
October 10 - 13, 2018
Halifax Convention Centre, Halifax, Nova Scotia

Certificate of Attendance

for

Luat Cong Nguyen

Attendee at the 2018 Diabetes Canada/CSEM Professional Conference
Halifax, NS October 10 – 13, 2018

This event is an accredited group learning activity under Section 1 as defined by Maintenance of Certification (MOC) program of the Royal College of Physicians & Surgeons of Canada (RCPSC). It is approved by the Canadian Society of Endocrinology and Metabolism (CSEM) for a maximum of 25 credits. This program was co-developed and planned with CSEM and Diabetes Canada to achieve scientific integrity, objectivity and balance.

Through an agreement between the RCPSC and the American Medical Association (AMA), physicians may convert Royal College MOC credits to AMA PRA Category 1 Credits™. More information on the process to convert Royal College MOC credit to AMA credit.

Live educational activities, occurring in Canada, recognized by the RCPSC as Accredited Group Learning Activities (Section 1) are deemed by the European Union of Medical Specialists (UEMS) eligible for ECMEC®."

CFPC Affiliate Members (members whose specialty is not family medicine) may count Royal College credits toward their Mainpro+ credit requirements. All other CFPC members and Non-member Mainpro+ participants may claim up to 50 certified credits per cycle for participation in Royal College MOC Section 1 accredited activities.

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