ORIGINAL ARTICLE

GESTATIONAL DIABETES MELLITUS IN PRIMIGRAVIDAE: A MILD DISEASE

Nor Azlin Mohamed Ismail[1], Norkhatijah Mohd Aris[2], Zaleha Abdullah Mahdy[1], Shuhaila Ahmad[1], Norzilawati Mohd Naim[1], Harlina Harlizah Hj Siraj[1], Syed Zulkifli Syed Zakaria[2]

Universiti Kebangsaan Malaysia, Faculty of Medicine, Kuala Lumpur, Malaysia: Department of Obstetrics & Gynaecology[1], UKM Medical Molecular Biology Institute[2]

Summary: This prospective observational study was done to analyse the prevalence of gestational diabetes mellitus (GDM) among primigravidae and its outcome. All healthy primigravidae with singleton pregnancies were offered universal glucose tolerance testing between 16 and 28 weeks gestation. GDM and non GDM groups were managed according to hospital protocol. The antenatal features and pregnancy outcomes were analysed. Out of 616 primigravidae, 113 (18.34 %) were GDM with slightly older (27.9 ± 4.2 versus 26.32 ± 3.3, $p < 0.001$) age. The mean fasting and two hours postprandial blood glucose in both groups were 4.99 ± 1.08 mmol/l, 8.86 ± 1.41 mmol/l(GDM) and 4.36 ± 0.43 mmol/l, 5.71 ± 1.11 mmol/l (Non GDM), respectively. Maternal family history of diabetes mellitus, weight exceeding 80 Kg, polyhydramnios (2.65 % versus 0.2 %, p=0.028) and neonatal hyperbilirubinaemia (9.73 % versus 2.98 %, p=0.01) occurred significantly more frequent in the GDM group compared to normal. There was no significant difference in other pregnancy outcomes and complications between the two groups. In conclusion GDM in primigravidae was detected at a relatively young age with more frequent maternal family history of DM, weight exceeding 80 Kg, polyhydromnions and neonatal hyperbilirubinaemia. The degree of disease was mild and treatment led to no significant complication.

Key words: *Gestational diabetes mellitus; Primigravidae; Macrosomia; Risk factors; Polyhydramnios*

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying degrees of severity with first onset or recognition during pregnancy. It has been reported that the incidence is approximately between 1–14 % (3) of all pregnancies although in actual fact a higher incidence was found in some countries with Asian ethnicity (19, 2). The prevalence of GDM was also shown to be increased in other parts of the world (7). GDM has known association with maternal and perinatal complications such as pre-eclampsia and macrosomia (12). Concern extends beyond these as GDM is a mirror to the development of Type 2 diabetes mellitus (9) in later life. Prompt diagnosis of GDM in pregnant women, education on the disease process and healthy lifestyle may delay possible complications. Although policy and methods of screening for GDM varies from one centre to another, most parts of the world now have screening tests to detect GDM. There is, as yet, no consensus on the ideal way (16) of screening hence this follows the preference of the obstetrician.

Among risk factors that are known to contribute to GDM are ethnicity, history of previous GDM and obesity. In countries with multiethnicity the prevalence may vary according to diffent ethnic groups. Several studies (2) advocated using a combination of serum fructosamine and glycated haemoglobin on a single fasting level for screening in countries with multiethnic and high risk populations. South East Asian women have an eight-fold preponderance to develop GDM compared to Caucasian women (6). The current study was done to analyse the prevalence of primigravidae alone with gestational diabetes mellitus and its outcome in our centre using the universal approach of screening.

Materials and methods

All primigravidae without medical problems, multiple pregnancies and regardless of risk to develop GDM, attending routine antenatal clinic between 2007 and 2008 were invited to enroll into the study. This prospective observational study done in a teaching hospital involved 616 primigravidae who were not known to be diabetic before. The patients' history and examination findings were recorded. Other antenatal screening tests such as blood group and infective screening were carried out as per hospital pro-

tocol. Following 72 hours of unrestricted carbohydrate intake and at least 8 hours overnight fast, the women were subjected to a glucose tolerance test (GTT). The test was performed between 16 and 28 weeks gestation using 75 g oral glucose dissolved in 250 ml water. Venous blood samples were taken at 0 hour (fasting blood glucose, FBG) and two hours post prandial (2HPPBG). The test was considered abnormal if FBG > 110 mg/dL (6.0 mmol/L) and/or 2HPPBG > 140 mg/dL (7.8 mmol/L), indicative of GDM.

Once diagnosed to have abnormal GTT, they were treated according to the usual hospital protocol which includes diet therapy and insulin treatment (if required) with a combined obstetrician-endocrinologist team managing the patients. Maternal and fetal monitoring were done as usual and the outcome of pregnancy and delivery were compared between the GDM group and those with normal GTT. All subjects were informed of the research procedure and signed the written informed consent. This study was performed according to the Declaration of Helsinki and approved by our Institutional Research Ethics Board.

Risk factors for GDM, antenatal features, delivery outcome and neonatal parameters were analysed using SPSS 12.0. The chi-square, student t-test and Fisher exact tests and one-way analysis of variance were used for normally distributed data. Mann-Whitney *U* and Kruskal-Wallis tests were used for non-parametric data. The test was considered significant if p value < 0.05.

Results

Out of 616 primigravidae, 113 (18.34 %) had abnormal GTT. The rest of the women were normal (503, 81.66 %). There was not much difference in the demographic features except the age, where the non GDM women were slightly but significantly younger than the GDM group (26.3 ± 3.3 versus 27.9 ± 4.2 p< 0.001). There was a relatively higher percentage of Chinese and Indian women in the GDM group compared to the non GDM group (see Tab. 1).

Tab. 1: Patients' demographic data.

Parameters	GDM n=113 (%)	NonGDM n=503 (%)	*P* value
Race	0.046[a]		
Malay	73 (64.6)	362 (72)	
Chinese	33 (29.2)	130 (25.8)	
Indian	7 (6.2)	11 (2.2)	
Age (mean±SD	27.9 ± 4.2	26.32 ± 3.3	<0.001[b]
Weight (mean±SD)	66.5 ± 14.4	60.3 ± 12.2	0.096[b]
Working	98 (86.7)	400 (79.5)	0.079[a]

[a]Pearson Chi Square P value; [b]T-test P value

The GTT results revealed that the mean fasting and two hours postprandial blood glucose in the GDM group were significant 4.99 ± 1.08 mmol/l, and 8.86 ± 1.41 mmol/l respectively compared to those of normal women (4.36 ± 0.43 mmol/l and 5.71 ± 1.11 mmol/l). Our study also showed that family history of diabetes and maternal weight exceeding 80 kg (at the time of screening) were both significant risk factors for GDM (see Tab. 2). Antenatally there was no statistically significant difference in the incidence of complications including evidence of large for gestational age (LGA) fetus and proteinuria except for incidence of polyhydramnios (2.65 % in GDM versus 0.2 % in non GDM, p=0.028).

Tab. 2: Risk Factors and antenatal features.

	GDM n=113 (%)	NonGDM n=503 (%)	*P* value
Risks			
Abnormal MGTT	113 (18.34)	503 (81.66)	0.635[a]
Fasting blood glucose*	4.99 ± 1.08	4.36 ± 0.43	<0.001[b]
2hr post prandial*	8.86 ± 1.41	5.71 ± 1.11	<0.001[b]
Family h/o diabetes mellitus	56(49.56)	182(36.18)	0.008[a]
Maternal wt > 80 Kg	24 (21.24)	40 (7.95)	<0.001[a]
Antenatal features			
LGA	4 (3.54)	11 (2.19)	0.495[c]
Polyhdromnion	3 (2.65)	1 (0.2)	0.028[c]
Glycosurea	13 (11.50)	50 (9.94)	0.609[a]
Protinurea	0	8 (1.59)	0.362[c]

*(mean±SD) mmol/l; [a]Pearson Chi Square P value; [b]T-test P value; [c]Fisher's exact test P value

Tab. 3: Maternal and neonatal complications.

Features	GDM n=113 (%)	NonGDM n=503 (%)	*P* value
Delivered	111 (98.2)	437 (86.88)	
Missing data	2 (1.8)	66 (13.12)	
Maternal			
Premature delivery	18 (15.93)	65 (12.92)	0.767[a]
Pre-eclampsia	2 (1.77)	17 (3.38)	0.391[a]
Ceaserean section	28 (24.78)	125 (24.85)	0.554[a]
Post partum hemorrhage	0	0	-
Fetal			
> 4kg	6 (5.31)	9 (1.79)	0.094[a]
Anomalies	0	0	-
Neonatal death	0	0	-
Apgar at 1 min	8 (7.08)	9 (1.79)	0.933[b]
Apgar at 5 min	8 (7.08)	9 (1.79)	0.888[b]
cord pH*	7.24 ± 0.2	7.25 ± 0.1	0.467[b]
Neonatal			
Hypoglycaemia	1 (0.9)	2 (0.4)	0.492[a]
Hyperbilirubinaemia	11 (9.73)	15 (2.98)	0.01[a]
Hypocalcaemia	0	0	-
Polycythaemia	0	0	-
Birth trauma	1 (0.9)	2 (0.4)	0.494[a]
NICU admission	5 (4.42)	30 (5.96)	0.514[a]

*(mean±SD); [a]Fisher's exact test P value; [b]T-test P value

With regard to delivery details, two women were lost to follow up in the GDM group and 66 in the normal group. There was no statistically significant difference in terms of complications of pregnancy such as preterm delivery, pre-eclampsia or caesarean section (see Table 3) with no incidence of post partum hemorrhage during the period of study. Fetal outcome was also similar except for macrosomia which was seen more frequently among women with GDM although the difference was not significant.

In the neonatal period, significantly more offspring of GDM mothers developed jaundice compared to those of normal mothers (9.73 % versus 2.98 %, $p = 0.01$). Other neonatal complications were not statistically affected (Tab. 3).

Discussions

The prevalence of diabetes mellitus has increased globally with a higher incidence of GDM seen especially among Asian ethnics (7). In this study 18.34 % of primigravidae were noted to have GDM as compared to an overall incidence of 24.9 % irrespective of parity in a previous study at our centre (17). The previous study had also shown that maternal age of more than 35 years and family history of DM were significant risk factors for GDM. In the present study, GDM was detected even in a younger (27.9 ± 4.2 years) age group of primigravidae (Tab. 1), similar to an observation among the blacks who are the higher risk ethnic group for GDM in the United States (7). This finding was in contrast to our earlier study in all parities which indicated the older age (17) of more than 35 years noted to be one of the risks to GDM.

The present study indicated family history of DM as a significant risk factor for GDM as seen in the present study as well as documented in previous (14). This highlights the importance of inherited (genetic) and lifestyle elements. Although this may not be the principal determinant to gestational hyperglycaemia, in a previous study this factor has been identified to be a more relevant risk to GDM in primigravidae than in multiparous women. Therefore genetic factors in GDM and its association with type 2 diabetes mellitus in later life as pointed out by other studies (1,5,15) probably holds the explanation as to why even young primigravidae developed GDM that was seen in the present study.

Antenatal features of poorly controlled blood glucose such as uterus bigger than dates, proteinuria and glycosuria were not statistically significant in the GDM group despite a relatively high 2HPPBG result (8.86 ± 1.41 mmol/l). However, polyhydramnios which is a known complication of GDM (8) was a prominent feature in the current study although the actual number was very small (Tab. 2). Other maternal complications such as premature delivery, pre-eclampsia and caesarean section were not significantly increased in this study, most likely because of the relatively mild (FBG less than 5.30 mmol/l) form of GDM which antenatally had been treated. Nevertheless studies (13) had advocated those with mild hyperglycemia during pregnancy would have higher risk of hypertensive disorders, preterm labor, cesarean delivery followed by metabolic and cardiovascular risks at later years.

Potential GDM complications are growingly evidenced in fetuses with macrosomia complicating delivery and respiratory distress. The babies from GDM mothers have long term increased risk of glucose intolerance, obesity, metabolic syndrome and younger Type 2 DM (13). This theoretically explains why younger aged primigravidae were diagnosed with GDM in current study. Nevertheless, over a long term assessment, there was no evidence of lower cognitive ability in children of diabetic mothers (18) whom had been exposed to higher concentration of glucose and fatty acids while in utero that perhaps had enhanced brain development.

There was no major neonatal complication although they (GDM group) were noted to have a higher percentage of macrosomic babies compared to the non-GDM (statistically was not significant) group (Table 3). A previous study (12) reported more macrosomic babies born to multiparous women with GDM compared to primigravidae which most likely explained the findings in the present study which comprised totally primigravidae. During the neonatal period no statistically significant complication was seen except for a higher incidence of hyperbilirubinaemia in the GDM group.

Recent studies (4, 11) have shown that treatment of mild GDM does not significantly reduce stillbirth and other neonatal complications but it has been seen to reduce the risk of fetal overgrowth, shoulder dystocia, caesarean delivery and hypertensive disorders. Therefore these studies (4, 11) have recommended treating mild GDM, although the exact timing of screening and initiating treatment has not yet been agreed upon. The benefits of treating mild GDM had been highlighted (10) after two recently conducted large-scale randomized trials. Perhaps this also could have been applied to our multiethnic population with mild GDM among primigravidae.

In conclusion, GDM in primigravidae was detected at a relatively young age with significantly more prevalent among those with maternal family history of DM, and maternal weight exceeding 80 Kg. Polyhydramnios and neonatal hyperbilirubinaemia were seen significantly more frequent in this group. Treating a mild degree of disease had led to no significant complications. Nevertheless for our centre, whether treating an already mild disease would not impose other major burden (ie including cost effectiveness), needs further evaluation.

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Conflict of interest

The authors have no conflict of interest in conducting this study.

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Corresponding author:

Dr M I Nor Azlin, Department of Obstetrics & Gynaecology, Faculty of Medicine, University Kebangsaan Malaysia, Jalan Yaacob Latiff, 56000 Cheras, Kuala Lumpur, Malaysia; e-mail: azlinm@ppukm.ukm.my