

## FACTORS ASSOCIATED WITH GESTATIONAL DIABETES MELLITUS AMONG PREGNANT WOMEN IN THE KLANG VALLEY, MALAYSIA



By

DEEPA A/P THILLIAMPALAM

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

June 2022

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### June 2022

### Chairman : Professor Rosita binti Jamaluddin, PhD Faculty : Medicine and Health Sciences

Diet and lifestyle were consistently linked with gestational diabetes mellitus (GDM) over the year. With multiple interventions, nutritional policies and campaign the prevalence of GDM still accelerating over the year. This highlights the need of different dietary approach to prevent and manage this disease. The current study aimed to study the factors associated with GDM among pregnant women. In addition, other dietary factors such as body adiposity, dietary energy, macronutrients, micronutrients, diet quality as well as physical activity were also assessed in relation to GDM. This is a case control study conducted among 264 samples (146 GDM subjects and 188 non GDM subjects) in selected health clinic in Klang Valley. A structure questionnaire was used to collect the data. The height and weight of study subjects were assessed to determine their body mass index. All the data was analysed using SPSS version 23. As age increases per year the probability to develop GDM increased by 15% among study subjects (AOR = 1.15, 95% CI = 1.07 - 1.23, p < 0.001). Study subjects who were 30 years old and above were more likely to develop GDM more than two-fold (AOR = 2.60, 95% CI = 1.53 - 4.43, p< 0.001). Compared to those with tertiary educational background (university), study subjects with secondary school background most likely to be diagnosed with GDM (AOR = 11.6, 95% CI = 4.40 - 30.9, p < 0.001) followed by those from high school/ college (AOR = 9.52, 95% CI = 3.90 - 23.2, p < 0.001). Compared to study subjects with lowest household income (< RM1000), those with higher household income (> RM 4000) were more likely to be diagnosed with GDM (AOR = 16.52, 95% CI = 3.30 - 82.71, p = 0.001). As BMI increases by 1kg/m<sup>2</sup> the probability to develop GDM increased by 9% among study subjects (AOR = 1.09, 95% CI = 1.01 – 1.18, p =0.030). Compared to study subjects with BMI below than 25.0kg/m<sup>2</sup>, those who were overweight or obese were twice more likely to be diagnosed with GDM (AOR = 2.10, 95% CI = 1.07-4.09, p = 0.029). As dietary energy increases per 1kcal the probability to develop GDM increased by 46% among study subjects (COR = 1.46, 95% CI = 1.12- 1.90, p = 0.005). As carbohydrate consumption increases per 1g the probability to develop GDM

increased by 63% among study subjects (AOR = 1.63, 1.12 - 2.36, p = 0.011). As calorie from carbohydrate increases per 1kcal the probability to develop GDM increased by 48% among study subjects (AOR = 1.48, 95% CI = 1.04 - 2.12, p = 0.031). As calories from protein and fat increases per 1kcal the probability to develop GDM reduced by 40% and 32% respectively among (AOR = 0.60, 95% CI = 0.42-0.85, p = 0.005 and AOR = 0.68, 95% CI = 0.48 - 0.97, p = 0.033). As calcium and saturated fat increases per 1mg and 1 g, the probability to develop GDM increased by 66% and 46% among study subjects (AOR = 1.66, 95% CI = 1.09 - 2.52, p = 0.018 and AOR = 1.45, 95% CI = 1.01 - 2.09, p = 0.047). The highest tertile (T3) of PRAL showed a significant association with GDM among study subjects (COR = 2.11, 95% CI =1.15-3.86, p = 0.016). As the frequency of acidic diet intake per day increases by 1 unit the probability to develop GDM increased by 2.63 times among study subjects (AOR = 2.63, 95% CI = 1.66-4.15, p< 0.001). Adherence to acidic diet was more likely to increase the odds to be diagnosed with GDM among study subjects (AOR = 8.51, 95% CI = 3.95 - 18.3, p < 0.001). Study subjects who adhere to cereals, cereal products and tubers intake recommendation have an increased odd of GDM (AOR = 40.54, 95% CI = 5.77 - 284.9, p < 0.001). Adherence to whole grain cereal intake recommendation significantly reduced the odd of GDM (AOR = 0.012, 95% CI = 0.001 - 0.20, p = 0.002). On the other hand, adherence to legume and their products intake recommendation was significantly reduced the odd of GDM by 83% (AOR = 0.17, 95% CI = 0.03, 0.81, p = 0.026). High diet quality (Q4) was found significantly reduced the odd of GDM by 75% (AOR = 0.25, 95% CI = 0.09 - 0.65, p = 0.004). Eight variables were selected against GDM among pregnant women as the important variables in the final model which were age, educational background. monthly household income, frequency of acidic diet intake per day, acidic diet adherence, calorie from protein, adherence to cereals, cereal products and tubers intake, and adherence to legume and their product. Hence, in preventing GDM among pregnant mother, nutritionists, dietitians, clinicians, ministries and policy makers can start a routine intervention by providing holistic support for those who have these associated factors to help them cope with these important factors and to improve the goal of achieving a good glucose level and other further complications.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

### FAKTOR-FAKTOR MEMPENGARUHI DIABETES MELLITUS GESTASI DALAM KALANGAN WANITA HAMIL DI LEMBAH KLANG, MALAYSIA

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Pemakanan dan gaya hidup dikaitkan secara konsisten dengan diabetes mellitus gestasi (GDM) selama bertahun-tahuan. Dengan pelbagai intervensi, dasar pemakanan dan kempen, kelaziman GDM masih meningkat setiap tahun. Ini menunjukkan keperluan pendekatan pemakanan yang berbeza untuk mencegah dan menguruskan penyakit ini. Kajian ini bertujuan untuk mengkaji perkaitan antara faktor- faktor dan GDM. Di samping itu, faktor-faktor seperti kegemukkan, tenaga, makronutrien, mikronutrien, pemakanan beracid dan beralkali, kualiti pemakanan serta aktiviti fizikal turut dinilai berhubung dengan GDM. Ini merupakan kajian kawalan kes yang dijalankan di kalangan 264 sampel (146 subjek GDM dan 188 subjek bukan GDM) di klinik kesihatan terpilih di Lembah Klang. Soal selidik struktur digunakan untuk mengumpul data. Ketinggian dan berat subjek kajian dinilai untuk menentukan indeks jisim tubuh mereka. Semua data dianalisis menggunakan SPSS versi 23. Apabila umur meningkat setiap tahun kebarangkalian untuk mengembangkan GDM meningkat sebanyak 15% dalam kalangan subjek kajian (AOR = 1.15, 95% CI = 1.07 - 1.23, p < 0.001). Subjek kajian yang berumur 30 tahun dan ke atas lebih berkemungkinan menghidap GDM lebih daripada dua kali ganda (AOR = 2.60, 95% CI = 1.53 -4.43, p< 0.001) diikuti oleh mereka dari sekolah menengah/ kolej (AOR = 9.52, 95% CI = 3.90 - 23.2, p < 0.001). Berbanding subjek kajian yang berpendapatan isi rumah terendah (< RM1000), mereka yang berpendapatan isi rumah lebih tinggi (> RM 4000) lebih berkemungkinan untuk didiagnosis dengan GDM (AOR = 16.52, 95% CI = 3.30 – 82.71, p = 0.001). Apabila BMI meningkat sebanyak 1kg/m2 kebarangkalian untuk membangunkan GDM meningkat sebanyak 9% dalam kalangan subjek kajian (AOR = 1.09, 95% CI = 1.01 - 1.18, p =0.030). Berbanding dengan subjek kajian dengan BMI di bawah 25.0kg/m2, mereka yang berlebihan berat badan atau obes dua kali lebih berkemungkinan untuk didiagnosis dengan GDM (AOR = 2.10, 95% CI = 1.07-4.09, p = 0.029). Apabila pemakanan tenaga meningkat setiap 1kcal, kebarangkalian untuk membangunkan GDM meningkat sebanyak 46% dalam kalangan subjek kajian (COR = 1.46, 95% CI = 1.12- 1.90, p = 0.005). Apabila penggunaan karbohidrat meningkat setiap 1g kebarangkalian untuk membangunkan GDM meningkat sebanyak 63% dalam kalangan subjek kajian (AOR = 1.63, 1.12 - 2.36, p = 0.011). Apabila kalori daripada karbohidrat meningkat setiap 1kcal, kebarangkalian untuk membangunkan GDM meningkat sebanyak 48% dalam kalangan subjek kajian (AOR = 1.48, 95% CI = 1.04 – 2.12, p = 0.031). Apabila peratusan kalori daripada protein dan lemak meningkat setiap 1%, kebarangkalian untuk membangunkan GDM berkurangan sebanyak 40% dan 32% masing-masing antara (AOR = 0.60, 95% CI = 0.42-0.85, p = 0.005 dan AOR = 0.68, 95% CI = 0.48 - 95% CI = 0.48 0.97, p = 0.033). Apabila kalsium dan lemak tepu meningkat setiap 1mg dan 1 gram, kebarangkalian untuk membangunkan GDM meningkat sebanyak 66% dan 46% dalam kalangan subjek kajian (AOR = 1.66, 95% CI = 1.09 – 2.52, p = 0.018 dan AOR = 1.45, 95% CI = 1.01 - 2.09, p = 0.047). Tertil tertinggi (T3) PRAL menunjukkan perkaitan yang signifikan dengan GDM dalam kalangan subjek kajian (COR = 2.11, 95% CI =1.15-3.86, p = 0.016). Apabila kekerapan pengambilan diet berasid setiap hari meningkat sebanyak 1 unit, kebarangkalian untuk membangunkan GDM meningkat sebanyak 2.63 kali dalam kalangan subjek kajian (AOR = 2.63, 95% CI = 1.66-4.15, p< 0.001). Pematuhan kepada diet berasid lebih berkemungkinan meningkatkan kemungkinan untuk didiagnosis dengan GDM dalam kalangan subjek kajian (AOR = 8.51, 95% CI = 3.95 – 18.3, p < 0.001). Pematuhan kepada cadangan pengambilan bijirin bijirin penuh mengurangkan ganjil GDM (AOR = 0.012, 95% Cl = 0.001 - 0.20, p = 0.002). Sebaliknya, pematuhan kepada kekacang dan cadangan pengambilan produk mereka telah mengurangkan ganjil GDM dengan ketara sebanyak 83% (AOR = 0.17, 95% CI = 0.03, 0.81, p = 0.026), Kualiti diet tinggi (Q4) didapati secara signifikan mengurangkan ganjil GDM sebanyak 75% (AOR = 0.25, 95% CI = 0.09 - 0.65, p = 0.004). Lapan pembolehubah telah dipilih terhadap GDM dalam kalangan wanita hamil sebagai pembolehubah penting dalam model akhir iaitu umur, latar belakang pendidikan, pendapatan isi rumah bulanan, kekerapan pengambilan diet berasid sehari, pematuhan diet berasid, kalori daripada protein, pematuhan kepada bijirin, produk bijirin, dan pengambilan ubi, dan pematuhan kepada kekacang dan produknya. Oleh itu, dalam mencegah GDM dalam kalangan ibu hamil, pegawai pemakanan, doktor, pegawai pemakanan, kementerian, penggubal polisi boleh memulakan intervensi rutin dengan menyediakan sokongan holistik bagi mereka yang mempunyai faktor berkaitan ini untuk membantu mereka menghadapi faktor penting ini dan untuk meningkatkan matlamat mencapai tahap glukosa yang baik dan mencegah komplikasi yang lain.

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## LIST OF ABBREVIATIONS

ACOG	American College of Obstetrician and Gynecologist
ADA	American Diabetes association
ADIPS	Australasian Diabetes in Pregnancy Society
AOR	Adjusted odds ratio
BMI	Body mass index
CI	Confidence interval
CVD	Cardiovascular disease
DM	Diabetes Mellitus
DIPSI	Diabetes in Pregnancy Study Group in India
EASD	European Association for the Study of Diabetes
FIGO	International Federation of Gynaecology and Obstetrics
GDM	Gestational Diabetes Mellitus
HbA1c	Hemoglobin A1c
IADPSG:	International Federation of Gynaecology and Obstetrics
IDF	International Diabetes Federation
IOM	Institute of Medicine
NICE	National Institute of Clinical Excellence
NOR	National Obstetric Registry
OGTT	Oral Glucose Tolerance Test
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

### CHAPTER 1

### INTRODUCTION

### 1.1 Study Background

'International disaster' is the term given by The International Diabetes Federation (IDF) to classify Diabetes Mellitus (DM) based on the consequences, impact and prevalence worldwide. Diabetes is a chronic disease characterized by hyperglycemia. It has already affected 387 million populations worldwide in 2014 which is beyond the estimated number which is 300 million by 2025 as predicted by World Health Organization (World Health Organization, 2020). Type 1 diabetes, Type 2 diabetes, and gestational diabetes are the most common classifications. Insulin resistance and a relative lack of insulin production characterise type 2 diabetes (T2DM). The absolute plasma insulin concentration (both fasting and meal-stimulated) normally is increased, yet "relative" to the intensity of insulin resistance, the plasma insulin concentration is insufficient to preserve normal glucose homeostasis. In most T2DM patients, insulin secretion ability deteriorates over time. Type 1 DM leads to an absolute deficit in beta-cell activity at most. Autoimmune destruction of beta-cells is a prevalent cause, however instances are nonetheless categorised as idiopathic.

In recent years, hyperglycemia often occurs in pregnant women with a significant increase in the global prevalence of diabetes. This phenomenon provides a large amount of research data for studying the relationship between pregnancy and blood glucose. A systematic review shows that pregnant women with hyperglycemia during pregnancy have a higher risk of adverse pregnancy outcomes. Positive and correct treatment of gestational diabetes has a very large effect on reducing adverse birth outcomes (WHO 2013a.). Gestational diabetes mellitus (GDM) is any degree of glucose intolerance with onset or first recognition during pregnancy. Hyperglycemia in pregnancy may be suggested by the presence of glycosuria, a fetus that is large for date, or polyhydramnios. Overt diabetes mellitus may be found in women presenting with risk factors for type 2 diabetes during the first prenatal visit (before 13 weeks of gestation) and usually this will be identified as on set of GDM. Gestational diabetes is easily overlooked, but its complications and adverse effects on mothers and children are very serious. Nearly half of the women who have had GDM will develop type 2 diabetes within 5-10 years (International Diabetes Federation, 2017).

Gestational diabetes is associated with risk of macrosomia, birth injury, dystocia, obesity, and sustained impairment of glucose tolerance among infants born to mothers with gestational diabetes (Farahvar, Walfisch & Sheiner, 2019). Maternal carbohydrate intake is the main energy source for fetus growth and fetal macrosomia occurs when there is excessive maternal weight gain due to high glycaemic carbohydrate food intake (Filardi et al., 2019). The mainstay of nutritional management for hyperglycemia in DM care includes improve glycaemic control and pharmacological preparation but still unable to lower

glucose concentration to within normal range and restore a normal pattern of glucose homeostasis for longer period of time, not only that, many medical authors have note that diabetes medications carries increase risk of inflicting harm and injury by causing hypoglycemia (Bodai et al., 2018).

Worldwide, GDM is a common metabolic disorder during pregnancy, whereby about 21.3 million of live births were affected by hyperglycemia and approximately 86.4% of the cases attributed to GDM (Dickens & Thomas, 2019). Among Asian countries, Malaysia reported a much higher prevalence of GDM (13.5%) compared to other Asian populations (2 – 7%) (World Health Organization, 2020). Prevalence of GDM appears to be high in South Asia and Southeast Asian women compared to African American, Caucasian and Hispanic women; prevalence rates are 3-21.2% in women with GDM who were born in Asian countries. Rates of fetal macrosomia are lower in South East Asian women than in American Caucasian women. Asian women with GDM have a higher incidence of abnormal postpartum glucose tolerance tests and risk of developing type 2 DM in the future is higher than in Anglo-European women (Yuen, Wong, & Simmons, 2018).Considering the magnitude of the problem and the multitude effects of GDM for both mother and child, the assessment risk factors associated with GDM is the crucial aspect to be assessed.

In terms of healthy diet, there are many strategies that have been identified and implemented in prevention and management GDM. One of the aspects that also become current concern is by maintaining a healthy pH balance in the body which should be around 7, where the body should be moderately alkaline. The rationale here is that with proper nutrition and lifestyle it can be returned to normal and prevent the body from becoming more acidic than it should be, which leads to various diseases and disorders in the body (Akter et al., 2016; Ikizler et al., 2016). In the context of pregnant women, there are inconsistent finding relating acidic food intake and GDM risk which ranged from poor to moderate significant association (Saraf-Bank et al., 2018) as well as with risk of diabetes as overall (Abshirini et al., 2019; Fagherazzi et al., 2014). Maintaining an optimal body pH not only essential for the mother but also for the baby. The fetus is extremely sensitive to changes in pH, and mothers' body pH changes throughout pregnancy, and pH imbalance underlies infertility and pregnancy complications (such as nausea/vomiting, heartburn, and swelling) (Akter et al., 2016; Ikizler et al., 2016).

The frequency of GDM is a function of multiple characteristics pertaining to diet, lifestyle, genetics, and the idiosyncrasies of an individual pregnancy; it also reflects the frequency of type 2 diabetes mellitus (T2DM) in the population as a whole. Established risk factors for GDM include ethnicity, obesity, and family history of diabetes (Farahvar, Walfisch & Sheiner, 2019). Body weight status is the main risk factor associated with increased odds of mother to develop GDM. High rates of gestational weight gain, especially early in pregnancy, may increase a woman's risk of GDM. Gestational weight gain during early pregnancy may represent a modifiable risk factor for GDM and needs more attention from health care providers (Kurtzhals et al., 2018). However, body weight is also

influenced by dietary intake and lifestyle factors which are also independent of GDM development among pregnant women. Therefore, an analytical study is needed to identify the individual risk factors and their odds in developing GDM for a better prevention strategy.

### 1.2 Problem statements

Diabetes is associated with a wide variety of harmful health complications especially during pregnancy. Gestational diabetes has two categories which are pre-gestational associated with Insulin dependent diabetes or Non-insulin dependent diabetes. Gestational diabetes mellitus (GDM) extends to increased risk of developing diabetes. GDM is a clinical disorder of the metabolic states during pregnancy. Current management methods have not yielded any benefit in eliminating the disorder, this is proven by increasing incidence in the data obtained from the National Obstetric Registration hospitals in Malaysia (Amarra et al., 2021). Therefore, rather than management, it is important to identify the risk factor that may contribute to the development of GDM for early prevention, treatment as well as for better prognosis.

Even though strict glycaemic control on randomized controlled trials have shown improvement and reduce the complications of GDM (Crowther et al.,2005; Landon et al.,2009), but still the development of GDM and its limited availability of treatment are challenging to predict precisely because most often GDM is diagnosed in the last trimester of pregnancy rather than early pregnancy. Therefore, for an early detection of GDM, modifiable risk factors such as diet, gestational weight gain, or physical activity, associated with GDM development need to be assessed despite the non-modifiable risk factors such as age, ethnicity, genetic or family history of GDM.

The effects of diet quality predominately on alkaline ash diets have been studied for its potential benefit to reduce hyperglycemia by correcting the acid base imbalance among non-insulin dependent diabetes mellitus patients (Akter et al., 2016; Ikizler et al., 2016). On the other hand, an acidic ash diet was associated with many health consequences not limited to diabetes. However, the effect of these types of diets is yet to be assessed comprehensively among GDM. These may be not only benefitting the mother, but also the foetus as the alkaline ash diet consists of many healthy foods and is rich in vitamins and minerals especially with higher intake of fruits and vegetables. A study conducted in Iran higher reported that dietary acidic load was associated with an increased risk of GDM by more than 9-fold (Saraf-Bank et al., 2018). However, to date no literature has studied in detail on these diets in predicting the risk of GDM especially in Malaysia.

Even though diet patterns were identified to have a better prediction of any health outcomes, the individual nutrients and total energy contribution towards the development of GDM is still under discussion. Since food is made up of a variety of nutrients, vitamins and minerals, it is important to identify which nutrients act as predictors affecting the odds of GDM development. In addition, the main principle of dietary intake which is the quality of diet should not be neglected. It is important to assess the adherence to the Malaysian dietary guideline (MDG, 2020) to ensure sufficient nutrients were consumed by the mother for better foetal growth.

An optimal health of the pregnant mother not only merely depends on their diet, but also on their lifestyle. Lifestyle factors that may deteriorate the mothers' and foetal health need to be identified and intervene as a primary target. Smoking and alcohol consumption among pregnant mothers are the most detrimental habit to both mother and infant; however, the prevalence of smoking and alcohol consumption was very low even to nil during pregnancy, even though the mother had reported previous smoking or alcohol consumption habits. However, another lifestyle factor that needs to be advocated to pregnant women is to be physically active. Unlike normal people, pregnant women are less likely to exercise vigorously or engage with sports, yet they need to stay active. Therefore, it is important to assess the physical activity level of pregnant mothers and the risk of GDM.

Body weight status, dietary pattern and intake as well as physical activity are the modifiable risk factors that have been found protective towards many health outcomes and may have similar protective effects towards GDM (Kurtzhals et al., 2018; Yong et al., 2020). Therefore, an analytical cross-sectional study was conducted in selected health clinics in Klang Valley to determine the association of acidic ash and alkaline ash diet, diet intake and quality, body weight status and physical activity with GDM among pregnant mothers. The novelty of this study is that a new multi-risk factor model can be identified in GDM risk assessment. New knowledge particularly on the association of acidic ash and alkaline ash diet with GDM can be generated after controlling multiple confounding factors. Based on the problems and research gaps identified above several research questions were deduced as follows:

- i. Are there any differences in socio-economic background, anthropometry measurement, dietary factors and physical activity between GDM and non-GDM pregnant women?
- ii. Are socio-economic background, anthropometry measurement, dietary factors and physical activity associated with increased odds of GDM?
- iii. Do socio-economic background, anthropometry measurement, dietary factors and physical activity form a predictive model for GDM?

## 1.3 Research objectives

## 1.3.1 General objective

To compare the influence of acidic and alkaline ash food consumption and nutritional factors between gestational diabetes mellitus (GDM) and non-GDM pregnant women in Klang valley, Malaysia

## 1.3.2 Specific objectives

- 1. To determine and compare the following factors between GDM and non-GDM pregnant women.
  - i. Socio-economic background
  - ii. Anthropometry measurements
    - Pre-pregnancy body mass index
    - Body mass index
    - Gestational weight gain
  - iii. Dietary factors
    - dietary energy consumption
    - macronutrients consumption
    - micronutrients consumption
    - acidic and alkaline ash diet consumption
    - diet quality
  - iv. Physical activity
- 2. To compared the associations of socio-economic background, anthropometry measurement, dietary factors and physical activity between GDM and non-GDM pregnant women.
- 3. To construct a predictive model of GDM among pregnant women.

## 1.4 Research hypotheses

There is a significant differences between gestational diabetes mellitus and nongestational diabetes mellitus pregnant women on these factors:

- i. Socio-economic background
- ii. Anthropometry measurements
  - Pre-pregnancy body mass index
  - Body mass index
  - Gestational weight gain

- iii. Dietary factors
  - dietary energy consumption
  - macronutrients consumption
  - micronutrients consumption
  - acidic and alkaline ash diet consumption
  - diet quality
- iv. Physical activity

## 1.5 Conceptual framework of the study

Age, ethnicity, and other socio-demographic factors were found significantly associated with GDM. Acidic Ash diets consist of meat, refined grain, sugary and processed food, while alkaline ash diets mainly consist of vegetables, fruits and whole grains. Individually many literatures have found significant effects towards diabetes mellitus; yet the consumption of these foods in combination was not widely assessed in diabetes mellitus as well as GDM.

Individual nutrient consumption as well as total dietary intake were identified as risk factors of diabetes mellitus among adults, but limited studies are available for GDM. The adherence to dietary guidelines is an indicator of diet quality that was found to be associated with many health benefits to the targeted population, yet the effect towards GDM is yet to be assessed. Pregnant women were encouraged to be active as it is protective towards many health consequences, but the effect to total physical activity intensity against GDM are yet to be studied. The association between the identified factors were shown in the conceptual framework in figure 1.1. This conceptual framework will be used and tested for the predictive model of GDM.

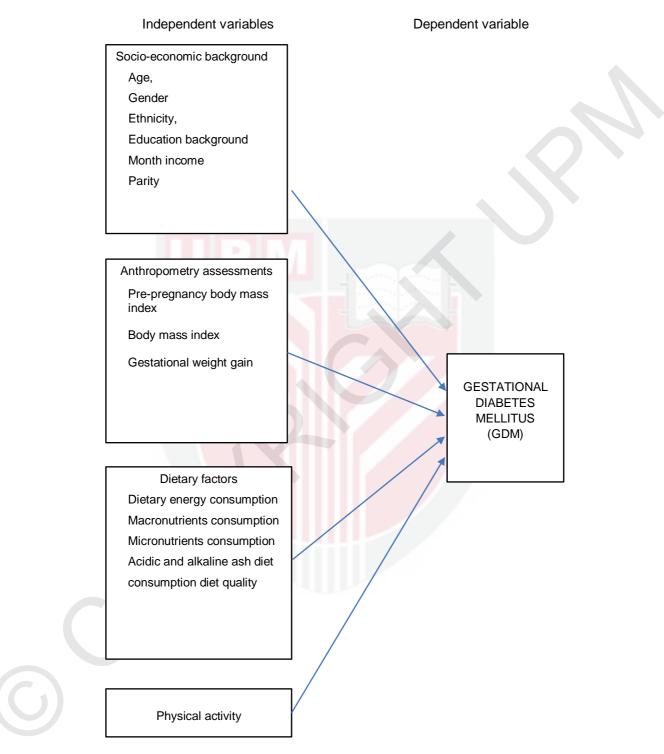


Figure 1.1 : Research Conceptual framework

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