Prevalence of glucose intolerance, and associated antenatal and historical risk factors among Malaysian women with a history of gestational diabetes mellitus

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INTRODUCTION Women with previous gestational diabetes mellitus (PGDM) are at increased risk of future glucose intolerance. This study aimed to determine the prevalence of prediabetes and type 2 diabetes mellitus (T2DM), and the associated antenatal and historical risk factors among women with PGDM.
METHODS This was a cross-sectional study conducted at University Malaya Medical Centre, Kuala Lumpur, Malaysia. A 75-g 2-hour oral glucose tolerance test was performed in a cohort of multiethnic women with PGDM. Body mass index, waist and hip circumferences, fasting lipid profile and blood pressure were obtained. Data pertaining to the index gestational diabetes mellitus (GDM) were obtained from medical records and interviews.
RESULTS 448 women were enrolled in the study. The prevalence of prediabetes and T2DM was 26.2% and 35.5%, respectively. On multinomial logistic regression analysis, fasting plasma glucose at diagnosis of index GDM and duration lapse after index GDM were shown to be significantly higher in women with isolated impaired fasting glucose (IFG), combined IFG/impaired glucose tolerance and T2DM, as compared to women with normal glucose tolerance (p < 0.05). 2-hour plasma glucose at diagnosis of index GDM was significantly higher only in women who progressed to T2DM when compared to those that remained normal glucose tolerant (p < 0.05).
CONCLUSION In this study, duration lapse after index GDM, fasting plasma glucose and 2-hour plasma glucose at diagnosis of index GDM were important risk factors for early identification of women at high risk for future glucose intolerance. These may be useful for developing potential preventive strategies.

INTRODUCTION

Women with a history of previous gestational diabetes mellitus (PGDM) are at increased risk of future glucose intolerance (impaired fasting glucose [IFG], impaired glucose tolerance [IGT] and type 2 diabetes mellitus [T2DM]).[1-3] These women have been reported to have a seven-fold increased risk of developing T2DM when compared to women without PGDM.[4] A meta-analysis that examined women who had PGDM from six weeks to 28 years postpartum showed that the cumulative incidence of developing T2DM after gestational diabetes mellitus (GDM) ranged from 2.6% to > 70%, depending on ethnicity and the diagnostic criteria used. The cumulative incidence increased markedly in the first five years after delivery and appeared to plateau after ten years.[5]

In Asian countries, prevalence data on glucose intolerance after GDM is scarce. In Korea, 11.5% of women with PGDM were found to have T2DM based on fasting plasma glucose (FPG) within six years of their index pregnancy with GDM.[6] In Trinidad, West Indies, the cumulative incidence of glucose intolerance was reported to be 32% among women with PGDM within 3.5–6.5 years postpartum.[7] Meanwhile in Beijing, China, the cumulative

incidence among women with PGDM within 5–10 years postpartum was 33.3%.[8] In Malaysia, there is a lack of data regarding the prevalence of glucose intolerance in women after GDM.

Studies have shown that risk factors commonly associated with T2DM, such as family history of T2DM[9] and obesity,[2] were found to be associated with an increased risk of developing postpartum glucose intolerance. Additionally, antenatal and historical characteristics such as gestational age at diagnosis of GDM,[10] requirement of insulin treatment during the index GDM pregnancy[11] and delivery of an infant with macrosomia[12] were also associated with an increased risk of developing postpartum glucose intolerance.

Recent well-designed randomised controlled trials have demonstrated that the onset of T2DM can be delayed among high-risk groups such as women with PGDM by means of lifestyle changes or the use of drugs.[13-16] Therefore, understanding and identifying the characteristics of women with PGDM who are at high risk of progressing to T2DM will assist in the risk stratification of the highest risk individuals for preventive strategies and

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programmes. In 2009, the prevalence of GDM at University Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia, was reported to be 12.3%.[17] However, data on the prevalence of glucose intolerance after an index pregnancy with GDM is lacking. The aim of this study was to determine the prevalence of prediabetes (isolated IGT, isolated IFG and combined IGT/IFG) and T2DM, as well as the associated antenatal and historical risk factors among women with PGDM being treated at UMMC.

METHODS

This was a cross-sectional study conducted at UMMC, Kuala Lumpur, Malaysia. Women with PGDM between 20–50 years of age were recruited using a systematic random sampling method from the hospital's database of women with GDM. The diagnosis of GDM was made based on the 1985 criteria of the World Health Organization (WHO).[18] The duration from the index pregnancy with GDM ranged from three months to 15 years postpartum. Women currently pregnant were excluded from the study. Ethical approval of the study was provided by the ethics committee at UMMC (ethics committee/IRB ref no. 375.13). Informed consent was obtained from all the participants prior to inclusion in the study.

The sample size required was calculated based on the following formula suggested by Naing et al in 2006:[19] $n = (Z^2 \times p[1-p])/d^2$. The prevalence data of T2DM and IGT for Malaysians was sourced from the National Health and Morbidity Survey (NHMS) II,[20] where 'n' was the required sample size, 'Z' was the Z-statistic for 95% confidence level (standard value = 1.96), 'p' was the estimated prevalence of diabetes mellitus (12.6%), and 'd' was the precision or margin of error at 5% (standard value = 0.05). Therefore, the formula used for this study was $n = (1.96^2 \times [0.126 \times 0.874])/0.05^2$, and the sample size needed was 156.

Participants were asked to fast overnight for at least 8–12 hours before the study visit. On the visit day, fasting venous plasma was obtained for the measurement of glucose, lipid and lipoprotein profiles, including serum total cholesterol, triglycerides (TGs), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol. A standard 75-g 2-hour oral glucose tolerance test (75-g 2-hour OGTT) was performed. After the fasting blood specimen was obtained, each participant ingested 75 g of anhydrous glucose dissolved in 250–300 mL of water over five minutes. Venous blood was drawn for the 2-hour plasma glucose (2-hour PG) measurement. PG was assayed by the glucose oxidase method using the Beckman glucose analyzer (Beckman Instruments, Fullerton, CA, USA). Analysis of lipid and lipoprotein profiles was done using the Dade Behring Dimension RxL Chemistry autoanalyser (Dade Behring, West Sacramento, CA, USA).

Results of the 75-g 2-hour OGTT were evaluated according to the 2002 WHO criteria for T2DM (FPG ≥ 7.0 mmol/L and/or 2-hour PG ≥ 11.1 mmol/L), isolated IGT (FPG < 5.6 mmol/L and 2-hour PG ≥ 7.8 mmol/L to < 11.1 mmol/L),[18] and the 2006 American Diabetes Association criteria for isolated IFG (FPG ≥ 5.6 mmol/L to < 7.0 mmol/L).[21] Combined IGT/IFG was defined as FPG ≥ 5.6 mmol/L to < 7.0 mmol/L and 2-hour PG ≥ 7.8 mmol/L to < 11.1 mmol/L.

The protocol used in this study for anthropometric measurements was based on the International Society for the Advancement of Kinanthropometry method.[22] Participants wore light clothing without shoes to facilitate the anthropometric measurements. Each measurement was taken twice and the mean of these measurements was calculated. Height was measured to the nearest 0.1 cm using a stadiometer (SECA Health o meter®; Continental Scale Corporation, Bridgeview, IL, USA). Weight was measured to the nearest 0.1 kg using a calibrated mechanical beam balance (SECA Health o meter®; Continental Scale Corporation, Bridgeview, IL, USA). Body mass index (BMI) was calculated as weight/height² (kg/m²).

Waist circumference (WC) and hip circumference (HC) were measured using a non-extendable measuring tape to the nearest 0.1 cm. WC measurement was made at the midpoint between the lower border of the ribs and the iliac crest on a horizontal plane. The measurement was taken at the end of normal expiration with arms relaxed by the side. HC measurement was made at the level of the greatest protuberance of the buttocks that corresponded anteriorly with the level of the pubic symphysis. Participants were asked to stand with feet together and without tensing the gluteal muscles while measurements were being taken.

Demographic and socioeconomic data were obtained. The following data pertaining to the index GDM pregnancy (first GDM pregnancy) were obtained from hospital medical records and by interviewing the participants: (a) presence or absence of family history of T2DM in a first-degree relative; (b) parity and gravidity; (c) frequency of macrosomia; (d) infant's birth weight during the index GDM pregnancy; (e) frequency of pregnancy with GDM; (f) duration lapse after the index GDM pregnancy; (g) OGTT results obtained during the index GDM pregnancy; (h) body weight and blood pressure at diagnosis of index GDM; (i) treatment for GDM during index GDM pregnancy; and (j) age at the index GDM pregnancy.

Statistical analysis was done using the Statistical Package for the Social Sciences for Windows version 18 (SPSS Inc, Chicago, IL, USA). Values were presented as mean ± standard deviation or number of participants (n). The sample data were tested for normal distribution by using the Kolmogorov-Smirnov test. To compare continuous variables among the groups, one-way analysis of variance was used (F test) and the post-hoc test performed using Bonferroni method. Categorical variables were compared for significance using the chi-square and Fisher's exact tests. If the distribution of data was not normal, it was transformed to the natural logarithm scale to improve the originally skewed distribution. Multinominal logistic regression analysis was used to determine the independent risk factors

Table I. Demographic and anthropometric characteristics of women (n = 342) with previous gestational diabetes mellitus, classified into glucose tolerance categories.

Characteristic	Mean ± SD				
	NGT (n = 172)	Isolated IGT (n = 42)	Isolated IFG (n = 46)	Combined IGT/IFG (n = 29)	T2DM (n = 53)
Age (yrs)	37.6 ± 5.3	37.7 ± 5.0	38.9 ± 5.6	39.7 ± 6.8	39.4 ± 4.5
Weight (kg)	61.6 ± 11.7[a]	63.5 ± 11.7[c]	63.4 ± 11.1[d]	66.5 ± 11.9	73.3 ± 12.5[a,c,d]
Height (m)	1.55 ± 0.06	1.55 ± 0.06	1.55 ± 0.06	1.53 ± 0.07	1.56 ± 0.05
BMI (kg/m^2)	25.69 ± 4.85[a,b]	26.59 ± 4.84[c]	26.22 ± 4.33[d]	28.53 ± 5.07[b]	30.26 ± 4.62[a,c,d]
Waist circumference (cm)	78.7 ± 9.6[a,b]	81.6 ± 10.3[c]	79.9 ± 9.7[d]	85.9 ± 11.7[b]	89.5 ± 10.5[a,c,d]
Hip (cm)	98.7 ± 9.4[a,b]	99.2 ± 8.8[c]	99.4 ± 8.3[d]	105.3 ± 12[b]	106.3 ± 10.5[a,c,d]
Waist-to-hip ratio*	0.80 ± 0.06[a]	0.82 ± 0.05	0.80 ± 0.06[d]	0.82 ± 0.06	0.84 ± 0.06[a,d]
Family history of DM (no. [%])	102 (59.3)	27 (64.3)	26 (56.5)	16 (55.2)	37 (69.8)

*Value was transformed to logarithm scale for analysis. One-way analysis of variance (ANOVA) was used for the comparison of continuous variables while the chi-square and Fisher's exact tests were used to compare categorical variables.
[a]NGT vs. T2DM (p < 0.05). [b]NGT vs. combined IGT/IFG (p < 0.05). [c]Isolated IGT vs. T2DM (p < 0.05). [d]Isolated IFG vs. T2DM (p < 0.05).
NGT: normal glucose tolerance; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; SD: standard deviation; T2DM: type 2 diabetes mellitus; BMI: body mass index
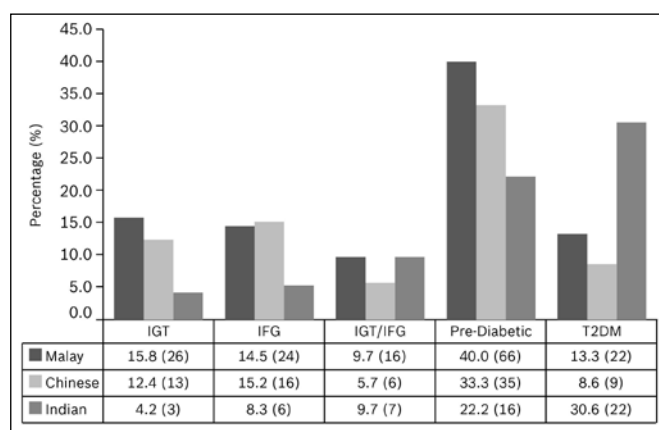

Fig. 1 Prevalence of isolated impaired glucose tolerance (IGT), isolated impaired fasting glucose (IFG), combined IGT/IFG, prediabetes and type 2 diabetes mellitus (T2DM) in women with previous gestational diabetes mellitus according to ethnicity (n = 342; p = 0.02; chi-square and Fisher's exact tests).

of T2DM or prediabetes. A p-value < 0.05 was considered statistically significant.

RESULTS

From a total of 592 potential participants who were selected using systematic sampling from the hospital's database of women with GDM, 448 women responded. The remaining participants were excluded from the study for a variety of reasons – 106 women declined to participate, 22 were not contactable due to a change in address, 14 were pregnant again at the time of the study, one woman died and one woman had a speech problem. 106 participants were excluded from the postpartum OGTT assessments because they had already progressed to T2DM. 342 participants were finally selected for enrolment and all women gave informed consent for OGTT assessments.

The prevalence of postpartum glucose intolerance was 61.7% in women with PGDM in (isolated IGT, 9.4%; isolated IFG, 10.3%; combined IGT/IFG, 6.5%; T2DM, 35.5%). Among the 35.5% of women with T2DM, 23.7% were known patients and 11.8% were newly diagnosed. The mean age of participants

was 38.2 ± 5.4 years. A majority of the participants were Malay (Malay 48.2%, Chinese 30.7%, Indian 21.1%), and significant association was found between the occurrence of glucose intolerance and ethnicity (p < 0.05). The highest prevalence of T2DM among the various ethnic groups was seen among Indian women (Indian 30.6%, Malay 13.3%, Chinese 8.6%), and the prevalence of prediabetes was highest among Malay women (Malay 40%, Chinese 33.3%, Indian 22.2%) (Fig. 1).

Table I shows the demographic and anthropometric characteristics among the different categories of glucose tolerance/T2DM in terms of normal glucose tolerance (NGT), isolated IGT, isolated IFG, combined IGT/IFG and T2DM. There was no significant difference in the mean age among the various groups (p > 0.05) although an increasing trend was noted across the groups from NGT to T2DM. Mean weight, BMI, WC and waist-to-hip ratio were significantly higher in participants with T2DM than NGT (p < 0.05). However, mean BMI and WC were significantly higher in participants with combined IGT/IFG than participants with NGT (p < 0.05). In addition, participants with T2DM were shown to have significantly higher mean weight, BMI and WC than participants with isolated IGT and isolated IFG (p < 0.05).

Mean TG was significantly higher in participants with combined IGT/IFG (1.61 ± 0.88 mmol/L) and in those with T2DM (1.58 ± 0.83 mmol/L) when compared to those with isolated IGT (1.13 ± 0.53 mmol/L) and NGT (1.18 ± 0.64 mmol/L) (p < 0.05). Participants with T2DM had significantly lower mean HDL cholesterol (1.22 ± 0.26 mmol/L) as compared to those with NGT (1.45 ± 0.54 mmol/L) (p < 0.05). Mean LDL cholesterol was significantly higher in participants with isolated IFG (3.40 ± 0.75 mmol/L), combined IGT/IFG (3.49 ± 0.85 mmol/L) and T2DM (3.45 ± 0.87 mmol/L) as compared to participants who had NGT (3.34 ± 0.95 mmol/L) (p < 0.05). No significant difference was found in the mean total cholesterol levels among the various groups (p > 0.05; Table II). Both systolic and diastolic blood pressures progressively increased across the groups from NGT

Table II. Biochemical characteristics of women with previous gestational diabetes mellitus (n = 342), classified into glucose tolerance categories.

Characteristic	Mean ± SD				
	NGT (n = 172)	Isolated IGT (n = 42)	Isolated IFG (n = 46)	Combined IGT/IFG (n = 29)	T2DM (n = 53)
Fasting plasma glucose* (mmol/L)	4.91 ± 0.40[a,b,c]	4.99 ± 0.41[e,f,g]	5.97 ± 0.36[a,e,h]	6.05 ± 0.25[b,f,j]	7.66 ± 1.85[c,g,h,j]
75-g 2-hour plasma glucose* (mmol/L)	6.01 ± 1.03[b,c,d]	8.75 ± 0.82[d,e,g]	6.44 ± 0.93[e,i]	9.21 ± 0.93[b,i,j]	13.90 ± 3.12[c,g,j]
Total cholesterol (mmol/L)	5.27 ± 1.09	4.98 ± 0.92	5.25 ± 0.75	5.66 ± 1.01	5.39 ± 1.00
Triglycerides* (mmol/L)	1.18 ± 0.64[b,c]	1.13 ± 0.53[f,g]	1.21 ± 0.49	1.61 ± 0.88[b,f]	1.58 ± 0.83[c,g]
HDL cholesterol (mmol/L)	1.45 ± 0.54[c]	1.35 ± 0.26	1.30 ± 0.30	1.39 ± 0.33	1.22 ± 0.26[c]
LDL cholesterol (mmol/L)	3.34 ± 0.95[a,b,c]	3.11 ± 0.81	3.40 ± 0.75[a]	3.49 ± 0.85[b]	3.45 ± 0.87[c]
Systolic BP (mmHg)	111 ± 14[a,b,c]	117 ± 16[g]	119 ± 21[a,h]	122 ± 19[b]	128 ± 13[c]
Diastolic BP (mmHg)	68 ± 11[c]	71 ± 9[g]	72 ± 12	73 ± 15	78 ± 9[c,g]

*Value was transformed to logarithm scale for analysis. One-way analysis of variance (ANOVA) was used for the comparison of continuous variables while the chi-square and Fisher's exact tests were used to compare categorical variables.
[a]NGT vs. isolated IFG ($p < 0.05$). [b]NGT vs. combined IGT/IFG ($p < 0.05$). [c]NGT vs. T2DM ($p < 0.05$). [d]NGT vs. isolated IGT ($p < 0.05$). [e]IGT vs. isolated IFG ($p < 0.05$). [f]IGT vs. combined IFG/IGT ($p < 0.05$). [g]Isolated IGT vs. T2DM ($p < 0.05$). [h]Isolated IFG vs. T2DM ($p < 0.05$). [i]Isolated IFG vs. combined IFG/IGT ($p < 0.05$). [j]Combined IGT/IFG vs. T2DM ($p < 0.05$).
NGT: normal glucose tolerance; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; SD: standard deviation; T2DM: type 2 diabetes mellitus; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BP: blood pressure

to T2DM. Participants with NGT had significantly lower systolic blood pressure (111 ± 14 mmHg) than participants with T2DM (128 ± 13 mmHg), combined IGT/IFG (122 ± 19 mmHg) and isolated IFG (119 ± 21 mmHg), respectively ($p < 0.05$). For diastolic blood pressure, a significant difference was found between participants with T2DM and those with NGT and isolated IGT ($p < 0.05$; Table II).

The analysis of historical and antenatal characteristics of the index pregnancy with GDM showed that participants with T2DM had significantly higher gravidity, parity, duration lapse after index GDM pregnancy, BMI, blood pressure at diagnosis of index GDM and need for insulin for glycaemic control during the index GDM pregnancy than women with NGT ($p < 0.05$). There was no significant difference between the groups with regard to maternal age at diagnosis of index GDM, frequency of GDM, infant birth weight and gestational age at diagnosis of index GDM. During the index pregnancy with GDM, FPG and 2-hour PG showed an increasing trend across groups from NGT to T2DM. Participants who progressed to T2DM had significantly higher FPG (5.36 ± 1.22 mmol/L) than those with isolated IGT (4.52 ± 0.61 mmol/L) and NGT (4.60 ± 0.64 mmol/L) ($p < 0.05$). Similarly, women with T2DM had significantly higher 2-hour PG (10.10 ± 2.24 mmol/L) than those with isolated IGT (8.76 ± 1.10 mmol/L), isolated IFG (9.15 ± 1.10 mmol/L) and NGT (8.89 ± 0.97 mmol/L) ($p < 0.05$; Table III).

There was a significant relationship among the categories of postpartum glucose intolerance and the requirement for insulin treatment during the index GDM pregnancy ($p < 0.05$). The percentage of participants with T2DM requiring insulin treatment during their index GDM pregnancy (24.5%) was higher than those with NGT (6.4%), isolated IGT (0%), isolated IFG (6.5%) and combined IGT/IFG (3.4%) (Table III). The duration lapse after the index GDM pregnancy was divided into three categories, and the analysis showed that the prevalence of
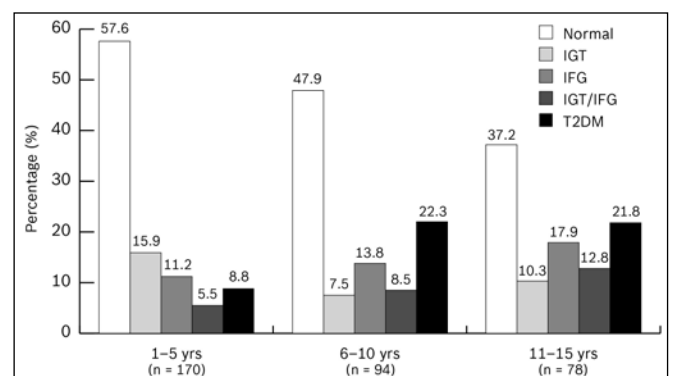

Fig. 2 Prevalence of normal glucose tolerance, isolated impaired glucose tolerance (IGT), isolated impaired fasting glucose (IFG), combined IGT/IFG and type 2 diabetes mellitus (T2DM) in women with previous gestational diabetes mellitus (GDM) according to duration lapse after index pregnancy with GDM (n = 342, p = 0.004; chi-square and Fisher's exact tests).

T2DM increased between women with a duration of 1–5 years (8.8%) and women with a duration of 6–10 years (22.3%), but appeared to plateau among those with a duration of 11–15 years (21.8%) (Fig. 2).

Multinominal logistic regression analysis was used to determine the independent historical and antenatal risk factors that were associated with postpartum glucose intolerance (Table IV). Current BMI, WC, age and ethnicity were adjusted for this analysis. FPG at diagnosis of index GDM and duration lapse after the index GDM pregnancy were shown to be significantly higher in participants who had T2DM, isolated IFG and combined IGT/IFG than women with NGT ($p < 0.05$). 2-hour PG at diagnosis of index GDM was significantly higher only in women with T2DM when compared to women with NGT ($p < 0.05$). There was no significant difference between women with isolated IGT and NGT with regard to these three parameters. There was also no significant association found for the other antenatal and historical characteristics analysed (such as maternal age at diagnosis of

Table III. Historical and antenatal characteristics during the index pregnancy with gestational diabetes mellitus (n = 342), classified into glucose tolerance categories.

Characteristic	Mean ± SD				
	NGT (n = 172)	Isolated IGT (n = 42)	Isolated IFG (n = 46)	Combined IGT/IFG (n = 29)	T2DM (n = 53)
Age (yrs)	32.0 ± 5.1	33.2 ± 4.8	32.1 ± 5.0	31.7 ± 5.2	32.2 ± 4.8
Gravidity*	4 ± 2[a]	4 ± 2	4 ± 2	4 ± 2	4 ± 2[a]
Parity*	3 ± 1[a]	3 ± 2	3 ± 1	3 ± 2	3 ± 2[a]
Frequency of GDM*	1 ± 1	1 ± 1	1 ± 1	1 ± 1	1 ± 1
Duration lapse after index GDM* (mths)	70 ± 48[a]	67 ± 48	91 ± 53	95 ± 47	97 ± 49[a]
At the time of diagnosis of GDM					
Fasting plasma glucose* (mmol/L)	4.60 ± 0.64[a,b]	4.52 ± 0.61[c,d]	5.00 ± 1.18	5.23 ± 1.11[b,c]	5.36 ± 1.22[a,d]
75-g 2-hour plasma glucose* (mmol/L)	8.89 ± 0.97[a]	8.76 ± 1.10[d]	9.15 ± 1.10[e]	9.36 ± 2.13	10.10 ± 2.24[a,d,e]
Weight (kg)	65.0 ± 10.3[a]	67.5 ± 11.1	64.4 ± 11.5[e]	69.8 ± 14.3	72.3 ± 12.1[a,e]
BMI (kg/m^2)	27.16 ± 4.3[a]	28.16 ± 4.63	26.60 ± 4.31[e]	29.93 ± 6.63	29.88 ± 4.68[a,e]
Systolic blood pressure* (mmHg)	111 ± 12[a]	112 ± 13	116 ± 13	112 ± 17	118 ± 15[a]
Diastolic blood pressure* (mmHg)	70 ± 9[a]	71 ± 10	72 ± 9	72 ± 14	74 ± 9[a]
Infant's birth weight (kg)	3.1 ± 0.4	3.3 ± 0.5	3.2 ± 0.6	3.3 ± 0.5	3.3 ± 0.4
Gestational age at diagnosis of index pregnancy with GDM* (wks)	29 ± 6	28 ± 6	28 ± 6	28 ± 7	28 ± 7
Need for insulin treatment† (no. [%])	11 (6.4)	0 (0)	3 (6.5)	1 (3.4)	13 (24.5)

*Value was transformed to logarithm scale for analysis. One-way analysis of variance was used for the comparison of continuous variables while the chi-square and Fisher's exact tests were used to compare categorical variables.
†p < 0.05 was significant for categorical variables.
[a]NGT vs. T2DM (p < 0.05). [b]NGT vs. combined IGT/IFG (p < 0.05). [c]IGT vs. combined IFG/IGT (p < 0.05). [d]Isolated IGT vs. T2DM (p < 0.05). [e]Isolated IFG vs. T2DM (p < 0.05).
GDM: gestational diabetes mellitus; BMI: body mass index; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; NGT: normal glucose tolerance; SD: standard deviation; T2DM: type 2 diabetes mellitus

Table IV. Multinominal logistic regression to compare the independent historical and antenatal risk factors of the various glucose tolerance categories with NGT.*

Historical and antenatal risk factor	Isolated IGT		Isolated IFG		Combined IGT/IFG		T2DM	
	B	p-value	B	p-value	B	p-value	B	p-value
Fasting plasma glucose at diagnosis of GDM	−0.048	0.868	0.695	0.001†	0.734	0.007†	0.689	0.007†
75-g 2-hour plasma glucose at diagnosis of GDM	−0.111	0.562	0.205	0.167	0.328	0.072	0.515	0.002†
Duration lapse after index GDM	0.000	0.919	0.009	0.015†	0.011	0.025†	0.012	0.004†

*NGT was the reference group. †p < 0.05 was statistically significant.
GDM: gestational diabetes mellitus; IFG: impaired fasting glucose; IGT: isolated impaired glucose tolerance; NGT: normal glucose tolerance; T2DM: type 2 diabetes mellitus

index GDM, parity, gravidity, frequency of GDM, weight at diagnosis of index GDM, BMI at diagnosis of index GDM, blood pressure at diagnosis of index GDM, infant's birth weight during the index GDM pregnancy, gestational age at diagnosis of index GDM and requirement of insulin treatment during the index GDM pregnancy) among the various categories of glucose tolerance/T2DM (p < 0.05).

DISCUSSION

Women with PGDM are at increased risk of developing postpartum glucose intolerance. The prevalence of T2DM in our study was 35.5%, which was higher than the prevalence reported by the NHMS III study among the general female population in Malaysia (11.3%).[23] However, it is possible that the reason why the findings of these two studies are not comparable to each other is because the age groups of the women in the two cohorts are not the same.

Our study showed that the prevalence of postpartum glucose intolerance was different among the various ethnic groups (p < 0.05). Indian participants had the highest prevalence of T2DM (30.6%) compared to Malay (13.3%) and Chinese (8.6%) women. This was consistent with the findings of previous national health surveys – NHMS II in 1996 and NHMS III in 2006 – where Indian participants were noted to have the highest prevalence of T2DM (NHMS II 11.5%; NHMS III 19.9%).[20,23] In contrast, Indian participants had the lowest prevalence of prediabetes (22.2%) in our study when compared to Malay (40%) and Chinese (33.3%) women. When the interethnic anthropometric characteristics were evaluated among prediabetic women (isolated IGT, isolated IFG and combined IGT/IFG) with PGDM, Indian and Malay women were found to have comparable BMI and WC, although the measurements in these two ethnic groups were higher than that in Chinese prediabetic women (p < 0.05; Table V). Based on anthropometric surrogate markers (BMI and WC) of insulin

Table V. Interethnic anthropometric characteristics among prediabetic women with previous gestational diabetes mellitus (n = 342).

Characteristic	Mean ± standard deviation			Total (n = 117)
	Malay (n = 65)	Chinese (n = 35)	Indian (n = 16)	
Body mass index* (kg/m²)	27.86 ± 4.73[a]	24.08 ± 3.32[a,b]	29.26 ± 4.90[b]	26.91 ± 4.75
Waist circumference* (cm)	83.5 ± 11.2[a]	77.5 ± 8.4[a,b]	85.9 ± 9.2[b]	82.0 ± 10.6
Waist-to-hip ratio*	0.82 ± 0.06	0.80 ± 0.05	0.81 ± 0.07	0.81 ± 0.06

Note: prediabetic patients were those with isolated impaired glucose tolerance (IGT), isolated impaired fasting glucose (IFG) and combined IGT/IFG. [a]Malay vs. Chinese (p < 0.05). [b]Chinese vs. Indian (p < 0.05). *One-way analysis of variance was used for the comparison of continuous variables.

resistance, Chinese prediabetic women had a significantly higher prevalence than Indian women with a lower BMI and WC. Even though our finding appears to be consistent with that of Khoo et al,[24] this result probably deserves further investigation in larger PGDM populations. It is also possible that the lowest prevalence of prediabetes observed among Indian women in our study was most likely due to insufficient power.

Elevated FPG during index pregnancy with GDM was reported to be a predictor of postpartum glucose intolerance in some studies.[5,25] Our results were similar to these studies, as FPG was found to be an independent risk factor for the development of T2DM, combined IGT/IFG and isolated IFG (p < 0.05), but not for isolated IGT (p > 0.05), during the index GDM pregnancy. 2-hour PG was also found to be significantly higher in women with T2DM when compared to those with NGT (p < 0.05). This finding is consistent with earlier studies that have reported that elevated 1-hour or 2-hour PG levels after OGTT were a risk factor for either early[11,26,27] or long-term development of T2DM.[28]

The duration lapse after an index GDM pregnancy has also been shown to be an independent predictor of postpartum glucose intolerance.[11,29] In our study, the duration lapse after index GDM pregnancy was significantly higher in women with T2DM, combined IFG/IGT and isolated IFG than in those with NGT (p < 0.05). In addition, we found that the prevalence of T2DM increased in women with durations 1–5 years (8.8%) and 6–10 years (22.3%), but appeared to plateau in those with duration 11–15 years (21.8%). This finding was also consistent with a study by Kim et al.[5]

The anthropometric and biochemical characteristics of participants with isolated IGT were not significantly different than those with NGT (p > 0.05), except for 2-hour PG levels. Participants with isolated IFG had significantly higher mean LDL cholesterol and systolic blood pressure, as compared to those with NGT (p < 0.05) while participants with combined IGT/IFG had significantly higher triglycerides, LDL cholesterol level and systolic blood pressure compared to those with NGT and isolated IGT. This is consistent with other studies where isolated IFG was shown to have a stronger association with cardiometabolic risk factors in women with PGDM than isolated IGT.[30] Furthermore, combined IGT/IFG was shown to be associated with higher diabetic and cardiometabolic risk compared to isolated IGT and isolated IFG.[31-33] For this reason, regular follow-up with OGTT is essential to identify women with PGDM who may be prediabetic.[34] A meta-analysis by Gerstein et al reported that individuals with prediabetes were approximately 5–10 times more likely to

develop diabetes mellitus within one year than people without IFG or IGT.[35]

This is the first study from Malaysia that examines the prevalence of postpartum glucose intolerance in women with PGDM. However, the participants in the present study only represented an urban cohort from one institution in Malaysia. Furthermore, the effect of ethnicity could not be established beyond doubt due to the small sample size in our study. A larger multiethnic cohort study, involving both urban and rural populations is therefore warranted. Such studies would be vital for healthcare professionals in Malaysia to enable them to plan appropriate interventional programmes for this high-risk group of patients, in order to prevent or delay the occurrence of postpartum glucose intolerance/T2DM. In conclusion, women with PGDM are at increased risk of future glucose intolerance. The duration lapse after index GDM pregnancy and FPG at diagnosis of index GDM were found to be important variables that could be used for potential preventive strategies aimed at early identification of high-risk women.

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