



UNIVERSITI PUTRA MALAYSIA

***FACTORS ASSOCIATED WITH VITAMIN D AND GESTATIONAL
DIABETES MELLITUS AMONG PREGNANT WOMEN IN SELECTED
MATERNAL AND CHILD HEALTH CLINICS IN SEREMBAN, NEGERI
SEMBILAN, MALAYSIA***

LALITHA PALANIVELOO

FPSK(m) 2021 1



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By

LALITHA PALANIVELOO

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,
in Fulfilment of the Requirements for the Degree of Master of Science**

February 2021

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

FACTORS ASSOCIATED WITH VITAMIN D AND GESTATIONAL DIABETES MELLITUS AMONG PREGNANT WOMEN IN SELECTED MATERNAL AND CHILD HEALTH CLINICS IN SEREMBAN, NEGERI SEMBILAN, MALAYSIA

By

LALITHA PALANIVELLOO

February 2021

Chairman : Professor Zalilah Mohd Shariff, PhD
Faculty : Medicine and Health Sciences

The prevalence of Vitamin D deficiency (VDD) is high among pregnant women in Malaysia despite abundance of sunlight all year round. VDD had been associated with many adverse effects in pregnancy and one of them is gestational diabetes mellitus (GDM). Thus, this study aimed to investigate the association between Vitamin D status in first trimester with GDM among pregnant women in selected maternal and child health clinics in Seremban, Negeri Sembilan.

This study was a part of the ‘Seremban Cohort Study (SECOST): A prospective study of determinants and pregnancy outcomes of maternal glycemia in Malaysia’. In this study, 170 pregnant women were recruited using purposive sampling method from Senawang and Ampangan Maternal and Child Health Clinics in Seremban, Negeri Sembilan between 2014 - 2015 and followed-up until 2016. A set of pre-tested Malay language interviewer-administered questionnaire was used to obtain information on demographic, socio-economic, dietary intake and physical activity. Obstetrical data were obtained from the antenatal cards of the women. Height and weight of the women were measured in the clinics at the study enrollment (<10 weeks), during Visit 1 (10-14 weeks of gestation) and Visit 2 (24-30 weeks of gestation).

Blood samples were obtained during Visit 1 to quantify serum 25-Hydroxy Vitamin D [25(OH)D] and during Visit 2 for a standard 75g Oral Glucose Tolerance Test (OGTT). VDD is defined as serum 25(OH)D <50nmol/L. GDM is diagnosed if fasting plasma glucose \geq 5.6 nmol/L or 2-hours post prandial plasma glucose \geq 7.8 nmol/L. All data were analysed using SPSS version 22 and significant level was set at $p < 0.05$. Logistic regression was performed to determine the association between serum Vitamin D status in first trimester and GDM.

The prevalence of VDD in first trimester and GDM in the present study was 93% and 14.1% respectively. Pregnant women who had pre-pregnancy BMI of overweight/ obese were 6 times more likely to have mild VDD compared to pregnant women with normal BMI while pregnant women with a family history of Type 2 Diabetes Mellitus (T2DM) were 3 times more likely to have GDM compared to pregnant women who do not have any family history of T2DM. In this study, pregnant women with GDM had a significantly higher mean Vitamin D level compared to non-GDM pregnant women in bivariate analysis. However, serum Vitamin D status was not significantly associated with GDM in the multivariate analysis. In the study, pregnant women with GDM had a higher mean pre-pregnancy BMI and age compared to non-GDM pregnant women. These two factors could have contributed to the onset of GDM regardless of Vitamin D level. A more comprehensive study with a bigger sample size is suggested to obtain concrete evidence on the association between VDD in pregnancy and GDM as only 24 women were diagnosed with GDM in this study.



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FAKTOR BERKAITAN DI ANTARA VITAMIN D DAN ‘GESTATIONAL DIABETES MELLITUS’ DI KALANGAN IBU HAMIL DI KLINIK KESIHATAN IBU DAN ANAK TERPILIH DI SEREMBAN, NEGERI SEMBILAN, MALAYSIA

Oleh

LALITHA PALANIVELOO

Februari 2021

Pengerusi : Profesor Zalilah Mohd Shariff, PhD
Fakulti : Perubatan dan Sains Kesihatan

Prevalens kekurangan Vitamin D dalam kalangan ibu hamil di Malaysia adalah tinggi walaupun terdapat pancaran matahari sepanjang tahun di negara ini. Kekurangan Vitamin D dikaitkan dengan pelbagai masalah kesihatan dalam kehamilan, di antaranya adalah ‘gestational diabetes mellitus’ (GDM). Oleh itu, kajian ini dijalankan untuk mengkaji perkaitan di antara status Vitamin D pada trimester pertama kehamilan dan GDM dalam kalangan ibu hamil di klinik kesihatan yang terpilih di Seremban, Negeri Sembilan.

Kajian ini adalah sebahagian daripada ‘Seremban Cohort Study (SECOST)’ Kajian Kohort Perspektif Faktor Penentu dan Kesan Status Glukosa Darah Ibu Hamil Terhadap Kehamilan di Malaysia. Kajian ini melibatkan 170 ibu hamil yang dipilih menggunakan kaedah persampelan bertujuan dari Klinik Kesihatan Ibu dan Anak Senawang dan Ampangan sepanjang tahun 2014 – 2015 dan mereka disusuli sehingga tahun 2016. Borang soal selidik yang telah dibuat pra uji dalam bahasa Melayu digunakan untuk mendapat maklumat sosio-demografi, pemakanan dan aktiviti fizikal menggunakan borong soal-selidik dalam Bahasa Melayu yang telah dipra-uji manakala data obstetrik diperolehi melalui kad antenatal. Pengukuran berat dan tinggi diambil untuk kali pertama semasa responden mula menyertai kajian (<10 minggu kehamilan), temujanji 1 (minggu ke-10 hingga ke-14) dan seterusnya pada temujanji 2 (minggu ke-24 hingga ke-30 kehamilan).

Sampel darah diambil semasa temujanji pertama untuk analisis tahap serum 25-Hydroxy Vitamin D [25(OH)D] manakala ujian standard 75g oral glukos tolerans (OGTT) dibuat semasa temujanji kedua. Kekurangan Vitamin D ditakrifkan sebagai tahap serum 25(OH)D <50nmol/L manakala GDM ditakrifkan apabila tahap glukosa darah berpuasa

ibu hamil ≥ 5.6 nmol/L atau tahap glukosa darah selepas 2 jam pengambilan glukos ≥ 7.8 nmol/L. Kesemua data dianalisis menggunakan perisian statistik SPSS versi 22 dan tahap signifikan ditetapkan pada $p < 0.05$. Regresi logistik dijalankan untuk menentukan perkaitan antara serum Vitamin D di trisemester pertama dan GDM.

Prevalens kekurangan Vitamin D dalam trimester pertama dan GDM yang diperolehi melalui kajian ini adalah 93% dan 14.1%. Ibu hamil yang berlebihan berat badan /obes sebelum mengandung mempunyai 6 kali lebih tinggi risiko untuk mengalami kekurangan Vitamin D yang sederhana berbanding ibu hamil yang mempunyai berat badan normal manakala ibu hamil yang mempunyai sejarah keluarga diabetes melitus jenis 2 (T2DM) mempunyai 3 kali lebih tinggi risiko mengalami GDM berbanding ibu hamil yang tidak mempunyai sejarah keluarga T2DM. Hasil analisis dalam model bivariat menunjukkan ibu hamil yang mengalami GDM mempunyai purata aras Vitamin D yang lebih tinggi berbanding ibu hamil yang tidak mengalami GDM, dan perkaitan ini adalah signifikan. Walaubagaimanapun, aras serum Vitamin D tidak menunjukkan perkaitan yang signifikan di antara ibu hamil yang mengalami GDM dan yang tidak dalam model analisis multivariat. Ibu hamil yang mengalami GDM didapati mempunyai purata Indeks Jisim Tubuh (IJT) sebelum hamil yang tinggi dan lebih berumur berbanding ibu hamil yang tidak mengalami GDM dalam kajian ini. Oleh itu, kemungkinan dua faktor ini menjadi factor penyebab kepada masalah GDM di kalangan ibu hamil tanpa mengambil kira aras serum Vitamin D. Adalah disarankan agar satu kajian yang berskala besar yang melibatkan lebih ramai ibu hamil dapat dijalankan bagi membuktikan perkaitan antara kekurangan Vitamin D dalam trimester pertama kehamilan dan GDM, memandangkan hanya 24 ibu hamil yang mengalami GDM dalam kajian ini.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Zalilah Mohd Shariff, PhD

Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Loh Su Peng, PhD

Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

ZALILAH MOHD SHARIFF, PhD

Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 9 September 2021

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Name and Matric No: Lalitha Palaniveloo, GS40669

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Signature: _____

Name of Chairman
of Supervisory
Committee:

Professor Dr. Zalilah Mohd Shariff

Signature: _____

Name of Member
of Supervisory
Committee:

Associate Professor Dr. Loh Su Peng

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetrics and Gynaecology
ADA	American Diabetes Association
BMI	Body Mass Index
BIGCS	Born in Guangzhou Cohort Study
CMIA	Chemiluminescent Microparticle Immuno Assay
DIP	Diabetes in Pregnancy
DM	Diabetes Mellitus
DPSG	Diabetes Pregnancy Study Group
DRI	Dietary Reference Intake
EI	Energy Intake
ER	Energy Requirement
EVITA	The Epidemiology of Vitamin D Study
GDM	Gestational Diabetes Mellitus
GWG	Gestational Weight Gain
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IOM	Institute of Medicine
IPH	Institute for Public Health
MCH	Maternal and Child Health
MET	Metabolic Equivalent
MOH	Ministry of Health
MREC	Medical Research Ethics Committee
NCCFN	National Coordinating Committee on Food and Nutrition

NDDG	National Diabetes Data Group
NOR	National Obstetric Registry
OGTT	Oral Glucose Tolerance Test
PA	Physical Activity
PED	Pre-Existing Diabetes
PIH	Pregnancy Induced Hypertension
PIN	Pregnancy, Infection, and Nutrition
PPAQ	Pregnancy Physical Activity Questionnaire
RAS	Renin-Angiotensin System
RNI	Recommended Nutrient Intake
ROS	Reactive Oxygen Species
SECOST	Seremban Cohort Study
SGA	Small-For-Gestational Age
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
UPM	Universiti Putra Malaysia
UVB	Ultraviolet B
VDD	Vitamin D Deficiency
WINGS	Women in India with GDM Strategy
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background

Vitamin D deficiency (VDD) (serum 25(OH)D level <50 nmol/L) is a global public health problem that cuts across all age and ethnic groups (Institute of Medicine, 2011). It has been estimated that nearly 1 billion of the world population are affected by VDD, which include countries in lower latitude with abundance of ultraviolet B (UVB) radiation and industrialized nations where Vitamin D fortification of food and beverages has been implemented for years (Palacios & Gonzalez, 2014; Aguiar et al., 2017). The prevalence of VDD among European adults age 18 – 65 years old was 40 – 75% (Larose et al., 2014; Hoge et al., 2015; Bettencourt et al., 2018; Deplanque et al., 2017) while in Middle Eastern countries, the prevalence was 64 – 83% (Al-Dabhani et al., 2017, Al-Alyani et al., 2018; Zhang et al., 2016). In the United States and Australia, the prevalence of VDD among adults age 18 – 65 years was 39 – 40% (Liu et al., 2018; Mitchell et al., 2012; Parva et al., 2018) and 23 – 31% (Malacova et al., 2019; Gill et al., 2014) respectively. In Asia, the prevalence of VDD ranged between 41 – 57% among adults of 18 – 65 years old (Akter et al., 2016; Bi et al., 2016; Mechenro et al., 2018; Yu et al., 2015, Choi, 2013).

In healthy women of reproductive age, the prevalence of VDD ranged between 32 – 73% (Contreras-Manzano, Villalpando & Robledo-Pérez, 2017; Junaid et al., 2015; Lopes et al., 2017). VDD is also common during pregnancy with a prevalence of 21 – 91% in developed and developing countries (Noble, Markenson & Chasan-Taber, 2015; Ekeroma, Camargo & Scragg, 2015; Ravinder et al., 2015; Ates et al., 2016; Pirdehghan et al., 2016; Richard et al., 2017). Among children and adolescents, the prevalence of VDD ranged between 40 – 50% (El Maataoui et al., 2016; Cairncross et al., 2017; Vierucci et al., 2014; Wang et al., 2016). Among the elderly aged 65 years and above, the prevalence of VDD was 37 – 45% (Carrillo-Vega et al., 2017; Cheng et al., 2017; Brouwer-Brolsma et al., 2016).

Vitamin D is an essential fat-soluble vitamin that has two major forms, Ergocalciferol (Vitamin D₂) and Cholecalciferol (Vitamin D₃). Ergocalciferol is found mainly in plants and some fish while Cholecalciferol is synthesized in the skin by UVB rays from the sunlight. The synthesized Vitamin D₃ is transported to the liver by Vitamin D binding proteins to undergo hydroxylation where it is converted to 25(OH)D, which is the inactive form of Vitamin D. The 25(OH)D is then transported to the kidneys where it is hydroxylated further by the enzyme 1- α hydroxylase to the active form, 1,25(OH)D (Pludowski et al., 2018). As a fat-soluble vitamin, 25(OH)D is mostly stored in adipose tissues in the body (Holick et al., 2011). The receptors for 25(OH)D are found on cells throughout the body, mainly in skin, parathyroid gland, intestine, bone, kidney, pituitary gland, ovary, lymphocytes, liver, brain, heart and skeletal muscles (McAree et al., 2013). The main sources of Vitamin D are exposure to sunlight (endogenous synthesis) and

dietary intake. Endogenously synthesized Vitamin D accounts for nearly 80% of Vitamin D for humans while the remaining 20% is derived from dietary intake. However, due to limited food sources of Vitamin D (fatty fish, fortified dairy products, butter, margarines and egg yolk), exposure to sunlight is regarded as the main source (Saraff & Shaw, 2015; Holick, 2017; Moulas & Vaiou, 2018). Endogenous synthesis of Vitamin D is reduced when there is a limited exposure to sunlight due to clothing covering most of the skin surface while outdoors, usage of sunscreen lotion and frequent indoor or limited outdoor activities (Al-Wassia & Abo-Ouf, 2016). High presence of melanin in darker skin and limited sunshine due to geographical location and winter season also affect endogenous synthesis of Vitamin D (Dawodu & Akinbi, 2013).

Although the role of vitamin D in musculoskeletal health and bone mineralization is well established (Kumar et al., 2016), there is increasing evidence associating VDD with cardiovascular disease, cancer, autoimmune diseases and diabetes (Pludowski et al., 2018; Wang et al., 2017). The beneficial effects of vitamin D on reducing the risk of cardiovascular disease are through its role in the regulation of blood pressure, weakening the actions of the renin-angiotensin-aldosterone system and suppressing cellular inflammation of cardiac cells (Wimalawansa, 2016). In autoimmune diseases, Vitamin D acts as an anti-inflammatory agent and assists in maintaining the equilibrium between pro- and anti-inflammatory situations (Dankers et al., 2017). Furthermore, vitamin D and its metabolites reduce the incidence of cancer by inhibiting cell proliferation, stimulating apoptosis, suppressing inflammation, as well as inhibiting tumor angiogenesis, invasion and metastasis (Krishnan et al., 2012). The role of vitamin D in glucose tolerance is established by its ability to affect insulin secretion through the β -cells in the pancreas and insulin sensitivity (Martin & Campbell, 2011).

VDD in pregnancy has been associated with adverse pregnancy outcomes, including gestational diabetes mellitus (GDM), preeclampsia, bacterial vaginosis, a shorter gestation period, increase in cesarean section births and post-partum depression (Christesen et al., 2012; Charatcharoenwitthaya et al., 2013; Arnold et al., 2015). Adverse effects of VDD on newborns include higher incidence of small-for-gestational age (SGA), reduced infant bone mineral density and rickets (Hogler, 2015; Mulligan et al., 2010; Uday et al., 2018). Infants born to women with VDD are also at risk for developing respiratory infections, asthma, type 1, diabetes and schizophrenia later in life (Mulligan et al., 2010; Hart et al., 2015).

Hyperglycemia detected in pregnancy can be classified into pre-existing diabetes (PED) and gestational diabetes mellitus (GDM). PED comprises of Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM) while GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy at 24-28 weeks of gestation (IADPSG, 2010; Dirar and Doupis, 2017). Prevalence of GDM in Europe and United States were 5.4% (Eades, Cameron & Evans, 2017) and 7.6% (Casagrande, Linder & Cowie, 2018) respectively. In Asia, the prevalence was 11.5% (Lee et al., 2018). The prevalence of GDM varies between 14-28% In Malaysia (Institute for Public Health, 2016; Logakodie et al., 2016; Hasbullah et al., 2019). Women with GDM are at risk of developing gestational hypertension, preeclampsia and having higher rate of

caesarean section while women with a history of GDM are significantly at higher risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular diseases later in life (Benhalima et al., 2014; Nyugen et al., 2018; Lee et al, 2018). Infants born to GDM mothers have a higher risk of being macrosomic, having neonatal hypoglycemia and developing T2DM later in life (Lee et al., 2018; Begum, Dey & Fatima, 2018).

1.2 Problem Statement

Despite Malaysia being a tropical country with abundance of sunlight all year round, high prevalence of VDD has been reported in all age groups. The prevalence of VDD in adults aged 25-55 years old was 67% (Shafinaz and Moy, 2016) while among the elderly aged 55 years old and above, the prevalence was 41% (Mat et al., 2018). In children and adolescents, the prevalence ranged between 33-93% (Khor et al., 2011; Quah et al., 2019; Al-Sadat et al., 2016). Prevalence of VDD among females aged between 18-60 years was 91% (Jamil et al., 2019) while the prevalence in healthy women of reproductive age was 60% (Green et al., 2008). Correspondingly, studies reported a high prevalence of VDD, ranging between 60 – 90%, among pregnant women (Jan Mohamed et al., 2014; Bukhary et al., 2016). This is an indication that further investigations are needed to identify the factors contributing to the high prevalence of VDD among Malaysians, particularly among vulnerable groups such as pregnant women, besides establishing prevalence data of VDD for the country.

Studies have indicated that pregnant women in the country had an inadequate dietary intake of Vitamin D (<15µg/day) (Lee et al., 2020; Woon et al., 2019; Bukhary et al., 2016). A study by Lee et al. (2020) among 217 pregnant women in Selangor showed that nearly 68% of the pregnant women had an inadequate dietary intake of Vitamin D. Another study conducted among pregnant women in Kuala Lumpur and Selangor indicated that nearly 74% of the women had an inadequate dietary intake of Vitamin D (Woon et al., 2019). As the previous studies were all conducted among pregnant women in the locality of Kuala Lumpur/ Selangor, this research would provide an opportunity to study on dietary intake of Vitamin D among pregnant women in a locality in Negeri Sembilan besides contributing to the existing database of dietary intake of Vitamin D among pregnant women in the country.

Findings from the National Health and Morbidity Survey 2019 (NHMS 2019) showed that 50.1% of adults in Malaysia were overweight/ obese. The report also indicated an overweight and obesity prevalence of 30% and 25% respectively among the women population (Institute for Public Health, 2019). These findings indicate that nearly 25-30% of women in Malaysia will be entering pregnancy either in the state of overweight or obese. In line with NHMS 2019 findings, a study by Muthupalaniappen and Danasamy (2018) among 315 pregnant women who were in their first trimester of pregnancy found that nearly 61% of them had overweight/obese pre-pregnancy BMI. Another local study conducted among pregnant women in the first trimester of pregnancy in Kelantan reported a prevalence of pre-pregnancy overweight/obese BMI of 44% (Farhan, Rohana and Alina, 2015). As body weight and pre-pregnancy BMI are regarded as important risk factors for VDD and diagnosis of GDM among pregnant

women, findings from this study could strengthen the association between BMI status of the women and risk of VDD and GDM.

Pregnant women with normal pregnancy were recommended of at least 150 minutes/week of moderate-intensity exercise by The American College of Obstetricians and Gynaecologists (ACOG, 2017). In a study conducted in Kelantan, Jan Mohamed et al. (2014) reported that nearly 58% of pregnant women in the second trimester and 63% in the third trimester of pregnancy recorded a low physical activity level. Anjana et al. (2016) found that only 10.7% of pregnant women met the recommended ACOG 2017 guideline for physical activity in pregnancy from a study conducted among 795 pregnant women in India. Meanwhile, a study in Singapore found that pregnant women diagnosed with GDM had a higher percentage of insufficient level of physical activity compared to non-GDM women (Padmapriya et al. (2017). Physical activity is a modifiable risk factor associated with GDM (Gilbert et al., 2019). The establishment of the association between physical activity levels and the onset of GDM is crucial for an effective intervention among women with a high risk of GDM as existing data shows pregnant women generally has a low physical activity level.

The prevalence of GDM in Malaysia, ranged between 14-28%, is very much higher compared the to the prevalence of 5.4% in Europe, 7.6% in the United States and 14.6% in China (Institute for Public Health, 2016; Logakodie et al., 2016; Hasbullah et al., 2019; Eades, Cameroon and Evans, 2017; Casagrande, Linder & Cowie, 2018; Song et al., 2017). The relatively high prevalence of GDM among pregnant women in Malaysia warrants a more comprehensive study to identify risk factors of GDM in addition to updating the prevalence data of GDM in the country.

There have been numerous studies aimed to establish a link between serum Vitamin D with T2DM (Nakashima et al., 2016; Wimalawansa, 2016; Berridge, 2017; Lips et al., 2017; Lee et al., 2018). These studies have been extended to GDM since the pathophysiology of T2DM and GDM are similar (Zajdenverg and Negrato, 2017; Xu, Ma and Wang, 2018; Xia et al., 2019; Al-Ajlan et al., 2018; Dwarkanath et al., 2019). Despite a high prevalence of GDM reported among Malaysian pregnant women (Institute for Public Health, 2016; Logakodie et al., 2016; Hasbullah et al., 2019), limited information is available on the association between serum Vitamin D and GDM among Malaysian pregnant women (Woon et al., 2019). Thus, this study was conducted to investigate the association between serum Vitamin D in first trimester with GDM among Malaysian pregnant women. This study attempted to address the following questions:

- a) What is the Vitamin D status of Malaysian pregnant women in first trimester?
- b) What is the GDM status of Malaysian pregnant women?
- c) What are the factors associated with serum Vitamin D in first trimester among Malaysian pregnant women?
- d) What are the factors associated with GDM among Malaysian pregnant women?

- e) Is there any association between serum Vitamin D in first trimester with GDM among Malaysian pregnant women?

1.3 Research Objectives

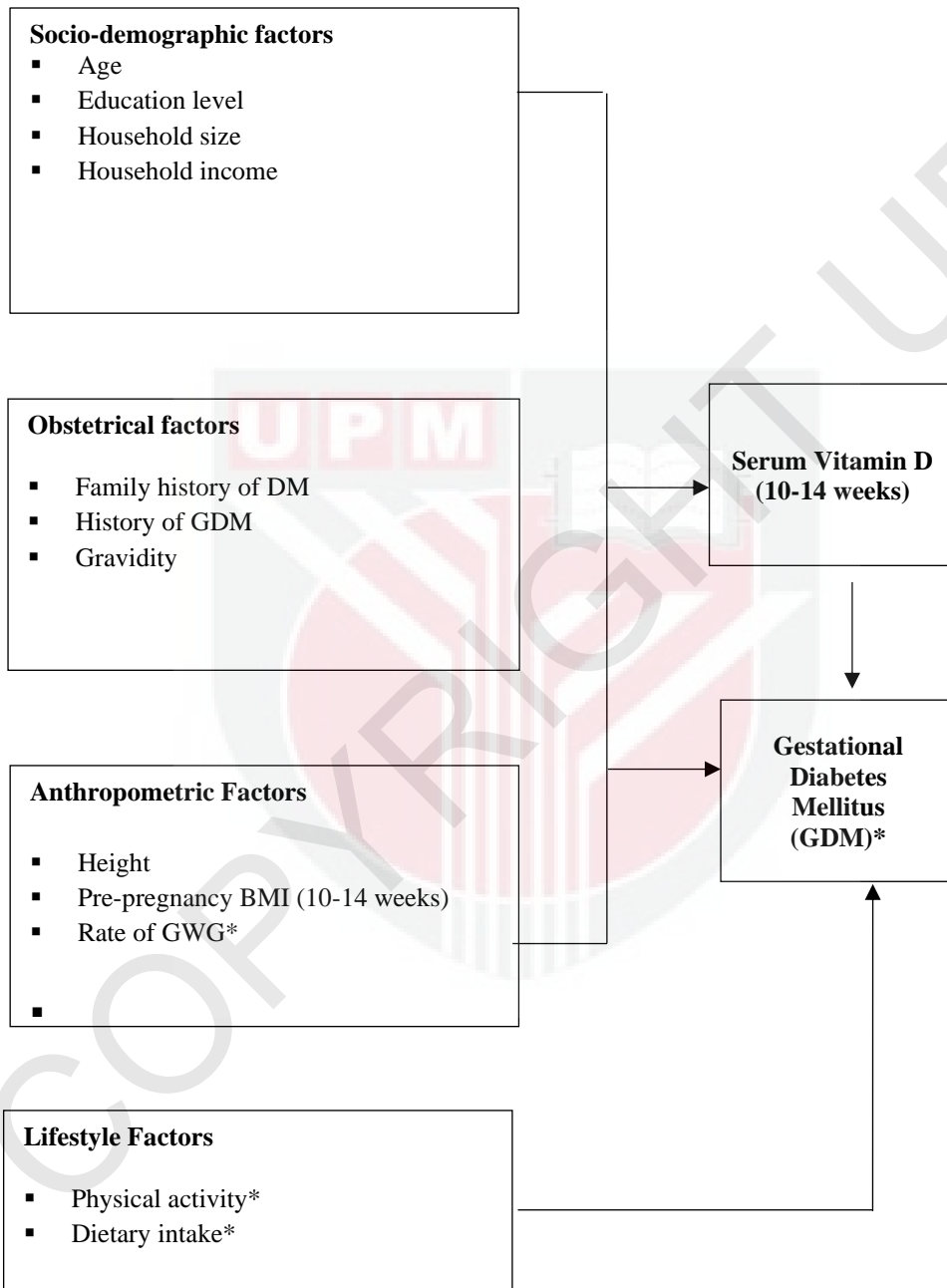
General Objective:

To determine the factors associated with Vitamin D status in first trimester and GDM, and its association among pregnant women in Seremban, Negeri Sembilan.

Specific Objective:

1. To assess
 - a. socio-demographic characteristics
 - b. obstetrical characteristics
 - c. anthropometric characteristics
 - d. lifestyle characteristics (dietary intake and physical activity status) of pregnant women
2. To identify
 - a. serum Vitamin D status in first trimester
 - b. Gestational Diabetes Mellitus (GDM) among pregnant women
3. To determine the contributing factors for VDD among pregnant women.
4. To determine the contributing factors for GDM among pregnant women.
5. To determine the association between Vitamin D status in first trimester with GDM among pregnant women.

1.4 Research Framework



*24 – 28 weeks – Second trimester

Figure 1.1 : Research framework

The research framework for this study is presented in Figure 1.1. The present study examined socio-demographic, obstetrical and anthropometric factors in relation to Vitamin D status and GDM. Lifestyle factors at 24-28 weeks of gestation were also included as risk factors for GDM.

Vitamin D status in pregnancy is associated with maternal age, education level and economic status (Bener et al., 2013; Van Den Berg et al., 2013; Ustuner et al., 2011). There is a growing evidence to suggest gravidity as a risk factor for VDD in pregnancy (Andersen et al., 2013; Al-Musharaf et al., 2018). Studies also found pre-pregnancy BMI is significantly associated with lower serum Vitamin D in pregnancy (Agarwal S, Kovilam & Agrawal DK, 2018; Karlsson et al., 2015; Vandevijvere et al., 2012). While history of GDM and family history of T2DM are known risk factors for GDM, numerous studies supported that maternal obesity is an important risk factor for GDM (Pleskacova et al., 2015; Logakodie et al., 2017; Padmanabhan, McLean and Cheung, 2014; Duman, 2015; Leng et al., 2015). Additionally, lifestyle factors that include dietary intake and physical activity levels during pregnancy have been associated with GDM (Meinila et al., 2015; Zhang et al., 2014; Anjana et al., 2016; Liu et al., 2014). Several studies showed that VDD in pregnancy is significantly associated with GDM (Bener et al., 2013; Aghajafari et al., 2013; El Lithy et al., 2014). Low serum Vitamin D is shown to be associated with increased insulin resistance and decreased beta cell function among pregnant women (Mutlu et al., 2015; Yeow et al., 2015).

1.5 Significance of Study

Vitamin D deficiency (VDD) is associated with musculoskeletal, cardiovascular, inflammatory and autoimmune diseases and also cancers. Low Vitamin D level is also associated with adverse effects in pregnancies for both mother and child. Though the prevalence of VDD is high among all age groups in Malaysia, little is known on prevalence of VDD specifically in pregnancy and its risk factors associated among pregnant women in Malaysia. Findings from this study will contribute to the existing limited prevalence data on VDD in pregnancy and its risk factors among pregnant women in the country.

The prevalence of diabetes mellitus (DM) is gradually increasing worldwide but markedly in middle-income countries, with an estimated of 1.6 million from deaths yearly caused by DM (WHO, 2020). In Malaysia, the national prevalence of T2DM among Malaysian adults has been rising steadily from 11.2% in 2011 to 18.3% (2019) (Institute for Public Health, 2011 & 2019). With research findings indicating a 7-fold increased risk of T2DM later in life among women with a history of GDM and the high prevalence of GDM among pregnant women in Malaysia, effective preventive actions should be taken to ensure a safe pregnancy for all the pregnant women. Besides contributing to the existing literature on maternal glycemia, this study will also establish the risk factors for GDM among Malaysian women. Related government and health agencies could use these findings to improvise current health policies and programmes in the country.

Numerous studies have established the effect of VDD in pregnancy and its link to onset of GDM. However, studies on VDD in pregnancy and its association to GDM in Malaysia is limited and the findings have been inconsistent. Thus, the findings from this study could contribute to the existing studies on VDD in pregnancy and ascertain the association between Vitamin D and GDM.

Findings from this study could contribute in development of simple yet effective preventive measures in curbing incidence of VDD and also GDM among pregnant women in Malaysia. This will enable pregnant women to have a healthy pregnancy and less complications in delivery.

1.6 Operational Definition

- 1.6.1 Gestational diabetes mellitus (GDM) - any degree of glucose intolerance diagnosed in the second or third trimester of pregnancy that is clearly not overt diabetes (American Diabetes Association, 2014).
- 1.6.2 Vitamin D deficiency (VDD) – Serum Vitamin D level < 50 nmol/L (Institute of Medicine, 2011).
- 1.6.3 Body Mass Index (BMI) – calculated as weight (kg)/ height (m²).
- 1.6.4 Pre-pregnancy BMI – BMI calculated from weight and height recorded at the study enrolment (<10 weeks of gestation).
- 1.6.5 Rate of gestational weight gain – the difference of weight measured in the clinic between the last and current antenatal visit and dividing it with the corresponding difference of gestational weeks (Huang et al., 2016).
- 1.6.6 Physical activity – household, caregiving, occupational, sports or exercise activities (Ainsworth et al., 2011).

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