PREVALENCE OF GOOD GLYCAEMIC CONTROL AND ITS ASSOCIATED FACTORS AMONG GESTATIONAL DIABETES PATIENTS IN BACHOK, KELANTAN

by

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ABBREVIATIONS

BMI	Body Mass Index
BSP	Blood Sugar Profile
DM	Diabetes Mellitus
FBG	Fasting Blood Glucose
GDM	Gestational Diabetes Mellitus
MNT	Medical Nutritional Therapy
OGTT	Oral Glucose Tolerance Test
SMBG	Self Monitoring Blood Glucose
2HPP	2-Hours Post Prandial

ABSTRAK

KELAZIMAN KAWALAN GLISEMIK YANG BAIK DAN FAKTOR-FAKTOR BERKAITAN DALAM KALANGAN PESAKIT DIABETES GESTASI DI BACHOK, KELANTAN

Pengenalan: Kelaziman diabetes gestasi telah menunjukkan kecenderungan peningkatan dari tahun ke tahun. Diabetes gestasi adalah keadaan perubatan yang boleh dikawal dan diabetes gestasi yang tidak terkawal telah dikaitkan dengan pelbagai morbiditi dan mortaliti kepada ibu dan bayi. Oleh itu, adalah penting untuk memastikan bahawa ibu-ibu dengan diabetes gestasi mempunyai kawalan glisemik yang baik untuk mengelakkan kesan-kesan negatif ini.

Objektif: Untuk menentukan kelaziman kawalan glisemik yang baik dan faktor-faktor yang berkaitan di kalangan pesakit diabetes gestasi yang menghadiri klinik antenatal di Bachok.

Kaedah: Ini merupakan kajian keratan rentas dengan tinjauan rekod retrospektif sebanyak 129 pesakit diabetes gestasi yang didiagnos dari Jun sehingga November 2014. Ciri-ciri sosio-demografi dan perubatan pesakit telah dikumpulkan dari kad antenatal dan direkodkan dalam borang laporan kes. Ciri-ciri perubatan yang diambil kira termasukah indeks jisim tubuh badan pada permulaan, umur gestasi ketika diagnosis diabetes gestasi, berat badan sehingga diabetes gestasi didiagnosis, tahap FBG dan 2HPP pada masa diagnosis, sejarah pengguguran, sejarah diabetes gestasi yang terdahulu dan sejarah bayi macrosomik. Kawalan glisemik yang baik ditakrifkan sebagai sama ada: (i) yang mempunyai sekurang-kurangnya 75% daripada bacaan profil gula dalam darah dalam julat normal dalam dua bacaan berturut-turut atau (ii) yang tidak memerlukan insulin selepas dua bacaan profil gula dalam darah berturut-turut.

Data dimasukkan dan dianalisa menggunakan perisian SPSS versi 22.0.

Keputusan: Kelaziman kawalan glisemik yang baik adalah 61.2% (95% CI, 0.53, 0.70)(n=79). Purata (SD) umur dan pariti (SD) pesakit dalam kajian ini adalah 31.2(6.00) dan 3.4(2.08). Regresi logistik pelbagai menunjukkan umur gestasi ketika diagnosis diabetes gestasi (OR= 0.93, 95% CI: 0.87, 1.00, p= 0.048), tahap FBG pada masa diagnosis (OR=0.28, 95% CI:0.15, 0.50, p=0.001), sejarah diabetes gestasi terdahulu (OR= 0.23, 95% CI: 0.06, 0.84 p= 0.026) dan sejarah bayi makrosmik (OR= 10.45, 95% CI: 1.80, 60.69 p= 0.009) sangat berkait dengan kawalan glisemik yang baik.

Kesimpulan: Kelaziman kawalan glisemik yang baik di kalangan pesakit diabetes gestasi dalam kajian ini adalah munasabah. Umur gestasi ketika diagnosis diabetes gestasi, tahap FBG ketika diagnosis diabetes gestasi, kehadiran sejarah diabetes gestasi terdahulu dan ketiadaan sejarah bayi makrosmik dikaitkan dengan kawalan glisemik yang baik.

ABSTRACT

PREVALENCE OF GOOD GLYCAEMIC CONTROL AND ITS ASSOCIATED FACTORS AMONG GESTATIONAL DIABETES PATIENTS IN BACHOK, KELANTAN

Introduction: The prevalence of GDM has shown an increasing trend from year to year. GDM can be effectively controlled and uncontrolled GDM had been associated with a wide range of morbidities and mortalities to mothers and infants. Hence, it is important to ensure that mothers with GDM have good glycaemic control in order to prevent these negative outcomes.

Objectives: To determine the prevalence of good glycaemic control and its associated factors among GDM patients attending antenatal clinic in Bachok.

Methodology: This is a cross sectional study with retrospective record review of 129 GDM patients who were diagnosed from June to November 2014 The socio-demographic and medical characteristics of patients were gathered from the antenatal cards and recorded in the case report form. The medical characteristics of interest includes BMI at booking, gestational age when GDM was diagnosed, weight gain until GDM was diagnosed, level of FBG and 2HPP at diagnosis, abortion history, previous history of GDM and history of macrosomic baby. Good Glycaemic Control was defined as either: (i) having at least 75% of the blood sugar profile (BSP) readings within the normal range in two consecutive BSP readings or (ii) those who do not require insulin after two consecutive blood sugar profile (BSP) readings. Data was entered and analysed using SPSS version 22.0.

Results: The prevalence of good glycaemic control was 61.2% (95% CI, 0.53, 0.70) (n =79). The mean (SD) age and parity (SD) of patients in this study were 31.2(6.00) and 3.4(2.08) respectively. Multiple logistic regression showed that gestational age at GDM diagnosis (OR= 0.93, 95% CI: 0.87, 1.00, p= 0.048), level of FBG at GDM diagnosis (OR= 0.28, 95% CI: 0.15, 0.50, p= 0.001), previous history of GDM (OR= 0.23, 95% CI: 0.06, 0.84 p= 0.026) and history of macrosomic baby (OR= 10.45, 95% CI: 1.80, 60.69 p= 0.009) were significantly associated with good glycaemic control.

Conclusion: The prevalence of good glycaemic control among GDM patients in this study was acceptable. Gestational age at GDM diagnosis, level of FBG at GDM diagnosis, presence of previous GDM history and no history of macrosomic baby were associated with good glycaemic control of GDM.

CHAPTER 1: INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity, with first recognition of hyperglycaemia during pregnancy (WHO Guideline Development Group, 2013). Based on WHO 2013 guideline, GDM includes women with diabetes, impaired fasting glucose and impaired glucose tolerant of which the latter two were also referred as intermediate hyperglycaemia. In Malaysia, screening for GDM is done selectively in patients with risk factors using 75g glucose at least once at 24 to 28 weeks of gestation. However, screening should be done earlier at 16-18 weeks of gestation if patient has high risks (MOH, 2015). The risk factors includes BMI more than 27kg/m2, previous macrosomic baby weighing 4kg or more, previous GDM, having first degree relative with diabetes, bad obstetric history, glycosuria at prenatal visit, current obstetric problems and age above 25 years old (MOH, 2015).

The concern for GDM arises because uncontrolled GDM will increase morbidity and mortality to both fetus and mother whereas GDM is a condition that can be effectively controlled. GDM will increase risk of macrosomia, birth injuries such as shoulder dystocia, bone fracture and nerve palsies, hypoglycaemia and hyperbilirubinemia for the infants while for the mothers, they are at increased risk of developing pre-eclampsia and have an increased chance of need for induction of labour and caesarean section (Ju *et al.*, 2008).

American Diabetes Association in their latest guideline released in January 2017, suggested that medical nutritional therapy (MNT), physical activity and weight management should be started first in the treatment of GDM. However, pharmacological therapy should be initiated in women with greater degree of hyperglycaemia (American Diabetes Association, 2017).

1.1 Justification of study

It was estimated that the prevalence of diabetes mellitus was 17.5% nationwide and Kelantan contributed 18.5% (National Health and Morbidity Survey, 2015). This prevalence had been significantly raised from year to year (National Health and Morbidity Survey, 2015). The increment in the prevalence is worrying since it is a known fact that GDM is a risk factor for the development of DM type 2 later in life (American Diabetes Association, 2017). Thus, identifying the women with GDM early in their pregnancy and treat them accordingly is crucial to intercept the development of diabetes mellitus. Unfortunately, the data on GDM and the level of control once it had been diagnosed is sparse. Local studies had shown various data of prevalence of GDM in Malaysia. An earlier study in 2007 quote the prevalence to be 11.4% (Tan *et al.*, 2007) but in 2009 another study quote it to be 18.4% (Idris *et al.*, 2009). However, a more recent study in 2013 quoted that prevalence of GDM is 5.2% (Kampan *et al.*, 2013). These studies were however small scale studies, and the prevalence was based on their population. Hence, the true prevalence of GDM in Malaysia is still not known.

Nevertheless, what is more important is to estimate the number of GDM women who has good glycaemic control once they are diagnosed with the disease to ensure prevention of the unwanted sequelae. Therefore, this study aimed to determine the prevalence of good glycaemic control among GDM patients as well as the factors associated with it.

This information will assist the health care workers in their patient's evaluation, treatment planning and rationalized the health care planning. In return, it will facilitate the health care team in optimising the utilising of time, human and economic resources. Furthermore, it may guide the health care workers in planning more appropriate short-term and long-term goals for GDM patients.

CHAPTER 2: LITERATURE REVIEW

2.1 Prevalence of GDM

The prevalence of DM in Malaysia has shown an increasing trend over the years from 6.3% in 1986 to 17.5% in 2015 (National Health and Morbidity Survey, 2015). According to American Diabetes Association, women with a history of GDM have greatly increased risk of conversion to type 2 diabetes over time (American Diabetes Association, 2017). It is estimated that about 35-60 % of women with history of GDM will develop type 2 diabetes mellitus within 10 years (Metzger *et al.*, 2007). Although the increasing in DM prevalence in Malaysia had been well recorded, the trend for GDM cannot be ascertained. In Europe, the prevalence of GDM mostly figures from 2 to 6 % while in Northern or Atlantic seaboard parts a lower prevalence at mostly less than 4% was reported. A higher prevalence of GDM was reported in South and Mediterranean seaboard at more than 6% (Buckley *et al.*, 2012). On the other hand, the prevalence of GDM in Asian continent showed higher prevalence. In Qatar, the prevalence of GDM was 16.3 % (Bener *et al.*, 2011) while in India the prevalence was 18.9 % (Seshiah *et al.*, 2004). As mentioned before, studies in Malaysia had reported various figures depending on their population (Tan *et al.*, 2007; Idris *et al.*, 2009; Kampan *et al.*, 2013). There is still the need for national study to ascertain the true prevalence of GDM among women in Malaysia.

2.2 Screening of GDM

Issues related to GDM screening had never been solved for years. Different countries and organizations have their own guidelines and distinctive methods in diagnosing GDM. Universal screening or selective screening based on the risk factors remained debatable. The most popular method for universal screening is 50g glucose challenge test (GCT). However it was reported that the glucose challenge test (GCT) is no longer part of diagnostic algorithm due to lacks sensitivity and specificity (Nankervis A *et al.*, 2013). A local study has recommended for universal screening over risk-based screening method in view of better predictive value in detecting GDM (Idris *et al.*, 2009). Selective screening based on the risk factors was thought not to be as cost effective as universal screening in a population with low risk of GDM. The International Federation of Gynaecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus in their guideline recommended for universal screening rather than risk factor based testing in order to include all pregnant women to be tested for hyperglycaemia in pregnancy (Hod *et al.*, 2015). They argued that the screening based approach has poor sensitivity for detection of GDM.

On the other hand, the National Institute for Health and Care Excellent (NICE) recommended that GDM should be screened with 75g oral glucose tolerance test (OGTT) in women with risk factors (NICE, 2015). The risks that are mentioned in the guideline are BMI above 30kg/m^2, previous macrosomic baby weighing 4.5kg or more, previous GDM, first degree family history of DM and minority ethnic family origin with a high prevalence of diabetes. They also suggested that the screening should be done at 24-28weeks of pregnancy or earlier in patient with previous history of GDM. The GDM can be diagnosed if the woman has either fasting plasma glucose of 5.6mmol/l or above or 2 hour plasma glucose of 7.8mmol/l or above. Another body,

The Australasian Diabetes in Pregnancy Society (ADIPS) recommended women not known to have pre-existing glucose abnormalities, but with risk factors for GDM which further classified into moderate and high risk group should be tested early in pregnancy.

Although it is recommended in the Malaysian guideline that screening for GDM should be done to all pregnant women with OGTT at 24-28 week of gestation due to high prevalence of DM type 2 in Malaysia, but taking into consideration of some limitation in resources, screening only be done to high risk group of pregnant women at booking and then should be repeated after 4 to 6 weeks if initial screening was normal (MOH, 2015).

2.3 Glycaemic control of GDM.

For the time being, there is no specific definition of controlled GDM. The definition of glycaemic control of GDM is also different in different parts of the world. The need for insulin therapy has been used repeatedly to indicate glycaemic control. Two studies in Germany and Turkey described good glycaemic control if patients were not converted to insulin therapy after receiving medical nutritional therapy (Schaefer-Graf *et al.*, 2003; Bakiner *et al.*, 2013). Bakiner *et al* in their study mentioned that the prevalence of GDM patients who were able to maintain optimum glycaemic control with medical nutritional therapy alone was 63.3% compared with 36.7% who needed antenatal insulin therapy (Bakiner *et al.*, 2013). In Germany, about 93.5% of GDM patients studied had good glycaemic control within therapeutic threshold (Schaefer-Graf *et al.*, 2003).

A more recent study in Turkey in 2015 found that about 65.2% of GDM patients were able to maintain good glycaemic control with diet therapy while another 34.8% were converted to insulin therapy after 15 days trial of diet therapy (Aktun *et al.*, 2015). The definition of good glycaemic control of GDM in the study by Aktun *et al* was the same with an earlier study by Bakiner *et al*.

One study done in India revealed that 90% of GDM patients have good glycaemic control and only 10% of them required antenatal insulin after failed medical nutritional therapy. The insulin was initiated after 2 weeks trial of medical nutritional therapy if more than 30% of glucose level measurements were above the recommended values (Mitra *et al.*, 2014). In USA, one study mentioned that 74.8% of GDM patients were able to maintain good glycaemic control with diet and exercise whereas 25.2% required insulin therapy which indicates of poor glycaemic control. In that study, patients were instructed to perform daily fasting blood glucose with postprandial glucose and insulin was prescribed by the physician depends on the blood glucose level (Tudela *et al.*, 2006). Meanwhile in Japan, a retrospective study which enrolled GDM patients between 2010 and 2016 found that 73% of them were able to maintain good glycaemic control with diet therapy while 27% were added insulin where it was started if three times of more of self-monitoring of blood glucose (SMBG) readings were not within target (Watanabe *et al.*, 2016).

In Netherland, a retrospective study showed about 56.1% of GDM patients from 2011 until 2014 were able to achieve good glycaemic control. In that study, the definition of good glycaemic control was made if patients were able to maintain SMBG levels within targets with diet therapy however the insulin therapy was commenced if two elevated blood glucose levels were found on two successive days (Koning *et al.*, 2016).

Meanwhile, a study in Brazil defined poor glycaemic control if more than 30% of the glucose measurements were above the recommended value or in which 20% or more of the measurements indicated hyperglycaemia and fetal weight was above the 75th percentile (Sapienza *et al.*, 2010). In the study by Sapienza *et al*, 39.8% of GDM patients were determined to have poor glycaemic control where they were initiated with insulin therapy based on their blood glucose measurements to achieve desired glycaemic control (Sapienza *et al.*, 2010).

It has been suggested that the control is based on the target range acceptable for women with diabetes. Since a more tight control is required, women with diabetes in pregnancy are required to monitor their blood sugar at fasting and before each meal as well as before bedtime. The ideal fasting or pre-prandial reading is set to be equal or less than 5.3mmol/l and pre-bed reading (2 hours post prandial) is set to be equal or less than 6.7mmol/l (MOH, 2015). If desired blood glucose levels are not met after 1-2 weeks of diet and exercise therapy, insulin therapy should be considered to achieve optimum glycaemic control (MOH, 2015). Based on NICE guidelines in 2015, pregnant women with any form of diabetes are advised to maintain their capillary blood sugar reading below the target levels; fasting: 5.3mmol/L, 1-hour post prandial: 7.8mmol/L or 2-hour post prandial: 6.4 mmol/L (NICE, 2015).

Role of Hba1c in measuring glycaemic control among GDM patients has little benefit. American Diabetes Association (ADA) in their latest guidelines in 2017 mentioned that HbA1c is used as a secondary measure of glycaemic control after self monitoring of blood glucose (American Diabetes Association, 2017). This is because Hba1c level falls during normal pregnancy due to the physiological increases in red blood cell turnover and the inability of Hba1c to fully capture postprandial hyperglycaemia (American Diabetes Association, 2017). National Institute for Health and Care Excellence (NICE)

had also suggested that Hba1c should be done to determine the level of risk to the pregnancy only in women with pre-existing diabetes at booking appointment and during second and third trimester (NICE, 2015).

2.4 Factors Associated with Glycaemic Control

Various publications and studies showed some factors predicting the glycaemic control of GDM (Tudela *et al.*, 2006; Akinci *et al.*, 2008; Sapienza *et al.*, 2010; Tania Pertot *et al.*, 2011; Wong and Jalaludin, 2011; Bakiner *et al.*, 2013; Mitra *et al.*, 2014; Aktun *et al.*, 2015; Barnes *et al.*, 2016; Koning *et al.*, 2016; Watanabe *et al.*, 2016). The predictors in their study were based on the existing risk factors of GDM which incorporated medical and socio-demographic profile of the patients. These studies determined the predictors for the need of insulin therapy among GDM patients which indirectly indicate poor glycaemic control. One study in Turkey classified the existing risk factors into pre-gestational (family history of DM, previous history of GDM, parity, abortion history and previous history of macrosomic baby), and gestational (BMI, gestational age at diagnosis, weight gain until diagnosis, maternal age, level of fasting blood glucose and level of 2 hours post prandial glucose during OGTT) (Bakiner *et al.*, 2013) . On the other hand, a study done in India showed the socio-economic background and educational status of the pregnant lady play a role in the development of GDM but did not study further on glycaemic control of their subjects (Rajput *et al.*, 2013).

2.4.1 Socio-demographic Factors Associated with GDM and Glycaemic Control.

Women with age of more than 40 years old is considered to be in high risk group for GDM (Nankervis A *et al.*, 2013). A study in Gaza by Zaki *et al* did not find any significant association between maternal age and developing GDM (Zaki *et al.*, 2013). However a study in Pakistan reported maternal age as a risk factor for GDM (Khan *et al.*, 2013). That study was on the same line with another study in India (Rajput *et al.*, 2013). When considering age as factor for predicting the glycaemic control, one study reported maternal age as a predictor for the need of insulin therapy. In this study, age was found to be a significant predictor for the need of insulin therapy where insulin was initiated if GDM patients were not able to maintain optimum glycaemic control by medical diet therapy after 15 days (Aktun *et al.*, 2015).

Gravidity and parity were thought to be risk factor for development of GDM. Rajput et al reported that women with gravida 3 and more had significantly higher prevalence of GDM compared to gravida less than 3 (Rajput *et al.*, 2014). However a study in Gaza did not find significant correlation between an increase in parity and an increase in the number of pregnancies with GDM (Zaki *et al.*, 2013). On the other hand, Anna *et al* reported that parity was associated with GDM (Anna *et al.*, 2008). In one study in Netherland, parity was determined to be a significant predictor for glycaemic control (Koning *et al.*, 2016). In that study, parity of 1 to 2 was determined as one of the predictors for the need of insulin therapy after failed medical nutritional therapy in order to achieve optimum glycaemic control. However, another predictive study for the need of insulin therapy among GDM patients in Brazil which include nulliparity in the study did not find any significant finding (Sapienza *et al.*, 2010). That study was supported by other two studies in Turkey where parity was not found to be a predictor for glycaemic control (Bakiner *et al.*, 2013; Aktun *et al.*, 2015).

Family history of DM is a known risk factor for development of GDM. Rajput *et al* in their study found that there was a significantly higher percentage of women with GDM who had positive family history of DM (Rajput *et al.*, 2013). Few predictive studies reported family history as a predictor for glycaemic control. One study in Netherland in 2016 reported family history of diabetes was a predictor for need of insulin therapy to maintain good glycaemic control (Koning *et al.*, 2016). This study was supported by other predictive studies with similar finding (Sapienza *et al.*, 2010; Mitra *et al.*, 2014). Sapienza *et al* reported that family history of diabetes was the predictor for the need of insulin therapy among GDM patients in order to achieve optimum glycaemic control after failed diet therapy (Sapienza *et al.*, 2010). Mitra *et al* in 2014 also concluded in their study that family history of diabetes was a predictor for antenatal need of insulin in which it was commenced if the blood sugar readings were above the recommended values (Mitra *et al.*, 2014).

A study in Gaza in 2013 showed that GDM was twice as high in illiterate when compared to non GDM pregnant ladies and there was no significant difference between women with GDM and the non GDM group regarding place of residency (Zaki *et al.*, 2013). Meanwhile, a study by Rajput *et al* in 2013 in India revealed that GDM rate increased with increasing educational qualification and the prevalence of GDM was found to be higher in women belonging to upper and upper middle class (Rajput *et al.*, 2013). The socioeconomic status in the study was based on Kuppusamy'scale where it comprised of education, occupation and monthly income score.

However, a study by Bener *et al* in Qatar showed there was no significant difference in the level of education and occupation between GDM and non GDM groups but most of GDM patients were from lower economic group (Bener *et al.*, 2011). Another study in Australia supported the similar statement where it concluded that women living in the

lowest socioeconomic postcodes had two-thirds higher risk of developing GDM compared with women in the highest group (Anna *et al.*, 2008). The socioeconomic status in the study was assigned according to the maternal postcode using the index of advantage/disadvantage from the Australian Bureau of Statistics Socio-Economic Indexes for Areas (SEIFA). A more recent study in Pakistan in 2013 showed there was no difference in term of monthly income, female occupation and education level between GDM and healthy pregnant women (Khan *et al.*, 2013).

2.4.2 Medical Characteristics Associated with GDM and Glycaemic Control.

Obesity is one of risk factors for developing of GDM. Hence, various guidelines suggested women with high BMI should be screened for GDM (Nankervis A *et al.*, 2013; MOH, 2015; NICE, 2015). This was supported by various studies where there was significant association between prevalence of GDM and increasing BMI (Bener *et al.*, 2011; Khan *et al.*, 2013; Rajput *et al.*, 2013; Zaki *et al.*, 2013). There were also various predictive studies that reported pre-pregnancy BMI as a predictor for need of insulin therapy in order to achieve better glycaemic control (Sapienza *et al.*, 2010; Tania Pertot *et al.*, 2011; Wong and Jalaludin, 2011; Barnes *et al.*, 2016; Koning *et al.*, 2016).

Koning *et al* reported that pre-pregnancy BMI of more than 30kg/m2 was a significant predictor for insulin need to achieve good glycaemic control (Koning *et al.*, 2016). That study was on the same line with other studies which reported BMI more than 30kg/m2 as a predictor for insulin need among GDM patients after failed medical nutritional therapy in order to achieve optimum glycaemic control (Sapienza *et al.*, 2010; Wong and Jalaludin, 2011).

Tudela *et al* in their study reported that gestational age at diagnosis was a predictor for need of insulin therapy to achieve good glycaemic control (Tudela *et al.*, 2006). In this study, gestational age at GDM diagnosis which less than 28 weeks was determined to be a predictor for need of insulin therapy. That study was supported by another study in Australia where it was reported that gestational age at diagnosis of GDM was a predictor for undesirable glycaemic control where insulin was added to those who failed to maintain good glycaemic control with medical nutritional therapy (Wong and Jalaludin, 2011).

Rajput *et al* reported that women with GDM had higher weight gain compared to non-GDM women (Rajput *et al.*, 2013). GDM mothers who were on diet therapy had a more significant weight gain compared to insulin group but this factor was not a predictor for need of insulin therapy to achieve better glycaemic control (Koning *et al.*, 2016). Other studies which reported the similar finding with this study were Bakiner *et al* and Aktun *et al*. (Bakiner *et al.*, 2013; Aktun *et al.*, 2015).

Various predictive studies reported oral glucose tolerance test (OGTT) readings as the predictor for glycaemic control. A study in Netherland which studied on predictors of poor glycaemic control among GDM patients reported that both fasting and 2-hour post-prandial in the OGTT reading were predictors for the need of insulin therapy to achieve glycaemic control (Koning *et al.*, 2016). This was similar to finding by Wong and Jalaludin in Australia (Wong and Jalaludin, 2011). Akinci *et al* supported this finding through their report that the level of fasting blood glucose was a significant predictor for insulin need in patients with GDM (Akinci *et al.*, 2008). In that study, they found that 68.7% of patients with fasting blood glucose level equal or higher than 95mg/dl or 5.3mmol/L required insulin therapy to achieve better glycaemic control. Similar finding were reported by Bakiner *et al* and Aktun *et al* (Bakiner *et al.*, 2013; Aktun *et al.*,

2015). In addition, Watanabe *et al* in 2016 reported that the level of 1-hour post prandial blood glucose level in OGTT during diagnosis of GDM was also the predictor for insulin therapy to achieve better glycaemic control (Watanabe *et al.*, 2016).A study by Idris *et al* had included history of recurrent miscarriage as a risk factor for a pregnant lady to be screened for GDM (Idris *et al.*, 2009). This was seconded by a few other studies which reported that women with history of miscarriage (more than once) were at higher risk for developing GDM (N. Wah Cheung *et al.*, 2001; Bener *et al.*, 2011; Zaki *et al.*, 2013).

Women with previous history of GDM were advised to test for GDM as soon as possible after booking and further at 24- 28 weeks if the first test was normal (NICE, 2015). This is because studies had demonstrated that previous history of GDM is a strong predictor for development of GDM on next pregnancy (Bhat *et al.*, 2010; Rajput *et al.*, 2013). However, there were mixed findings in the previous studies about the previous history of GDM as a predictor for glycaemic control of GDM. Koning *et al* in their study concluded that previous history of GDM was a predictor for glycaemic control where glycaemic control was portrayed by the need of insulin therapy to achieve good control of GDM (Koning *et al.*, 2016). On the contrary, Sapienza *et al* in their study found that previous history of GDM was not a predictor to insulin treatment in order to achieve good glycaemic control (Sapienza *et al.*, 2010). Similar finding were noted in other studies where previous history of GDM was not determined as predictor for glycaemic control (Tudela *et al.*, 2006; Bakiner *et al.*, 2013; Aktun *et al.*, 2015; Watanabe *et al.*, 2016).

Previous history of macrosomic baby is an established risk factor for developing of GDM in various guidelines (Nankervis A *et al.*, 2013; MOH, 2015; NICE, 2015). Various studies reported that the history of macrosomic baby was found to have an independent association with prevalence of GDM (N. Wah Cheung *et al.*, 2001; Bener *et al.*, 2011; Zaki *et al.*, 2013; Rajput *et al.*, 2014). A study by Koning *et al* demonstrated that previous history of macrosomic baby of more than 4.5kg was a predictor for glycaemic control (Koning *et al.*, 2016). In that study, previous history of macrosomic baby was determined to be a predictor for insulin therapy in which patients who were unable to achieve optimum blood glucose levels were added insulin therapies.

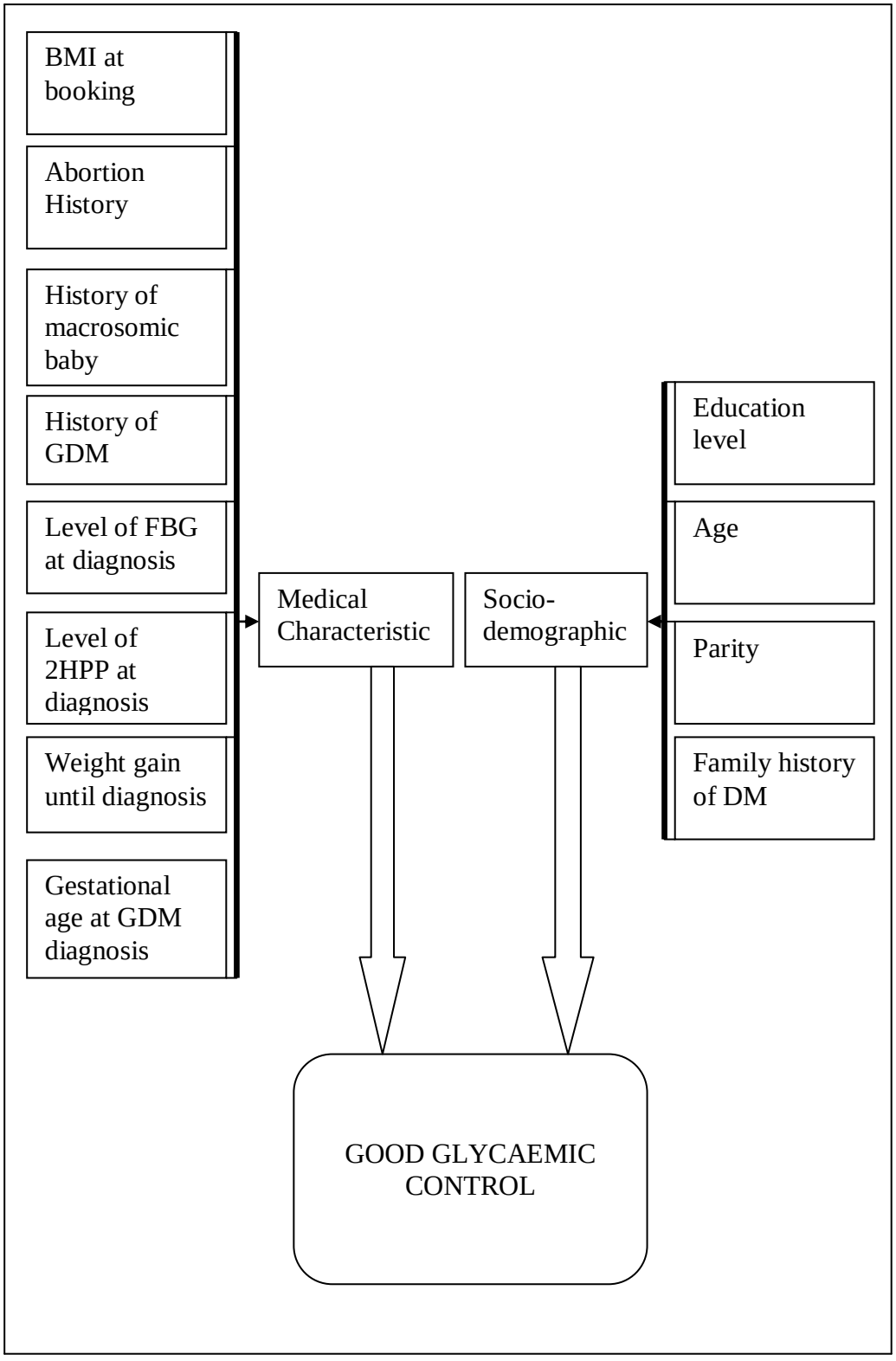

Figure 1 Conceptual Framework

CHAPTER 3 : OBJECTIVES

3.1 General Objective

To determine the prevalence of good glycaemic control and its associated factors among GDM patients attending antenatal clinic in Klinik Kesihatan in Bachok.

3.2 Specific Objectives :

1. To determine the prevalence of good glycaemic control among GDM patients attending antenatal clinic in Klinik Kesihatan in Bachok.

2. To determine the associated factors for good glycaemic control among GDM patients attending antenatal clinic in Klinik Kesihatan in Bachok.

3.3 Operational Definition:

Gestational Diabetes Mellitus (GDM) is a type of diabetes mellitus that is first recognized during pregnancy using oral glucose tolerance test (OGTT) of 75g anhydrous glucose. It is diagnosed if fasting blood glucose level is equal or more than 5.6 mmol/l or postprandial glucose is equal or more than 7.8mmol/l (WHO Guideline Development Group, 2013)

Good Glycaemic Control is defined as either: (i)GDM patients in whom at least 75% of the blood sugar profile (BSP) readings are within the normal range as stated in the Malaysian guideline (MOH, 2015) in two consecutive BSP readings after dietary advice. The normal limit for pre-breakfast and pre-prandial is equal to 5.3 or less and for two hours post prandial (pre-bed) reading is equal to 6.7 or less (MOH, 2015), or (ii)GDM patients who are not requiring insulin after two consecutive blood sugar profile (BSP) readings.

3.4 Hypothesis

Socio-demographic (age, parity, education level and family history of diabetes) and medical characteristics of GDM patients (BMI at booking, gestational age at diagnosis of GDM, weight gain until diagnosis of GDM, level of FBG and 2HPP at diagnosis of GDM, abortion history, previous history of GDM and history of macrosomic baby) are significant factors associated with good glycaemic control in gestational diabetes mellitus patients.

CHAPTER 4: METHODOLOGY

4.1 Study Design

This is a cross-sectional study with a retrospective record review.

4.2 Study Area

This study was conducted in Bachok district involving all Klinik Kesihatan. The district of Bachok is one of 10 districts in Kelantan. Bachok is among the district which has high rate of GDM in Kelantan. Based on 2014 local unpublished data from Bachok health district office, the proportion of GDM among new antenatal cases was 14.9%. Bachok has eight Klinik Kesihatan which are Klinik Kesihatan Bachok, Klinik Kesihatan Balai, Klinik Kesihatan Beris Panchor, Klinik Kesihatan Beris Kubur Besar, Klinik Kesihatan Mahligai, Klinik Kesihatan Gunong, Klinik Kesihatan Kuchelong and Klinik Kesihatan Kandis. All health clinics provide antenatal service with varies patients' attendance based on their population coverage.

4.3 Study period/duration.

This study period was from June to November 2015.

4.4 Reference population

The reference population was all GDM patients in Bachok district.

4.5 Source population

All GDM mothers attending antenatal clinic in Klinik Kesihatan in Bachok, Kelantan

4.6 Study sample

The study sample was all GDM mothers attended antenatal clinic in Klinik Kesihatan in Bachok who fulfilled the inclusion and exclusion criteria.

4.7 Inclusion Criteria

GDM mothers with at least two consecutive blood sugar profiles reading after dietary advice given by nutritionist.

4.8 Exclusion Criteria

Patients with established type 1 or type 2 diabetes mellitus.

4.9 Sampling Method

Universal sampling method was used in this study due to the limited samples within the given time period.

4.10 Sample Size Calculation

4.10.1 Sample size determination for objective 1.

Sample size to determine the prevalence of good glycaemic control among GDM patients was calculated based on single proportion formula (Daniel, 2005).

$$n = \left[\frac{Z_{\alpha/2}}{\Delta}^2\right] P(1-P)$$

n = Minimum required sample size

$Z_{\alpha/2}$ = Value of standard normal distribution was 1.96

Δ = Precision of 0.05

p = proportion of good glycaemic control = 93.5% (Schaefer-Graf *et al.*, 2003)

The proportion of good glycaemic control was 93.5% (Schaefer-Graf et al., 2003) and taking the precision of 0.05 with 95% confidence, the minimum required sample size was 94. After considering a non-response rate of 10%, the calculated sample size was 103 antenatal cards.

4.10.2 Sample size determination for objective 2

Sample size was calculated using PS-Power and sample size calculation. Sample to identify the associated factors for good glycaemic control among GDM patients are based on comparing two proportions for categorical variables and comparing two means for numerical variables (Appendix B). The variable that yielded the biggest sample size for this objective was that of previous history of GDM.

$\alpha = 0.05$

power = 0.8

P_0 = proportion of history of GDM among poor control = 29.0% (Bakiner *et al.*, 2013)

P_1 = proportion of history of GDM among good control = 9% (Expert opinion)

m = ratio of poor control to good control GDM = 1

The proportion of previous history of GDM among poor control was 0.29 (Bakiner *et al.*, 2013) and the minimum required sample size was 118. After considering the non-response rate of 10%, the calculated sample size for each group of cases and controls was 129.

The biggest sample size was from Objective 2 (n = 129) and was taken as the study sample.

4.11 Research Tool

The case report form (Appendix A) obtained responses on sociodemographic and medical data, namely, maternal age, parity, level of education, family history of DM, previous history of GDM, previous macrosomic baby, abortion history, BMI at booking,

weight gain until GDM diagnosis, gestational age at diagnosis of GDM, level of fasting blood glucose at diagnosis, level of 2 hours post prandial at diagnosis, date of receiving dietary advice and level of blood sugar profile monitoring.

4.12 Data Collection

All antenatal cards of GDM mothers diagnosed from June 2014 until November 2014 in Bachok district were collected. The antenatal cards were then reviewed in accordance to each health clinic visits. The socio-demographic and medical characteristics from a copy of antenatal card (Rekod Kesihatan Ibu KIK/ 1(b) /96) were obtained (Figure 2).

4.13 Data Entry and Statistical Analysis

All collected data were entered, cleaned and analysed using the SPSS software version 22. Data checking and cleaning were performed before analysis. The distributions and frequencies of variables were examined. Categorical variables were described in frequencies and percentage. Small cell categories were identified and collapsed accordingly. Categories with small sample size were identified and meaningful combinations of categories were done when indicated.

Descriptive analysis was performed to calculate the prevalence of good glycaemic control of GDM and each variable. Simple and multiple logistic regression analyses were performed to identify the factors associated with good glycaemic control of GDM. The dependent variable was glycaemic control (0 = Poor glycaemic control, 1 = good glycaemic control). The independent numerical variables in this study which were age, parity, BMI at booking, gestational age at diagnosis of GDM, weight gain until diagnosis of GDM, level of FBG and 2HPP at diagnosis were described as mean and

standard deviation (SD) for normally distributed data and median and inter quartile range (IQR) for not normally distributed data. The independent categorical variables which were education level, family history of diabetes, abortion history, previous history of GDM and history of macrosomic baby.

The numerical variables were defined as follows. Parity is defined as the number of times that a woman has given birth to a fetus with a gestational age of 24 weeks or more, regardless of whether the child was born alive or was stillborn. Body Mass Index (BMI) at booking is defined as BMI at the time of first antenatal visit and was calculated with the formula of (weight(kg)/Height(m)^2). Weight gain until GDM diagnosis is defined as amount of weight gained in kilogram by a patient from her first antenatal visit until diagnosis of GDM. Gestational age at diagnosis of GDM is defined as gestational age (expressed in week) of patient at the time of diagnosis of GDM. Level of fasting blood glucose at diagnosis is defined as the level of fasting blood glucose (expressed in mmol/l) in Oral Glucose Tolerance Test (OGTT) during diagnosis of GDM. Level of 2 hours postprandial at diagnosis is defined as the level of blood glucose after 2 hours of 75g anhydrous glucose ingestion (expressed in mmol/l) in Oral Glucose Tolerance Test (OGTT) during diagnosis of GDM.

The categorical variables were defined as follows. Level of education is categorised into (i) Lower education level (Primary school and Secondary school) and (ii) Upper education level (Diploma / Degree / Postgraduate level). Family history of Diabetes Mellitus is categorised into (i) presence of family history of diabetes among first degree family member or siblings, and (ii) absence. Previous history of GDM is categorised into (i) presence of history of being diagnosed of GDM in previous pregnancy and (ii) absence. Previous macrosomic baby is categorised into (i) history of giving birth 4kg and more in previous pregnancy and (ii) absence.

The procedure of simple and multiple logistic regression analyses

Simple logistic regression, was used as a screening in the selection of variables. All variables with *p* value less than 0.25 and clinically significant variables were included in multiple logistic regression. The *p* value was set larger than the level of significance to allow more important variables in the model. Multiple logistic regression using backward LR method was applied in this analysis. The preliminary main effect model was obtained.

Multicollinearity and all possible 2 way interactions were assessed. The preliminary final model was obtained. Model fitness tested with Hosmer-Lemeshow test, overall classification percentage and area under receiver operating characteristics (ROC) curve. The high overall classification percentage of more than 70% and area under curve of more than 70% showed the model is fit. The final model was presented as Wald statistic (Wald stat), adjusted odds ratio (adj OR), 95% confidence interval (95% CI) and *p* value.

4.14 Ethical Consideration

Ethical approval was obtained from Human Research Ethics Committee USM (USM/JEPeM/14090318) on 5 March 2015 and Medical Research & Ethics Committee (NMRR-14-1299-22330) on 12 February 2015. Permission from Kelantan State Health Department and Bachok District Health Office were obtained prior to data collection. All collected data was kept in confidential and for the eyes of involved researchers only. Each patient record was identified with coded number so that the true identity of the patient was kept confidential

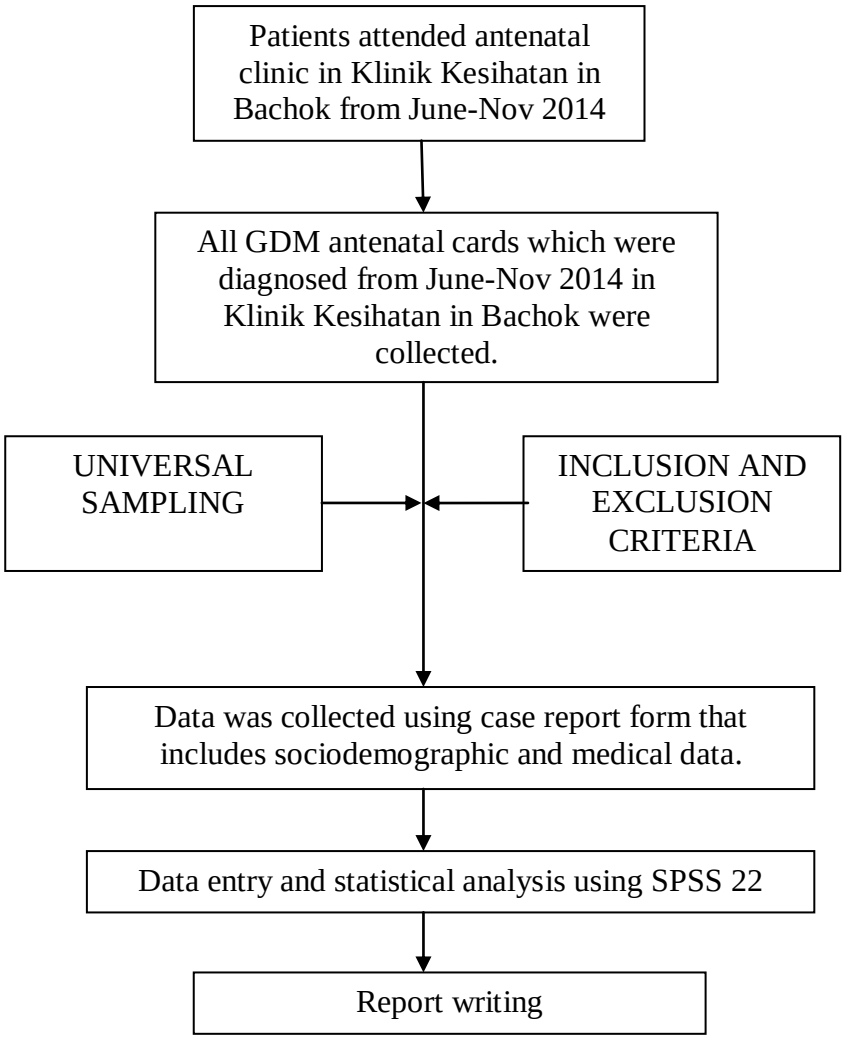

Figure 2 Flow chart of the study