SCREENING FOR GESTATIONAL DIABETES MELLITUS AND ASSOCIATED RISK FACTORS BEFORE 20 WEEKS OF GESTATION IN HEALTH CLINICS, TANAH MERAH, KELANTAN

by

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ABBREVIATIONS

ADA	American Diabetic Association
ACOG	American College of Obstetricians and Gynecologists
DM	Diabetes Mellitus
GDM	Gestational Diabetes Mellitus
GW	Gestational Weeks
NHMS	National Health and Morbidity Survey
OGTT	Oral Glucose Tolerance Test
WHO	World Health Organization

ABSTRAK

Saringan Diabetes Gestasi di Kalangan Ibu-ibu Mengandung di Klinik Kesihatan Tanah Merah, Kelantan dan Faktor-faktor Risiko yang Berkaitan Sebelum 20 Minggu Kandungan .

Kejayaan rawatan diabetes gestasi di kalangan ibu-ibu mengandung adalah bergantung kepada diagnosa dan rawatan awal. Pengesanan awal diabetes gestasi membolehkan diagnosa dan rawatan awal dimulakan. Objektif kajian ini adalah untuk menentukan insiden diabetes gestasi sebelum 20 minggu, pada 24-28 minggu dan pada 32-34 minggu kandungan dan mengenalpasti faktor-faktor risiko berkaitan dengan diabetes gestasi khususnya sebelum 20 minggu kandungan.

Kajian ini merupakan kajian irisan lintang yang melibatkan sejumlah 376 ibu-ibu mengandung yang mempunyai faktor risiko untuk mendapat diabetes gestasi dan memulakan rawatan antenatal di Klinik Kesihatan Batu Gajah dan Klinik Ibu dan Anak Tanah Merah, Kelantan sebelum kandungan berusia 20 minggu. Kesemua ibu mengandung menjalani 75g ujian tolerans glukosa yang pertama sebelum kandungan berusia 20 minggu, jika negatif , 75g ujian tolerans glukosa kedua diulang pada 24-28 minggu dan ketiga pada 32-34 minggu. Hasil utama analisa adalah insiden diabetes gestasi sebelum 20 minggu, 24-28 dan pada 32-34 minggu kandungan dan faktor-faktor risiko berkaitan dengan diabetes gestasi sebelum 20 minggu kandungan. Analisis dilakukan menggunakan SPSS versi 12.0. Keputusan kajian menunjukkan 47.9% ibu-ibu mengandung mempunyai diabetes gestasi. Insiden diabetes gestasi sebelum 20 minggu

kandungan adalah 33.0 %, pada 24-28 minggu kandungan adalah 13.5% manakala pada 32-34 minggu kandungan adalah 10.1%. Tiga faktor risiko yang telah dikenalpasti mempunyai kaitan yang signifikan untuk mendapat diabetes gestasi sebelum 20 minggu kandungan ialah umur $\geq$ 35 tahun , mempunyai diabetes gestasi pada kandungan yang lalu dan mempunyai ahli keluarga yang menghidap diabetes mellitus .

Kesimpulannya, saringan diabetes gestasi di kalangan ibu-ibu mengandung di Klinik Kesihatan Tanah Merah, Kelantan menunjukkan lebih dari separuh ibu-ibu yang menghidap diabetes gestasi (124 dari 180 , 68.9%) dapat dikesan diperingkat awal kandungan. Tiga kumpulan utama wanita iaitu wanita berumur $\geq$ 35 tahun , wanita yang mempunyai diabetes gestasi pada kandungan lalu dan wanita yang mempunyai ahli keluarga yang menghidap diabetes mellitus harus diberi kaunseling mengenai kepentingan saringan diabetes gestasi dan penjagaan antenatal di peringkat awal kandungan .

ABSTRACT

Screening for Gestational Diabetes Mellitus and Associated Risk Factors Before 20 Weeks of Gestation in Health Clinics, Tanah Merah, Kelantan.

Early diagnosis and treatment is the most important issue for the successful management of gestational diabetes mellitus. Thus lays the importance of screening for gestational diabetes mellitus, which allows for early initiation of appropriate therapy which remains the cornerstone of management of gestational diabetes mellitus. The objectives of this study were to determine the incidence of gestational diabetes mellitus before 20 weeks, at 24-28 weeks and at 32-34 weeks of gestation and to evaluate factors associated with gestational diabetes mellitus before 20 weeks of gestation.

This is a cross sectional study. A total of 376 pregnant women started their antenatal care at health clinics Tanah Merah, Kelantan before 20 weeks of gestation and were at risk of developing gestational diabetes mellitus were enrolled. All pregnant women had initial two hours 75-g oral glucose tolerance test before 20 weeks of gestation. If the results were negative, second OGTT were performed at 24-28 weeks and subsequently at 32-34 weeks if still negative. A diagnosis of gestational diabetes mellitus was made if fasting glucose $\geq$ 6.1 mmol/l or 2 hours $\geq$ 7.8 mmol/l. The main outcome measures were incidences of gestational diabetes mellitus before 20 weeks, at 24-28 and at 32-34 weeks of gestation and the association between clinical risk factors and gestational diabetes mellitus below 20 weeks of gestation. Data was analyzed using SPSS version 12.0. The

results showed that the overall incidence of gestational diabetes mellitus was 47.9 %. The incidence of GDM before 20 weeks of gestation was 33.0 %, another 13.5 % were diagnosed between 24-28 weeks and 10.1% between 32-34 weeks. The three independent risks for developing gestational diabetes mellitus before 20 weeks of gestation were age ≥ 35 years, history of gestational diabetes mellitus in previous pregnancy and family history of diabetes mellitus.

In conclusion, screening for gestational diabetes mellitus in Tanah Merah, Kelantan is crucial in detecting early onset of gestational diabetes mellitus since more than half of women with gestational diabetes mellitus (124 of 180 , 68.9%) were diagnosed early in their pregnancies. The three specific groups of women (women age ≥ 35 years, women who had gestational diabetes mellitus in previous pregnancy and women with family history of diabetes mellitus) should be promptly identified, counseled regarding the important of early booking and early screening for gestational diabetes mellitus.

CHAPTER 1 : INTRODUCTION

Gestational Diabetes Mellitus (GDM) is the most common medical complication and metabolic disorder seen in pregnancy. It is characterized as carbohydrate intolerance resulting in hyperglycaemia with onset or first recognition during pregnancy (WHO Consultation 1999) .It includes patients with undiagnosed pre-existing type 2 diabetes mellitus (type 2 DM) discovered during pregnancy. Diabetes in the first trimester is more likely to be type 2 DM that was present but undiagnosed before pregnancy (Virjee *et al.*, 2001).

Most clinical complications caused by GDM can be prevented by early diagnosis and tight control of blood glucose levels. So it is important for early screening of women at high risk of developing GDM. A study by Bartha *et al.*, 2003 showed that early glucose intolerance screening could avoid some diabetes-related complications such as polyhydramnios, fetal anomalies and preterm births.

Super (1991), Bartha (2000) and Meyer (1996), reported that 28–66 % of all cases of GDM could be detected during early pregnancy. A study by Asmah Yun, (1998) showed that the prevalence of GDM in high risk obstetric population was 12.5%. However, Shamsuddin and colleagues, (2001) reported that among women with at least one risk factor, the prevalence of GDM in Malaysia was 26.9%.

Traditionally a risk based selective screening program has been developed and practiced for many years especially in public or government health settings in Malaysia. Women defined as at high risk for the development of GDM were significant glycosuria on two or

more occasions during pregnancy, maternal obesity (Maternal weight > 80 Kg or BMI > 27 at booking), family history of diabetes mellitus in first degree relatives, previous big baby (weighing > 4 Kg), women aged > 35 years old, previous unexplained stillbirths, recurrent abortions, birth defects, previous history of gestational diabetes mellitus and polyhydramnios in current pregnancy. A high risk woman should undergone first oral glucose tolerance test (OGTT) after 12-14 weeks gestation or as soon as the risk factors have been identified. If the initial testing was negative, the woman should be retested at 24-28 weeks and subsequently at 32-34 weeks if still negative (Division Of Family Health Development and Ministry Of Health Malaysia., 2002). Malaysia has adopted the WHO definition using the 75g OGTT for diagnosis of GDM.

National Health and Morbidity Survey (NHMS) reported that the prevalence of DM in Malaysia has steadily increased over the years from 6.3% (NHMS 1, 1986) to 8.3% in 1996 (NHMS 2, 1996). Women with GDM and their offspring are at increased risk of developing DM (Metzger *et al.*,1998). Although increases in DM prevalence have been reported in Malaysia, it is unknown whether this trend is also occurring for GDM. Unfortunately, in Malaysia, the data on GDM is sparse. Although it is well known that the prevalence of type 2 DM has been increasing in Malaysia, no reports have described current data with respect to the development of GDM. There were no local data available on the incidences of early and multiple screening of GDM throughout pregnancy among high risk pregnant women. There were no study evaluating the effectiveness of a risk based selective screening program in early detection of GDM .This study was therefore

conducted to estimate the incidences of GDM at various stages of gestation and evaluated risk factors associated with early diagnosis of GDM.

CHAPTER 2 : LITERATURE REVIEW

2.1 Diagnosis of Gestational Diabetes Mellitus

Diagnosis of GDM has been based on OGTT. World Health Organization (WHO) panel characterizes GDM as the joint category of diabetes and impaired glucose tolerance. The WHO approach is simpler to perform, one-step approach to detect glucose alterations, less expensive and is especially convenient when financial resources are scarce and the ethnic characteristics of the population are associated with high rates of type 2 DM (Gerardo *et al.*, 2005). WHO recommends the same OGTT in pregnant and non-pregnant adults that consists of a glucose load of 75 g and a blood sample at fasting and 2 hours later. The diagnosis of GDM is made if the patient has a plasma glucose >7.0 mmol/l (fasting) or ≥7.8 mmol/l (2 h) (WHO Consultation., 1999).

According to diagnostic criteria recommended by the American Diabetes Association (ADA), GDM is diagnosed if two or more plasma glucose levels meet or exceed the following thresholds: fasting glucose concentration of 95 mg/dl, 1-hour glucose concentration of 180 mg/dl, 2-hour glucose concentration of 155 mg/dl, or 3-hour glucose concentration of 140 mg/dl (ADA 2004). However, Schmidt *et al.*, 2001 concluded that, GDM defined by either WHO or ADA criteria are valid options for the diagnosis of GDM and the prediction of adverse pregnancy outcomes.

2.2 Why screen for GDM?

2.2.1Adverse Health Outcomes

Evidence has shown that preexisting diabetes, diagnosed for the first time during pregnancy as GDM with fasting plasma glucose > 6.7mmol/l (120mg/dl), may be associated with a rate of congenital anomalies that is higher than in the general obstetrics population (Metzger *et al.*, 1998). Fetal macrosomia, hypoglycaemia, jaundice, respiratory distress syndrome, polycythaemia and hypocalcemia have been reported with varying frequency in the infants of women with GDM (Kjos and Buchanan 1999 , ADA 2003, Metzger 1998, O'Sullivan 1973 and Sheffield 2002). GDM has been linked to increase maternal and perinatal morbidity, principally through its association with fetal macrosomia (U.S. Preventive Services Task Force 2003). Macrosomia was defined as birth weight > 4000g (Cianni 2003). Approximately 20-30% of infants whose mothers have GDM developed macrosomia. (Kjos and Buchanan 1999)

Apart from that GDM is also associated with increased incidence of maternal hypertension, pre-eclampsia and obstetric intervention (Schmidt *et al.*, 2001). The Toronto Tri-Hospital Gestational Diabetes Project 1995, found a clear graded relationship between OGTT values and adverse outcomes, including operative delivery, macrosomia and preeclampsia (Naylor *et al.*,1997). A meta-analysis by Cheung and Byth, 2003 calculated the relative risk for developing diabetes after GDM to be 6.0.

2.2.2 Therapeutic interventions

Prevention of adverse perinatal outcome remains the primary focus of antepartum management of GDM. Controlling maternal glycemia with medical nutritional therapy (MNT), close monitoring of blood glucose levels, and treatment with insulin if blood glucose levels are not at goal have been shown to decrease fetal and maternal morbidities (Metzger *et al.*, 1998). Evidence showed that women who were intensively managed during pregnancy had significantly fewer macrosomic and large gestational age infants (Langer *et al.*,1994).O'Sullivan and colleagues,1973 found significantly more perinatal mortality in untreated women with GDM. Crowther *et al.*, 2005 reported that the rate of serious perinatal complications (defined as death, shoulder dystocia, bone fracture, and nerve palsy) was significantly lower among the infants of the women in the intervention group. Thus lays the importance of screening for GDM, which allows for early initiation of appropriate therapy which remains the cornerstone of management of GDM.

2.3 Risk factor for screening

Some authors reported that selective screening on the basis of historical risk factors would miss 40 % to 50 % of women with GDM(O'Sullivan 1973 ,Naylor 1997 and Coustan 1989) and therefore recommend that all women should undergo a screening test. Other recent studies have focused on the advantages of selective screening. (Naylor *et al.*, 1997 and Jimenez-Moleo *et al.*, 2000). Davey and Hamblin, 2000 concluded that selective screening on the basis of risk factors for GDM is practicable. They concluded that selective screening using four criteria (age, family history of DM, obesity and high-

risk racial heritage) would have missed only 0.6 % cases and could have saved screening up to 17% of women without GDM.

The WHO recommends screening by means of maternal risk factor selection. Groups defined as at high risk for the development of GDM by WHO are older age, previous glucose intolerance and previous history of large-for-gestational-age infant, certain ethnic groups and raised fasting or casual blood glucose. The Canadian Task Force on Preventive Health Care concluded in 1991 that the available evidence did not support a recommendation for or against universal screening for GDM .The Australasian Diabetes in Pregnancy Society (ADIPS) recommends that screening for GDM should be considered in all pregnant women. However, if resources are limited, screening may be reserved for those at highest risk. Risk factors include glycosuria, age over 30 years, obesity, family history of diabetes, past history of GDM or glucose intolerance, previous adverse pregnancy outcome; and certain ethnic group with a high risk for GDM (Beischer *et al.*, 1991). A 2001 Practice Bulletin of the American College of Obstetricians and Gynecologists (ACOG) recommends a similar risk-based approach but since only a small percentage of patients meet the criteria for low risk, universal 50-g 1-h GCT screening may be a more practical approach. ACOG recommends universal screening between 24 and 28 weeks of gestation for women of average risk and an increased risk of GDM. The American Diabetic Association (ADA) 2002, recommends screening all women at risk for GDM.

Increased parity (Dornhost *et al.*, 1992), twins pregnancy (Schwartz *et al.*, 1999), weight

gain between pre-pregnancy and post-partum (Dornhost *et al.*, 1992) are additional risk factors. A study by Yang *et al.*, 2002 concluded that independent predictors for GDM in Tianjin, China were maternal age, short stature, weight gain in pregnancy before screening, diabetes in first-degree relatives, and habitual cigarette smoking during pregnancy.

2.4 Timing of the screening test

Women who develop GDM early in pregnancy are at higher risk for neonatal hypoglycemia and other GDM-related outcomes than are those who develop GDM later in pregnancy (Griffin *et al.*,2000). Screening earlier in pregnancy detects fewer women with GDM, but identifies those at highest risk and allows for earlier intervention. Screening for GDM later in pregnancy detects a larger number of women with GDM, many of whom are at lower risk, but who would be treated for a shorter time (U.S. Preventive Services Task Force 2003)

Super *et al.*, (1991) found 66 % of high risk women developed GDM during the first half of the pregnancy. A study by Meyer and colleagues revealed that factors associated with early detection of glucose intolerance included maternal age >30 years, black race and the presence of risk factors. Poor pregnancy weight gain was associated with the late development of glucose intolerance. In their study, 40 % of GDM were detected with the early screening protocol, prior to 24 weeks and 16 % was subsequently diagnosed in the third trimester, at 28 weeks. The results of the study recommended that women with risk factors should be screened at early prenatal visits (between 12 and 24 weeks gestation)

and at 24 to 28 weeks if the test result was negative. Results of a study in Siriraj Hospital in Thailand, (2004) showed that the incidence of GDM among high risk women diagnosed before 20 weeks of gestation was 5.3 %, and another 4.9 % were diagnosed during 28-32 weeks. The two independent risks for developing early GDM were age $\geq$ 30 years and GDM in previous pregnancy. The study concluded that approximately half of women with GDM could be diagnosed early in their pregnancies.

Dashora *et al.*, (2002) tested 564 patients attending the antenatal clinic in Oman by glucose tolerance test using 75 g anhydrous glucose performed at booking. If the results were normal, the test was repeated two or three times at two month intervals, the last being at the seven month of pregnancy. The study concluded that early and multiple screening for GDM has the potential to increase detection of GDM and to favorably influence pregnancy outcome. The study showed over 88% of the patients with GDM were diagnosed at first testing.

Apart from that, a study by Maegawa *et al.*, (2003) showed that 63.6 % of the GDM patients were diagnosed in the first trimester and 36.4% were diagnosed in the second trimester. This finding is also similar with other studies. This suggests the importance of screening for glucose intolerance in the first trimester .The study showed that women with early GDM were of likely to be obese.

Bartha *et al.*, (2000) concluded that women with an early diagnosis of GDM represent a high-risk subgroup. The study compared pregnancy complications, obstetric outcomes, and perinatal outcomes between women with early onset and late onset GDM. Women

with early onset GDM were likely to be hypertensive, had higher glycemic values and need for insulin therapy than those in whom GDM developed later. Barahona *et al.*, 2005, concluded that diagnosis of GDM earlier in pregnancy is a predictor of adverse maternal and neonatal outcome.

Hong *et al*, 1989 however found that there was an increasing likelihood of GDM as pregnancy progressed, suggesting that the screening test performed early in pregnancy is likely to miss affected individuals. Prevalence of GDM diagnosed between 14-23 weeks are 2.5 %, 5.7 % between 24-28 weeks and 6.4 % at gestational age more than 28 weeks. Jovanovic and Peterson, 1985 elucidated the optimum time to test for diabetes during gestation, and the indication for retesting. The prevalence of GDM in their study was 3.2 %. GDM detection increased by repeating the test at 33-36 weeks of gestation in high risk individuals (obese and age > 33 years).

CHAPTER 3 : OBJECTIVES

3.1 General Objective

To determine the incidence of gestational diabetes mellitus at various stages of pregnancy among pregnant women with risk in Tanah Merah, Kelantan.

3.2 Specific Objectives :

1. To determine the incidences of GDM before 20 weeks , at 24 – 28 weeks and at 32-34 weeks of gestation.

2. To identify factors associated with development of GDM before 20 weeks of gestation