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Original Research

High prevalence of diabetes and abnormal glucose tolerance in Thai women with previous gestational diabetes mellitus

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ABSTRACT

Aim: To determine the prevalence of and risk factors for abnormal glucose tolerance (AGT) in previous gestational diabetes mellitus (pGDM) women.
Methods: 100 pGDM women randomly selected from the database of the Department of Obstetrics/Gynecology. 75 g-OGTT were performed in subjects without known diabetes. AGT was diagnosed using the American Diabetes Association criteria.
Results: The mean age, pre-gestational BMI, and time since delivery were 38 ± 5 years, 24.5 ± 5.7 kg/m^2, and 46 ± 26 months. Overall, 81% of the subjects had AGT, including IGT (38%), IGT + IFG (5%), T2DM (38%). Plasma glucose (PG) at 1 h after a 50 g-glucose challenge test (GCT), PG at 1 h after 100 g-OGTT, HbA_{1c}, and HOMA-IR were significantly greater in women with AGT than normal glucose tolerance (NGT) women. The proportion of women with ≥3 abnormal PG values during 100 g-OGTT was greater in AGT than NGT group (50.7% vs. 15.8%). Multivariate analysis showed that PG ≥ 150 mg/dl at 1 h after a 50 g-GCT and ≥3 abnormal PG values in 100 g-OGTTs were risk factors for developing AGT.
Conclusions: Eighty-one percent of pGDM women developed AGT within 4 years after delivery. Risk factors for AGT were PG ≥ 150 mg/dl at 1 h after a 50 g-GCT and ≥3 abnormal PG values in a 100 g-OGTT.

Introduction

Type 2 diabetes mellitus (T2DM) is a common disease worldwide. The International Diabetes Federation (IDF) estimated that, in the next 20 years, the number of people with diabetes will increase from 366 million in 2011 to 552 million in 2030 [1]. According to the 4th Thai National Health survey, 7.5% of people aged >20 years old had type 2 diabetes and that the prevalence of diabetes was greater in women than in men (8.3% vs 6.6%) [2]. People with diabetes have higher morbidity and mortality and lower quality of life compared with people without diabetes. Thus, the identification of subjects at high risk of developing T2DM or abnormal glucose tolerance (AGT) and the implementation of programs aimed to prevent T2DM may be cost-effective.

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that develops or is first detected during pregnancy. The reported prevalence of GDM in Thailand ranged from 2.1% to 7% [3–6]. It was reported that the history of GDM is a strong risk factor for the development of T2DM in women with a relative risk of 7.43 (95% confidence interval [CI] 4.79–11.51) [7]. Several studies [8–10] had demonstrated that fasting plasma glucose (PG), PG at 1 and 2 h after an oral glucose tolerance test (OGTT), pre-gestational and gestational body weight, age at pregnancy, and previous GDM (pGDM) were risk factors for the development of T2DM in women with pGDM. However, the prevalence of T2DM and risk factors for developing T2DM in Thai women with a history of GDM are unknown. The objective of this study was to examine the prevalence of AGT and T2DM in women with pGDM and to identify risk factors for the development of AGT in women with gestational diabetes.

Subjects and methods

Subjects

This was a cross-sectional study. Women with pGDM who were registered on the database at the Department of Obstetrics and Gynecology (Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand) between 2001 and 2011 were randomly

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recruited and invited to participate in the study. Women who had the following conditions were excluded: pre-gestational diabetes, taking medications that affect glucose metabolism, pregnancy at the time of recruitment, and unwilling to participate in the study. This study was approved by the Siriraj Institutional Review Board. All of the subjects gave written informed consent.

Study protocol

After an overnight fast (10–12 h), the women visited the Metabolic Unit of the Division of Endocrinology and Metabolism, Siriraj Hospital. A complete medical and gestational history taking, physical examination, laboratory tests, including fasting PG, fasting insulin, HbA_{1c}, and lipid profiles, were assessed in all of the women. A 75 g oral glucose tolerance test (OGTT) was done in subjects without known diabetes.

Calculations

Homeostasis model assessment (HOMA) of insulin secretion (HOMA-%B) and insulin resistance (HOMA-IR) were calculated using the HOMA calculator [11].

Laboratory analyses

Plasma glucose (PG) concentrations were measured using a hexokinase assay (Modular P800; Roche, Mannheim, Germany). Plasma insulin concentrations were measured using an electrochemiluminescence assay (Modular Elecsys 170; Roche).

Assessment of glucose metabolism

The definitions of glucose metabolism defined by American Diabetes Association were used in this study. In brief, the impaired fasting glucose (IFG) was defined as fasting PG levels between 100 and 125 mg/dL, impaired glucose tolerance (IGT) as 2 h PG after 75 g OGTT levels between 140 and 199 mg/dL and overt T2DM as fasting PG levels of 126 or more mg/dL, or 2 h PG after 75 g OGTT levels of 200 or more mg/dL. [12]. T2DM was also defined as the diagnosis of T2DM after delivery and treatment with hypoglycemic agents. AGT was defined as the presence of IFG, IGT, or T2DM.

Diagnosis of GDM

Subjects in this study were part of the long-term ongoing project of GDM study in Thai women by Luengmettakul et al. [13] therefore we used a two-step approach for the diagnosis of GDM, as recommended by the National Diabetes Data Group [14] in this study. In brief, pregnant woman with clinical risk factors underwent a 50 g glucose challenge test (GCT) at the first antenatal care visit. Clinical risk factors included family history of diabetes, age ≥30 years, obesity, prior unexplained fetal death, prior fetal macrosomia, prior malformed baby, and pGDM. If the PG at 1 h after the 50 g-GCT was ≥140 mg/dl, a 100 g-OGTT was performed 1 week later for diagnosis of GDM. Women were diagnosed with GDM if ≥2 PG values on the 100 g-OGTT exceeded the cutoff values which were 105, 190, 165 and 145 mg/dL at fasting, 1 h, 2 h, and 3 h respectively. If PG values were normal in this 100 g-OGTT, the 50 g-GCT and 100 g-OGTT were repeated at 24–28 and 32–34 weeks of gestation. The first recognized GDM-complicated pregnancy was used as the index pregnancy.

Statistical analyses

Statistical analyses were performed using SPSS version 17 for windows (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD or percentage as appropriate. Between-group comparisons were done using t tests, χ^2 tests, or Fisher's exact test, as appropriate. Multiple logistic regression analysis was performed. For all analyses, values of $P < 0.05$ were considered statistically significant.

Results

Characteristics of the subjects at the time of GDM diagnosis

One hundred women with pGDM were enrolled in this study. Table 1 shows the clinical characteristics of the subjects at the time of GDM diagnosis. The mean age of the subjects was 38 ± 5 years and pre-pregnancy body mass index (BMI) was 24.6 ± 5.7 kg/m^2. Ninety subjects were prescribed a diet to manage their GDM. The glycemic status was scheduled to be evaluated after birth in only 21% of subjects.

Glycemic status at the time of enrolment

The women were enrolled into this study 46 ± 28 months (range 6–120 months) after the index pregnancy. The clinical and laboratory characteristics are shown in Table 2. Among the 100 subjects, 81% of the women had AGT, including IGT (38%), IGT plus IFG (5%), and T2DM (38%).

Factors associated with the development of AGT

To identify the risk factors for developing AGT after GDM, the clinical and laboratory characteristics of pGDM women with normal glucose tolerance (NGT) and those with AGT were compared. As shown in Table 3. There was no significant difference in age,

Table 1
Clinical and laboratory characteristics of the women during the index pregnancy.

Characteristic	Value
N	100
Age (years)	38 ± 5
Age at the diagnosis of GDM (years)	34 ± 5
Gestational age at the diagnosis of GDM (weeks)	20 ± 10
Women diagnosed with GDM before 24 weeks of gestation (%)	51
Family history of DM (%)	51
BMI (kg/m^2)	
Before gestation	24.5 ± 5.7
At the diagnosis of GDM	27.0 ± 5.7
PG (mg/dl)	
1 h after the 50-g OGTT	180 ± 28
During the 100-g OGTT	
0 h	87 ± 23
1 h	202 ± 37
2 h	193 ± 29
3 h	161 ± 68
Women with ≥3 abnormal PG values during the 100-g OGTT (%)	44
Pregnancy outcomes (%)	
Spontaneous abortion at a gestational age of 14 weeks	1
Mode of delivery	
Normal delivery	33
Cesarean section	64
Vacuum extraction	2
Birth weight (%)	
≥4000 g	3
<2500 g	7

Data are presented as the mean ± standard deviation or percentage.
GDM: gestational diabetes mellitus; BMI: body mass index; PG: plasma glucose; OGTT: oral glucose tolerance test.

Table 2
Clinical and laboratory characteristics of the women at the time of enrollment.

Characteristic	Values
N	100
Time since the index pregnancy (months)	46 ± 26
BMI (kg/m^2)	25.7 ± 5.8
HbA_{1c} (%)	6.3 ± 1.5
HOMA-%B	105 ± 47
HOMA-IR (median [range])	1.2 (0.4–4.0)
Normal glucose tolerance (%)	19
Abnormal glucose tolerance (%)	81
IFG	0
IGT	38
IGT + IFG	5
T2DM	38

Data are presented as the mean ± standard deviation or percentage.
BMI: body mass index; HOMA-%B, homeostasis model assessment of β cell function; HOMA-IR: homeostasis model assessment of insulin resistance; IGT: impaired glucose tolerance; IFG: impaired fasting glucose; T2DM: type 2 diabetes mellitus.

Table 3
Comparisons between women with NGT or AGT.

	NGT	AGT	*P*-value
N (%)	19 (19)	81 (81)	
Age (years)	38 ± 4	38 ± 5	0.82
Age at the diagnosis of GDM (years)	34 ± 5	34 ± 4	0.75
Gestational age at the diagnosis of GDM (weeks)	22 ± 9	20 ± 10	0.44
Time since delivery (months)	45 ± 23	46 ± 29	0.81
Family history of DM (%)	32	56	0.06
BMI (kg/m^2)			
Before gestation	23.3 ± 6.1	24.9 ± 5.6	0.32
At the diagnosis of GDM	26.0 ± 6.6	27.3 ± 5.5	0.40
At enrolment into this study	25.7 ± 5.8	25.9 ± 5.2	0.89
Women diagnosed with GDM before 24 weeks of gestation (%)	42.1	53.8	0.361
PG (mg/dl)			
1 h after the 50 g-GCT	162 ± 18	186 ± 28	0.001
During the 100 g-OGTT			
0 h	84 ± 15	88 ± 25	0.435
1 h	180 ± 46	207 ± 32	0.024
2 h	186 ± 20	195 ± 31	0.263
3 h	153 ± 34	163 ± 75	0.55
Women with ≥3 abnormal PG values during the 100 g-OGTT (%)	15.8	50.7	0.006
HbA_{1c} (%)	5.5 ± 0.4	6.4 ± 1.6	0.00
HOMA-%B	107 ± 33	104 ± 50	0.78
HOMA-IR (median [range])	0.9 (0.5–2.1)	1.3 (0.4–4.0)	0.013

Data are presented as the mean ± standard deviation or percentage.
NGT: normal glucose tolerance; AGT: abnormal glucose tolerance; GDM: gestational diabetes mellitus; BMI: body mass index; GCT: glucose challenge test; OGTT: oral glucose tolerance test; HbA_{1c}: hemoglobin A_{1c}; HOMA-%B, homeostasis model assessment of β cell function; HOMA-IR: homeostasis model assessment of insulin resistance.

gestational age, time since delivery of the index pregnancy, and BMI between women with NGT and women with AGT. The prevalence of AGT tended to be greater in women with a family history of diabetes than in women without a family history of diabetes, although this difference did not reach statistical significance. HbA_{1c} and HOMA-IR were significantly greater in women with AGT than in women with NGT, whereas HOMA-%B was not significantly different between the two groups.

Based on the results of the OGTTs conducted for the diagnosis of GDM, we found that the PG concentrations at 1 h after the 50 g-GCT and at 1 h after the 100 g-OGTT were higher in women with AGT than in women with NGT. The proportion of women with ≥3 abnormal PG values following the 100 g-OGTT was greater in the AGT group than the NGT group (50.7% VS 15.8, p 0.006).

Multivariate logistic regression analyses showed that the PG ≥ 150 mg/dL at 1 h after 50 g-GCT and the presence of ≥3 abnormal PG values during 100 g-OGTT were the independent risk factors for developing AGT in women with pGDM (Table 4).

Discussion

To our knowledge, this was the first study to show a high prevalence of postpartum AGT in Thai women with pGDM. During 4 years after GDM, 38% of women in this cohort had IGT, 5% had IGT plus IFG, and 38% had overt T2DM. We also demonstrated that PG ≥ 150 mg/dl at 1 h after a 50 g-GCT and ≥3 abnormal PG values during a 100 g-OGTT were the risk factors for the development of AGT within approximately 4 years of a GDM pregnancy.

The prevalence of AGT in this study was quite high as compared with prior studies, in which T2DM developed in 2.6–70% of GDM subjects within 5–10 years, corresponding to a rate of about 16% per year [15–18]. There are several possible explanations for this difference. First, at our institute, we only screen for GDM in women with clinical risk factors for GDM [6]. Therefore, these women with GDM were at greater risk of developing T2DM later in life because of their established clinical risk. Second, nearly half of the women enrolled in this study were diagnosed with GDM in early pregnancy. Therefore, it is possible that many of these women might have undiagnosed AGT or T2DM before pregnancy. Third, the women were enrolled in this study approximately 4 years (mean 46 ± 26 months) after the index GDM pregnancy, whereas earlier studies had a longer interval between the index pregnancy and enrollment in the study. It was reported that the incidence of T2DM was greatest in the first 5 years after delivery [8]. Finally, we conducted 75 g-OGTTs for the diagnosis of diabetes, which can detect diabetes earlier than using fasting plasma glucose alone. These factors might contribute to the differences in the prevalence of T2DM in women with pGDM between our study and earlier studies.

This study showed that the prevalence of combined IFG and IGT was 8-fold less frequent than IGT or T2DM. Because the progressive nature of Type 2 diabetes which started from insulin resistance to impaired 1st phase insulin secretion to impaired late phase insulin resistance then progressed to type 2 diabetes. Thus, the timing of performed 75-g OGTT was an important factor to determine the prevalence of IFG, IGT, combined IFG-IGT or T2DM.

According to the 4th Thai National Health survey, the prevalence of T2DM was greater in women than in men (7.7% vs. 6.0%). The present data indicate that women with pGDM are at high risk of developing of T2DM later in life and are suitable for receiving a diabetes prevention program. A previous study [19] showed that the risk for developing T2DM was greater in women who were aged ≥35 years, had a family history of diabetes, or had a high BMI both before and after the index pregnancy. In the present study, we identified two novel risk factors for developing T2DM in Thai women with pGDM including the presence of PG ≥ 150 mg/dl at 1 h after a 50 g-GCT and the presence of ≥3 abnormal PG values during a 100 g-OGTT. By using these risk fac-

Table 4
Multivariate analysis of factors associated with the development of AGT in women with pGDM.

Factors	OR	95% CI
Age	1.00	0.86–1.16
Family history of diabetes	2.30	0.57–9.27
PG ≥ 150 mg/dl at 1 h after the 50 g-GTT	22.02	3.78–128.31
Absolute PG at 1-h after the 100 g-OGTT	1.00	0.98–1.16
≥3 abnormal PG values during the 100 g-OGTT	4.75	1.08–20.96

AGT: abnormal glucose tolerance; pGDM: previous gestational diabetes mellitus; OR: odds ratio; CI: confidence interval; PG: plasma glucose; GCT: glucose challenge test; OGTT: oral glucose tolerance test.

tors, we may be able to better identify women at risk of developing T2DM and increase the cost-effectiveness of diabetes prevention programs, especially in countries with limited resources. We also found that HOMA-IR was greater in women with AGT than in women with NGT. These findings are consistent with these of Ryan et al. [20] who reported that non-obese glucose-intolerant women with pGDM displayed insulin resistance, an underlying pathophysiologic feature of T2DM. Improving insulin resistance by weight reduction and exercise, as in diabetes prevention programs, may have valuable health benefits in these women.

The American College of Obstetricians and Gynecologists has established guidelines for the care of women following a GDM pregnancy, including OGTTs at 2 and 6 weeks following delivery, and every 1–3 years thereafter [19]. Despite this recommendation, only 21% of women were scheduled for postpartum diabetes screening in our study, similar to the rates reported in earlier studies [21,22]. There are several reasons for the lack of follow-up care in the postpartum period in women with GDM, including the lack of primary care surveillance in relatively young women, the mobile population, loss to follow-up after delivery, and the busy lifestyle of women caring for young infants. However, one of the most important reasons is the women's denial or underestimation of their risk of developing T2DM. Therefore, a strategy aimed at increasing awareness of the association between GDM and future risk of T2DM should improve adherence to postpartum diabetes surveillance program.

Conclusions

This study showed that a large proportion of women with pGDM developed AGT within approximately 4 years of the GDM pregnancy. Women with pGDM together with a PG $\geq$ 150 mg/dl at 1 h after a 50 g-GCT or $\geq$3 abnormal PG values during a 100 g-OGTT are candidates for intensive postpartum care to prevent the future development of T2DM.

Conflict of interest

The authors have no conflict of interest to declare.

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