



**UNIVERSITI PUTRA MALAYSIA**

***EFFECTS OF LOW GLYCEMIC INDEX DIETARY INTERVENTION IN  
WOMEN WITH GESTATIONAL DIABETES MELLITUS***

**FARHANAH BINTI AHMAD SHUHAIMI**

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By

**FARHANAH BINTI AHMAD SHUHAIMI**

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

**December 2015**

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

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**December 2015**

**Chair : Barakatun Nisak Binti Mohd Yusof, PhD**  
**Faculty : Medicine and Health Sciences**

High maternal glycemia especially at the postprandial level have been associated with high rates of complications in women with Gestational Diabetes Mellitus (GDM). A low glycemic index (LGI) diet may offer some benefits since the LGI foods usually produce lower postprandial blood glucose (PPG) responses as compared to high GI (HGI) foods. This randomized controlled study was conducted to investigate the effect of a LGI diet on glycemic-related parameters, other metabolic responses and dietary intake in women with GDM.

A total of 40 participants (aged 32 years; mean  $\pm$  SD pre-pregnancy Body Mass Index (BMI)  $29.3 \text{ kg/m}^2 \pm 7.3$ ; mean  $\pm$  SD gestation age = 26 week  $\pm 3.5$ ) from Universiti Kebangsaan Malaysia Medical Centre (UKMMC) were randomized to either LGI group (n=20) or Standard Nutrition Therapy (SNT) (n=20) groups to receive intensive intervention in which the outcomes were measured after 4-weeks period. As part of the study, the acute study was performed at week 1, 2 and 4 to determine the acute effects of LGI and HGI meal on postprandial metabolic responses (at week 1 and 2) and to challenge the postprandial response after having intensive intervention at week 4.

At baseline, participants in both groups were homogenous. At 4 weeks, both groups reduced the fructosamine levels ( $p < 0.05$ ) with no different detected between group. LGI intervention had significantly better reduction on self-monitoring blood glucose (SMBG) at 1-hour post breakfast by 11.8% recorded at home than the participants in the SNT group ( $p < 0.05$ ). No significant different were reported in lipid profile and C- Reactive Protein (CRP) between both groups after the 4 weeks of intensive intervention. Dietary Glycemic Index (GI) of participants in LGI group was significant lower by 7 units than SNT group ( $p < 0.05$ ). In the acute study, the 3-hours PPG was significantly lower after consuming low glycemic index meal (LGI\_M) than the high glycemic index meal (HGI\_M). The 4 weeks of LGI dietary intervention however, was not able to improve the PPG and triglyceride response after re-challenge with HGI\_M at the end of the study.

In conclusion, LGI dietary intervention was able to improve SMBG at 1-hour post breakfast. A LGI diet was feasible in this study, as the dietary GI in LGI

group has reduced significantly at the end of the study. The improvement in PPG was also evident after having LGI meals as compared to HGI meals in women with GDM.



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

**KESAN INTERVENSI DIET RENDAH GLISEMIK INDEKS DI KALANGAN WANITA YANG MEMPUNYAI GESTASI DIABETES MELLITUS**

Oleh

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Paras glisemia ibu yang tinggi terutama sekali selepas makan telah dikaitkan dengan kadar tinggi mendapat komplikasi bagi wanita yang mempunyai diabetes mellitus semasa hamil (GDM). Diet indeks glisemik rendah (LGI) mungkin menawarkan kebaikan memandangkan makanan rendah indeks glisemik biasanya menghasilkan paras glukosa selepas makan (PPG) yang rendah berbanding makanan yang tinggi GI (HGI). Kajian terkawal secara rawak ini dijalankan bagi mengkaji kesan diet LGI ke atas parameter berkaitan glukosa, tindak balas metabolik yang lain dan pengambilan diet dalam kalangan ibu mengandung yang mempunyai GDM.

Seramai 40 orang peserta (berumur 32 tahun; mean  $\pm$  SD Indeks Jisim Badan (BMI) sebelum hamil  $29.3 \pm 7.3 \text{ kg/m}^2$ ; min  $\pm$  SD usia kehamilan = 26 minggu  $\pm$  3.5) dari Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM) telah ditempatkan secara rawak sama ada dalam kumpulan LGI (n=20) atau Piawai Terapi Pemakanan (SNT) (n=20) untuk intervensi intensif di mana kesannya akan dilihat selepas 4 minggu. Sebagai sebahagian dari kajian ini, kajian akut telah dijalankan pada minggu 1, 2 dan 4 bagi menentukan kesan akut makanan rendah GI dan tinggi GI (HGI) terhadap tindakbalas metabolik selepas makan (minggu 1 dan 2) dan untuk mencabar tindak balas metabolik selepas makan selepas menjalani intervensi intensif pada minggu 4.

Pada garis asas, peserta dari kedua-dua kumpulan adalah homogen. Pada minggu ke- 4, paras fruktosamin pada kedua-dua kumpulan telah menurun ( $p < 0.05$ ) tanpa ada perbezaan di antara kumpulan. Intervensi LGI telah memberi penurunan yang lebih baik sebanyak 11.8% secara signifikan berbanding kumpulan SNT pada pemeriksaan glukosa dalam darah secara sendiri (SMBG) yang dilakukan di rumah pada 1 jam selepas sarapan. ( $p < 0.05$ ). Tiada sebarang perbezaan signifikan dilaporkan dalam profil lipid dan protein C-reactive (CRP) di antara kedua-dua kumpulan selepas intervensi intensif selama 4 minggu. GI dietari dalam kalangan peserta LGI adalah 7 unit lebih rendah secara signifikan dari kumpulan SNT ( $p < 0.05$ ). Di dalam kajian akut, PPG selama 3 jam adalah lebih rendah secara signifikan selepas makan makanan rendah GI (LGI\_M) berbanding makanan tinggi GI (HGI\_M). Walaubagaimanapun, intervensi diet selama 4 minggu tidak dapat memperbaiki

PPG dan tindakbalas trigliserid selepas dicabar semula dengan HGI\_M di penghujung kajian.

Kesimpulannya, intervensi diet LGI mampu memperbaiki SMBG pada 1 jam selepas sarapan. Diet LGI sesuai dilaksanakan di dalam kajian ini kerana GI dietari di dalam kumpulan LGI telah menurun secara signifikan di akhir kajian. Penurunan di dalam PPG juga telah terbukti selepas makan LGI\_M berbanding makanan HGI\_M dalam kalangan wanita yang mempunyai GDM.



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

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## LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologist
ADA	American Diabetes Association
AUC	Area Under the Curve
BMI	Body Mass Index
BSP	Blood Sugar Profile
CHO	Carbohydrate
CRP	C-Reactive Protein
DAS	Dietary Adherence Scores
FBG	Fasting Blood Glucose
FFA	Free Fatty Acid
FFQ	Food Frequency Questionnaire
GDM	Gestational Diabetes Mellitus
GI	Glycemic Index
GL	Glycemic Load
GLM	General Linear Model
HAPO	Hyperglycemia and Adverse Pregnancy Outcome
HDL	High Density Lipoprotein
HGI	High Glycemic Index
HGI_M	High Glycemic Index Meal
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IAUC	Incremental Area Under the Curve
LDL	Low Density Lipoprotein
LGA	Large for Gestation Age
LGI	Low Glycemic Index
LGI_M	Low Glycemic Index Meal
MNT	Medical Nutrition Therapy
MoH	Ministry of Health
NEFA	Non-Esterified Fatty Acid
NICE	National Institute for Health and Care Excellence
NICHD	The National Institute of Child Health
OGTT	Oral Glucose Tolerant Test
O&G	Obstetrics & Gynecology
PCT	Post Challenge Test
PPG	Maternal Postprandial Blood Glucose
RM	Ringgit Malaysia
RNI	Recommended Nutrient Intake (RNI)
SNT	Standard Nutrition Therapy
SPSS	Statistic Package for Social Sciences
SUNDEC	Sunnybrook Diabetes Education Centre
SMBG	Self-Monitoring Blood Glucose
T2DM	Type 2 Diabetes Mellitus
TEI	Total Energy Intake
UKM MC	Universiti Kebangsaan Malaysia Medical Centre

## CHAPTER 1

### INTRODUCTION

#### 1.1 Background of the Study

Gestational Diabetes Mellitus (GDM) is a state of glucose intolerance that begins or is first detected during pregnancy (ADA, 2004). Most recent studies documented and concluded that GDM occurs in about 7% of all pregnancies ranging from 1% to 14% depending on population and diagnostic tests (ADA, 2014)

The prevalence of GDM in most countries is unknown, but it reflects on the background prevalence of type 2 diabetes mellitus (T2DM) as well as prevalence of pre-diabetes (IGT) in young reproductive women in the given population (Hunt et al., 2007). It is projected that, among several groups categorized as high, the prevalence rate may be as high as 30% (World Diabetes Foundation, 2009). Recent findings discovered that the GDM prevalence has increased by ~10 to 100% in several ethnicities for the past 20 years (Ferrara, 2007).

Maternal diet, especially dietary carbohydrate (CHO) is a major determinant of the maternal postprandial glucose excursion (ADA, 2008). Conventionally, blood glucose management in GDM may take into account the amount of CHO and consistency (ADA, 2007). The 2002 Dietary References Intake Report has documented a minimum of 130g/ day for non-pregnant women and 175g CHO per day for pregnant women. The additional of 33 g of CHO is meant for fetal brain development and functioning (ADA, 2007). This new minimum recommendation provides an essential basis for the level of CHO restriction for women with GDM (de Veciana et al., 1995). Nevertheless, CHO restriction may not be feasible in Asia including in Malaysia as Asian's staple food commonly consists of polished white rice and refined wheat that are high glycemic index (GI) and glycemic load (GL) values (Ludwig, 2002).

CHO restriction is not only the factor affecting postprandial blood glucose response as the type of CHO which known as a concept of GI could also affect postprandial glucose response (ADA, 2008), but the GI values of food, exert a strong influence on blood glucose response. It is reported that serum glucose is 2-folds higher after the consumption of a high GI (HGI) meal compared to a low GI (LGI) meal, although the amount of CHO remained constant (Galgani et al., 2006).

In principal, the GI values of CHO foods can be categorized according to three categories: low GI ( $\leq 55$ ), medium GI (56-69) and high GI ( $\geq 70$ ) (Kirpitch et al., 2011). Foods with lower GI enter the blood stream at a slower rate, which reduces both the glycemic response and the corresponding insulin release (Kirpitch et al., 2011). According to meta-analyses, there was a modest reduction in HbA1c by 0.27% units (Opperman et al., 2004) and fructosamine

level in diabetic patients who were on LGI dietary intervention (Brand-Miller et al., 2003). Based on the facts stated, there is a positive correlation between consumption of HGI foods and an increases incidence of T2DM (Kirpitch et al., 2011).

## 1.2 Problem Statement

The increase in maternal glycemic control, especially excessive rise at the postprandial level, even within current recommended target have been associated with a higher rate of maternal and obstetric complications (Medzger et al., 2008).

The impact of LGI diet in women with GDM has been investigated in a few well-designed randomized controlled trial (RCT) that have provided strong proof and evidence. The proof and evidence are well documented in the two studies conducted in Australia (Louie et al., 2011; Moses et al., 2009), one each for Iran (Afaghi et al., 2013), Canada (Grant et al., 2011) and Mexico (Parera et al., 2012). All of these studies suggested that LGI diet might become a new alternative strategy in reducing postprandial blood glucose in women with GDM without to restriction of the dietary CHO (Louie et al., 2011; Afaghi et al., 2013; Moses et al., 2009; Perera et al., 2012; Grant et al., 2011).

Although a number of clinical studies have shown that LGI diet appear to have some beneficial and favorable effects on glycemic control in women with GDM, the findings cannot be generalized to the Asian context because of the genetic, environment and food pattern divergences between Western countries and Asian countries (Barakatun Nisak et al., 2014). 97% of Malaysians consume white rice, which is high in GI value almost every day (Norimah et al., 2008). Studies on the effectiveness of LGI in maternal glycemic control in GDM were all done in Western countries.

Previously, there have been a few GI studies conducted in Malaysia, the studies were focused on T2DM (Barakatun Nisak et al., 2009) and women with history of GDM (Shyam et al., 2013). Although both studies showed positive and encouraging outcomes among the participants in the LGI group, the results could not be applicable to women with GDM as the metabolic response during pregnancy especially those complicated with GDM were totally different including the gastric motility (Wald et al., 1982), and insulin sensitivity (Butte et al., 2000) which influences the rate of CHO digestion and absorption.

To address this research gap, this randomized controlled study is proposed to investigate the effectiveness of the LGI diet on glycemic control for Malaysian women with GDM. This study investigates the effect of a LGI dietary intervention on glycemic-related parameters and metabolic responses in women with GDM.

### **1.3 Significant of Study**

Several findings concluded in Western countries have demonstrated the beneficial effects of LGI food on the glycemic control parameters especially on the postprandial glucose in women with GDM (Grant et al., 2011; Moses et al., 2009; Louie et al., 2013). Additionally, Barakatun Nisak et al. (2009) successfully proven that local food with LGI values produced significantly lower postprandial blood glucose than HGI foods among the patients with diabetes in Malaysia. Suggesting that, LGI diet is feasible for implementation in the management of diabetes in the Malaysian setting.

However at present, there is lack of information and data in the management of women with GDM to incorporate the GI concept in Malaysia. Recognizing the lack of local data on LGI in the management of women with GDM, this research provides firm and strong information on the acute effects of GI on postprandial metabolic response in women with GDM. The outcomes of this study could become a useful dietary guidance for dietitians to incorporate the concept of GI in the management of GDM and will enable better provision of care for pregnant women with GDM in this country.

As this study focused on the effects of LGI diet on glycemic control among women with GDM, the results could help the Ministry of Health (MoH) and dietitians to develop a specific guidelines to initiate the GI concept in managing women with GDM in Malaysia. The findings could also can be used as a reference for other research and health practitioners to help improve the management of women with GDM in future research.

### **1.4 Research Questions**

1. What are the short-term effects of intensive intervention of LGI and standard nutrition therapy (SNT) on maternal glucose-related parameter and other metabolic responses among participants with GDM?
2. What are the acute effects of low versus high GI (HGI) meal on postprandial blood glucose and other metabolic responses among participants with GDM?

### **1.5 Research Objectives**

To investigate the effects of a LGI dietary intervention in women with GDM

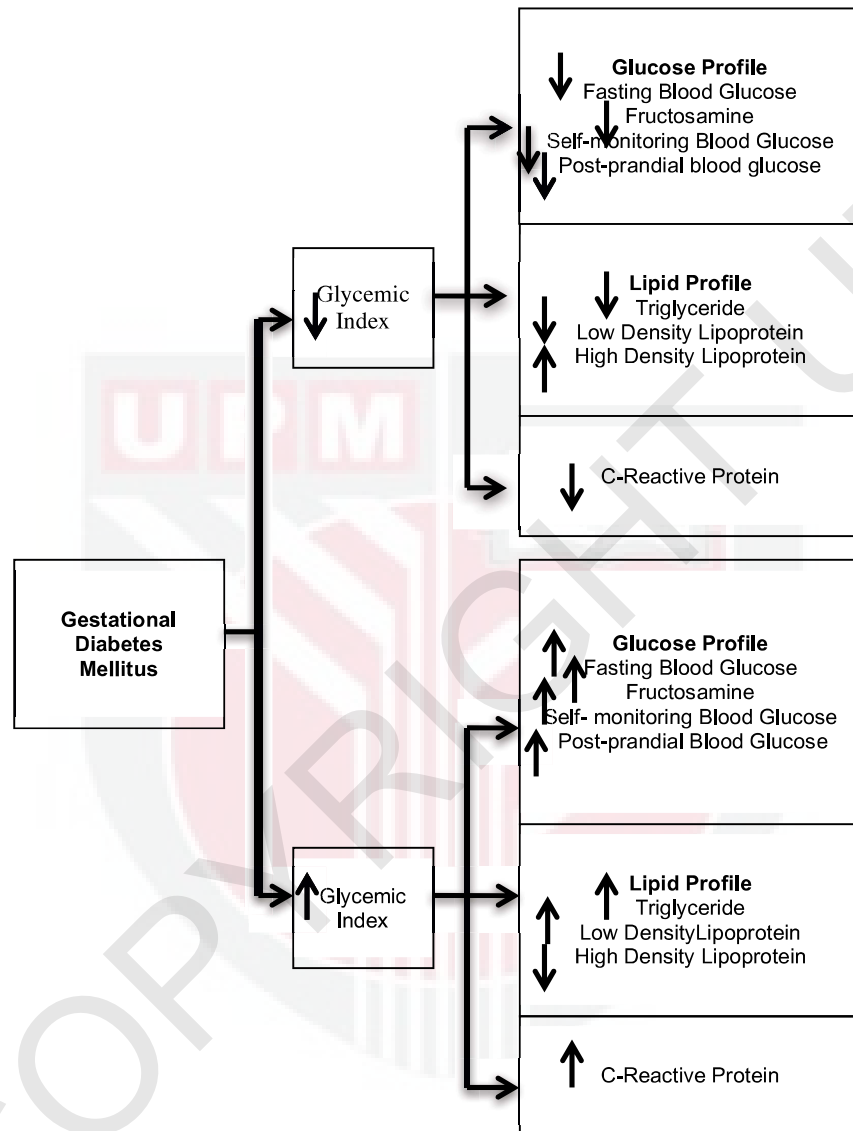
## **1.6 Specific Objectives Are:**

1. To compare the baseline characteristics between participants in LGI and SNT group.
2. To compare the effects of LGI against the SNT group on glucose-related parameter as assessed by fasting blood glucose (FBG), fructosamine and self-monitoring blood glucose (SMBG) after 4 weeks of intensive intervention.
3. To compare the effects of LGI against the SNT group on the other metabolic parameters (assessed by lipid profile and C-reactive protein (CRP)), dietary intake and adherence.
4. To compare acute effects of LGI meal (LGI\_M) against HGI meals (HGI\_M) on metabolic response assessed by capillary blood glucose, venous blood glucose and venous blood triglyceride for 3-hour period at week 1 and 4 of the study.

## **1.7 Hypothesis**

1. Participants with GDM in the LGI group achieve significant greater improvement in glucose-related parameter (assessed by FBG, fructosamine and SMBG) than SNT group.
2. Participants with GDM in the LGI group achieve significant greater improvement in other metabolic parameters (assessed by lipid profile and CRP), dietary intake and adherence than SNT group.
3. The LGI meal produces a significant slower rise in postprandial blood glucose and triglyceride levels than the HGI meal.

## 1.8 Conceptual Framework



**Figure 1.1. Conceptual Framework of the Study**

As shown in Figure 1.1, the incorporation of the LGI diet in the dietetic management resulted in a favorable glycemic control (Moses et al., 2009; Grant et al., 2011; Louie et al., 2011; Perera et al., 2012; Afaghi et al., 2013). From previous studies among women with GDM, the glucose-related parameters were assessed by FBG, HbA<sub>1c</sub>, fructosamine, and PPG (Moses et al., 2009; Grant et al., 2011; Louie et al., 2011; Perera et al., 2012; Afaghi et al., 2013).



Theoretically, CHO-rich foods with HGI value have been demonstrated to be more rapidly digested and absorbed, resulting greater fluctuations in PPG as compared to foods with lower GI values (Jenkins et al., 1987). In addition, LGI foods induced earlier hyperinsulinaemia compared to HGI foods resulting in more rapid glucose removal from the circulation (Jenkins et al., 1987).

Previous study has shown a significant reduction in SMBG and improvement in postprandial SMBG among women in the LGI group who have had pre-pregnancy  $\geq 25\text{kg/m}^2$  (Grant et al., 2011). Furthermore, Perera et al. (2012) showed that, LGI has successfully reduced the FBG and achieved glycemic goals in 2-hPPG at lunch, pre-prandial and 2hr postprandial glucose at dinner towards the end of pregnancy.

Apart from observing the effect of LGI on glucose profile, this study was also investigating the effect of LGI diet on other metabolic parameters as assessed by triglyceride, High-Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL) cholesterol and CRP levels.

Interestingly, LGI not only influences postprandial blood glucose but also gives an impact to lipid profile and CRP level. Based on previous research, LGI diet may result in lower LDL cholesterol and improved HDL cholesterol (Helibron et al., 2002) due to the decrease of gluconeogenesis after the ingestion of LGI foods and suppress the release of non-esterified fatty acid (NEFA), which eventually increases the HDL cholesterol levels (Opperman et al., 2004). Another finding suggested that, lowering the GI might decrease the inflammatory response, which can also result in higher HDL cholesterol levels (Augustin et al., 2002).

Nevertheless, the evidence of LDL cholesterol and triglyceride lowering- effect in LGI diet is less conclusive. A number of studies have showed a positive change in LDL cholesterol following the LGI diet but the results did not reach its statistical significance (Kirpitch et al., 2011). The consumption of HGI meals may trigger postprandial insulin resistance resulting in an increase in NEFA, which may increase triglycerides and LDL cholesterol levels in the body (Augustin et al., 2002). Hence, the effect of GI on total cholesterol was more pronounced (Opperman et al., 2004). However, further research is needed to confirm the relationship.

The mean CRP, a physiological marker of inflammation with LGI diets has been reported to be lower than that with HGI diets (Wolever et al., 2008). This may be due to the exposure of endothelial cell to glucose fluctuation concentration after ingestion of HGI meals, rather than to the stable and constant concentration, increased oxidative stress and apoptosis (Risso et al., 2001). These increases will eventually trigger pro-inflammatory responses and greater release of CRP (Leiter et al., 2005).

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