## Risk factors for abnormal postpartum glycemic states in women diagnosed with gestational diabetes by the International Association of Diabetes and Pregnancy Study Groups criteria

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#### **Keywords**

Diabetes mellitus, Gestational diabetes mellitus, Postpartum

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#### ABSTRACT

**Aims/Introduction:** To evaluate the rate of postpartum glycemic screening tests (PGST) in women with gestational diabetes mellitus (GDM), and to investigate risk factors for abnormal PGST results.

**Materials and Methods:** We retrospectively analyzed the obstetric data of 1,648 women with GDM who gave birth after 28 completed weeks of gestation between 1 July 2011 and 31 December 2019 at Taipei Chang Gung Memorial Hospital, Taiwan. GDM was diagnosed by the International Association of Diabetes and Pregnancy Study Groups criteria. PGST was carried out at 6–12 weeks postpartum with a 75-g, 2-h oral glucose tolerance test, and the results were classified into normal, prediabetes and diabetes mellitus. Multiple logistic regression was used to assess the associations between various risk factors and abnormal PGST results.

**Results:** In total, 493 (29.9%) women underwent PGST and 162 (32.9%) had abnormal results, including 135 (27.4%) with prediabetes and 27 (5.5%) with diabetes mellitus. Significant risk factors for postpartum diabetes mellitus included insulin therapy during pregnancy (adjusted odds ratio [OR] 10.79, 95% confidence interval [CI] 4.07–28.58), birthweight >4,000 g (adjusted OR 10.22, 95% CI 1.74–59.89) and preterm birth <37 weeks' gestation (adjusted OR 3.33, 95% CI 1.09–10.22); whereas prepregnancy body mass index >24.9 kg/m<sup>2</sup> (adjusted OR 1.99, 95% CI 1.24–3.21) was the major risk factor for postpartum prediabetes.

**Conclusions:** Less than one-third of women with GDM underwent PGST, and nearly one-third of these women had abnormal results. Future efforts should focus on reducing the barriers to PGST in women with GDM.

#### INTRODUCTION

Based on the diagnostic criteria that are applied<sup>1,2</sup>, gestational diabetes mellitus (GDM) complicates 3–13% of pregnancies and is a major risk factor for maternal gestational hypertensive diseases, as well as neonatal complications, including hypo-glycemia, hyperbilirubinemia and respiratory distress syndrome<sup>3,4</sup>. Furthermore, women with GDM are more likely to develop type 2 diabetes mellitus and cardiovascular diseases in

their later life than women without GDM<sup>5,6</sup>. The identification of women at risk for impaired postpartum glucose metabolism is crucial for the early initiation of effective interventional strategies, such as increased physical activity, healthy nutritional advice, weight reduction and maintenance of an ideal bodyweight, which can delay or prevent the progression from GDM to type 2 diabetes mellitus or other metabolic disorders in the immediate postpartum period or several years later<sup>5–7</sup>. Therefore, the American Diabetes Association and the American College of Obstetricians and Gynecologists recommend type 2

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diabetes mellitus screening with a 75-g, 2-h oral glucose tolerance test (OGTT) at 4–12 weeks postpartum for all women with GDM<sup>8,9</sup>. However, the rate of carrying out the postpartum glycemic screening test (PGST) shows a wide variation, which ranges from 33 to 73%, among different countries or studies<sup>10,11</sup>. Compared with the USA and European countries, the rate of PGSTs for women with GDM is lower in Asian countries<sup>11,12</sup>, despite the higher risk for type 2 diabetes mellitus after GDM among Asian women than among other ethnicities<sup>13–16</sup>.

Several risk factors have been reported to be associated with the development of postpartum type 2 diabetes mellitus in women who had GDM. These include a high glycated hemoglobin level at GDM diagnosis, high glucose parameters on the 100-g, 3-h OGTT, history of GDM, and a high prepregnancy body mass index (BMI)<sup>5,6</sup>. Based on the result of a postpartum 75-g, 2-h OGTT<sup>17</sup>, a woman can be categorized as normal, or diagnosed with prediabetes (including isolated impaired fasting glucose [IFG], isolated impaired glucose tolerance [IGT] and IFG plus IGT) or diabetes. It is unclear whether women with prediabetes have a similar risk factor profile as those who are diagnosed with diabetes. Furthermore, most previous studies examined the risk factors for postpartum type 2 diabetes mellitus in women with GDM that was diagnosed with the 100-g, 3-h OGTT (see reviews in Tovar et al.11, Nouhjah et al.12 and Benhalima et al.18). Just a few studies were carried out among women with GDM that was diagnosed with a 75-g, 2-h OGTT based on the criteria defined by the International Association of Diabetes and Pregnancy Study Groups (IADPSG)<sup>19-25</sup>; most of these studies had small sample sizes<sup>20-25</sup> and were conducted on non-Asian populations  $^{19-23}$ . Thus, it remains unclear whether Asian women with GDM that was diagnosed on the basis of the IADPSG criteria have a similarly increased risk and risk profile for abnormal postpartum glucose metabolism than those with a GDM diagnosis that was based on other screening strategies and diagnostic criteria.

Therefore, the present study was carried out to examine the risks and risk profile for abnormal postpartum glucose metabolism in women who were diagnosed with GDM based on the IADPSG criteria. The primary objective of this research was to ascertain the rate of PGST, and the secondary objective was to investigate the risk factors for prediabetes and diabetes at 6–12 weeks postpartum in a population of Taiwanese women with GDM.

#### **METHODS**

#### Data collection

Study data were extracted from the computerized obstetrics database of Taipei Chang Gung Memorial Hospital, Taiwan. Information on maternal demographic characteristics, and medical and obstetric histories, as well as the course of the index pregnancy and perinatal outcomes were recorded. The details of the database organization have been previously reported<sup>26–28</sup>. We retrospectively examined the data of all women who gave

birth after 28 completed weeks of gestation between 1 July 2011 and 31 December 2019. The institutional review board of Chang Gung Memorial Hospital approved the study (approval no. 201800894B0). The approving body waived the need for informed consent, given the retrospective nature of the study and the use of anonymized participant information.

#### **Diagnosis of GDM**

During the study period, all pregnant women who were treated at this hospital underwent universal screening for GDM with a one-step approach, as recommended by the IADPSG<sup>1,29</sup>. The IADPSG recommends testing to be routinely carried out between 24 and 28 weeks of gestation or at the first prenatal visit in high-risk women. Based on the results of a 75-g, 2-h OGTT, a woman was diagnosed with GDM when one or more of her plasma glucose concentrations were equivalent to or exceeded the following levels: fasting, 92 mg/dL; 1 h, 180 mg/ dL; or 2 h, 153 mg/dL<sup>29</sup>. After a GDM diagnosis, women were referred to dieticians for advice on dietary and lifestyle modifications, and underwent regular monitoring of blood glucose levels. Insulin therapy was indicated if medical nutritional therapy failed to consistently maintain a fasting glucose level <95 mg/dL and a 2-h postprandial level <120 mg/dL.

#### Postpartum glycemic screening test

After delivery, women with GDM are offered a PGST with a standard 75-g, 2-h OGTT that is usually undertaken at 6–12 weeks postpartum. Based on the levels of fasting and 2-h plasma glucose concentrations<sup>17</sup>, a woman was classified into one of the following diagnoses: (i) diabetes: fasting glucose  $\geq$ 126 mg/dL or 2-h glucose  $\geq$ 200 mg/dL; (ii) isolated IFG: fasting glucose  $\geq$ 100 and <126 mg/dL, and 2-h glucose <140 mg/dL; (iii) isolated IGT: fasting glucose <100 mg/dL, and 2-h glucose  $\geq$ 140 mg/dL and <200 mg/dL; (iv) IFG plus IGT: fasting glucose  $\leq$ 100 mg/dL and <200 mg/dL, and 2-h glucose <100 mg/dL and 2-h glucose <100 mg/dL. For this study, women with isolated IFG, isolated IGT and IFG plus IGT were grouped together as prediabetes.

#### Data analysis

The present study consisted of two parts. In the first part of the study, we investigated the rate of GDM women who underwent the PGST. We further evaluated maternal characteristics and pregnancy outcomes between GDM women with and without PGST by frequency (percentage), and compared the distribution differences using the  $\chi^2$ -test or Fisher's exact test. Multiple logistic regression analysis was then carried out to determine factors associated with undergoing PGST in women with GDM, after adjusting for potential confounders from maternal characteristics and pregnancy outcomes that were statistically significant in the univariate analysis. The maternal characteristics for analysis included age at delivery (stratified as <20, 20–34 and >34 years); prepregnancy BMI (stratified as

<18.5, 18.5–24.9 and >24.9 kg/m<sup>2</sup>); mode of delivery (spontaneous or operative vaginal delivery, or cesarean delivery [CS]); primiparity; history of induced or spontaneous abortions, preterm birth and fetal death; conception assisted by reproductive technology; cigarette smoking during pregnancy; multiple gestation; genetic amniocentesis; uterine fibroids; group B streptococcal colonization of the rectogenital tract; maternal diseases, such as chronic hypertension, pre-eclampsia, and hypo- and hyperthyroidism; and first- or second-degree family history of diabetes, GDM history in a previous pregnancy and insulin therapy for GDM during pregnancy. The pregnancy outcomes for analysis included fetal sex (male or female); preterm birth before 34 or 37 weeks of gestation, birthweight <1,500, <2,500 or >4,000 g; small-for-gestational age infants, defined as birthweight <10th percentile of mean weight corrected for fetal sex and gestational age<sup>30,31</sup>; large-for-gestational age infants, defined as birth weight >90th percentile of mean weight corrected for fetal sex and gestational age<sup>30,31</sup>; low 1- and 5-min Apgar scores (<7); neonatal intensive care unit admission; fetal death; neonatal death; congenital anomalies (chromosomal or structural); premature rupture of membranes; meconium-stained amniotic fluid; oligohydramnios; polyhydramnios; acute chorioamnionitis; placental abruption; placenta previa; placenta accreta; postpartum hemorrhage, defined as a blood loss >500 mL for vaginal delivery, 1,000 mL for CS or excessive bleeding that results in signs of hypovolemia, such as hypotension or tachycardia; and severe perineal injury, defined as thirdor fourth-degree perineal laceration.

The objective of the second part of the study was to investigate risk factors for abnormal PGST results, including prediabetes and diabetes. We compared the distribution differences in the aforementioned maternal characteristics and pregnancy outcomes between GDM women with normal and abnormal PGST results. Only variables with statistical differences in the univariate analysis among these three groups of women were selected for further multiple logistic regression analysis. We then generated two models for multiple logistic regression to determine independent risk factors for abnormal PGST results; model 1 adjusted for the confounding effects of maternal characteristics, whereas model 2 adjusted for the confounding effects of both maternal characteristics and pregnancy outcomes.

#### Statistical analysis

All statistical analyses were carried out in SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as the mean  $\pm$  standard deviation, and categorical variables as the number and frequency (%). Comparisons between GDM women with and without PGST were carried out with the Student's *t*-test,  $\chi^2$ -test or Fisher's exact test, as appropriate. Intergroup comparisons among women with normal PGST results and those with prediabetes and diabetes were undertaken with logistic regression or the Kruskal–Wallis test followed by Dunnett's post-hoc test. A *P*-value <0.05 was

considered statistically significant. In multiple logistic regression, adjusted odds ratios (OR) and associated 95% confidence intervals (CI) were calculated to identify factors associated with the attendance of PGST, and to assess the associations between various risk factors and abnormal PGST results.

#### RESULTS

# Differences in the rates of various maternal characteristics and pregnancy outcomes between women with GDM with and without PGST

During the study period, a total of 1,648 women with 1,696 infants (including 48 sets of twins) were diagnosed with GDM on the basis of the IADPSG criteria, and 493 (29.9%) women had a PGST at 6–12 weeks postpartum. Compared with women with GDM who did not undergo the PGST, the rates of operative vaginal delivery, family history of diabetes, insulin therapy during pregnancy and severe perineal injury were higher in women with GDM who underwent a PGST (Tables 1,2). In contrast, the rates of CS, male fetus, preterm birth <37 weeks and placenta previa were lower in women with GDM who underwent a PGST than that in women with GDM who did not undergo the PGST.

### Factors associated with undergoing the PGST in women with GDM

Multiple logistic regression with adjustment for the confounding effects of maternal characteristics and pregnancy outcomes showed that women with GDM with operative vaginal delivery (adjusted OR 1.87, 95% CI 1.11–3.15), insulin therapy during pregnancy (adjusted OR 1.63, 95% CI 1.10–2.40) and family history of diabetes (adjusted OR 1.30, 95% CI 1.05–1.61) were more likely to undergo the PGST (Table 3).

#### Differences in the rates of various maternal characteristics and pregnancy outcomes between women with GDM with normal and abnormal PGST results

Among the 493 women who underwent the PGST, 162 (32.9%) women were found to have abnormal PGST results, including 135 (27.4%) women diagnosed with prediabetes and 27 (5.5%) women with diabetes. Among the women with prediabetes, 51 were classified as isolated IFG, 70 as isolated IGT and 14 as IFG plus IGT. The maternal characteristics of these 493 women are shown in Tables 4 and Table S1. Compared with women who had normal PGST results, the rates of prepregnancy BMI >24.9 kg/m<sup>2</sup>, CS, history of fetal death and insulin therapy during pregnancy were higher in women with prediabetes. Furthermore, women diagnosed with diabetes were more likely to have a prepregnancy BMI >24.9 kg/m<sup>2</sup>, CS and insulin therapy during pregnancy than women with a normal postpartum glycemic status. Therefore, prepregnancy BMI >24.9 kg/m<sup>2</sup>, CS, history of fetal death and insulin therapy during pregnancy were selected as potential risk factors for abnormal PGST results for multiple logistic regression analysis in model 1.

	Not screened ( $n = 1,155$ )	Screened ( $n = 493$ )	Р
Age (years)			
<20	1 (0.1%)	0	1.000
20–34	467 (40.4%)	189 (38.3%)	0.442
>34	687 (59.5%)	304 (61.7%)	0.411
Prepregnancy body mass index (kg/m <sup>2</sup> )			
<18.5	103 (8.9%)	46 (9.3%)	0.851
18.5–24.9	748 (65.0%)	340 (69.0%)	0.125
>24.9	300 (26.1%)	107 (21.7%)	0.062
Cesarean delivery	580 (50.2%)	211 (42.8%)	0.006
Operative vaginal delivery	35 (3.0%)	32 (6.5%)	0.001
Primiparity	604 (52.3%)	277 (56.2%)	0.161
History of induced or spontaneous abortions	370 (32.0%)	160 (32.5%)	0.863
History of fetal death	26 (2.3%)	8 (1.6%)	0.456
History of preterm birth	20 (1.7%)	3 (0.6%)	0.106
Conception through reproductive technology	79 (6.8%)	28 (5.7%)	0.445
Cigarette smoking during pregnancy	1 (0.1%)	1 (0.2%)	0.509
Multiple gestation	34 (2.9%)	14 (2.8%)	0.909
Genetic amniocentesis	509 (44.1%)	222 (45.0%)	0.745
Uterine fibroids	34 (2.9%)	21 (4.3%)	0.179
Group B streptococcal colonization	160 (13.9%)	85 (17.2%)	0.082
Chronic hypertension	7 (0.6%)	5 (1.0%)	0.359
Pre-eclampsia	48 (4.2%)	15 (3.0%)	0.327
Hyperthyroidism	10 (0.9%)	8 (1.6%)	0.197
Hypothyroidism	7 (0.6%)	1 (0.2%)	0.448
Family history of diabetes mellitus	492 (43.1%)	247 (50.2%)	0.009
History of gestational diabetes	67 (5.9%)	28 (5.7%)	1.000
Insulin therapy during pregnancy	77 (6.7%)	48 (9.8%)	0.042

<b>Table 1</b>   Maternal characteristics of the women who did and did not undergo the postpartum glycemic screening test
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Data are presented as a number (%). P-values are based on the  $\chi^2$ -test or Fisher's exact test.

The pregnancy outcomes of the 493 women who underwent the PGST are shown in Tables 5 and S2. Univariate analysis showed that there were significant differences in the rates of preterm birth <37 weeks of gestation, birthweight <1,500 or >4,000 g, large-for-gestational age infants, and low 1-min Apgar score between newborns from women with normal PGST results and those from women with prediabetes or diabetes. Therefore, these variables, in association with prepregnancy BMI >24.9 kg/m<sup>2</sup>, CS, history of fetal death and insulin therapy during pregnancy, were included as potential risk factors for abnormal PGST results in the multiple logistic regression analysis in model 2. Although univariate analysis showed significant differences in the rates of low 5-min Apgar score and fetal death among these three groups of women, these two variables were not selected for model 2 because the numbers of individuals were small and no women with normal PGST results had fetal death or newborns with a low 5-min Apgar score.

#### Risk factors for postpartum prediabetes and diabetes

In model 1, we applied multiple logistic regression to adjust for the confounding effects of maternal characteristics, and found that prepregnancy BMI >24.9 kg/m<sup>2</sup> was the independent risk factor for postpartum prediabetes (Table 6). Prepregnancy BMI

>24.9 kg/m<sup>2</sup> remained as the major risk factor (adjusted OR 1.99, 95% CI 1.24–3.21) for postpartum prediabetes when the confounding effects of pregnancy outcomes were simultaneously adjusted in model 2 (Table 6).

The results of multiple logistic regression on the risk factors for postpartum diabetes are shown in Table 7. Insulin therapy during pregnancy was found to be the major risk factor for postpartum diabetes in model 1. After adjusting the confounding effects of maternal characteristics and pregnancy outcomes, significant risk factors for postpartum diabetes included insulin therapy during pregnancy (adjusted OR 10.79, 95% CI 4.07–28.58), birthweight >4,000 g (adjusted OR 10.22, 95% CI 1.74–59.89) and preterm birth <37 weeks of gestation (adjusted OR 3.33, 95% CI 1.09–10.22).

#### DISCUSSION

In the present retrospective study, we found that less than onethird of women with GDM received a PGST at 6–12 weeks postpartum. Women with GDM with operative vaginal delivery, insulin therapy during pregnancy and a family history of diabetes were more likely to undergo the PGST. Furthermore, among women who underwent the PGST, 32.9% had abnormal results, including 27.4% with prediabetes and 5.5% with

	Not screened ( $n = 1,189$ )	Screened ( $n = 507$ )	Р
Gestational age (weeks)	37.7 ± 2.4	37.9 ± 2.4	0.072
Birthweight (g)	3,049 ± 595	3,082 ± 589	0.286
Male fetus	647 (54.4%)	249 (49.1%)	0.049
Preterm birth <34 weeks	53 (4.5%)	18 (3.6%)	0.430
Preterm birth <37 weeks	227 (19.1%)	69 (13.6%)	0.006
Birthweight <1,500 g	24 (2.0%)	10 (2.0%)	1.000
Birthweight <2,500 g	165 (13.9%)	54 (10.7%)	0.082
Birthweight >4,000 g	35 (2.9%)	19 (3.7%)	0.450
Small-for-gestational age infants	99 (8.4%)	32 (6.3%)	0.165
Large-for-gestational age infants	175 (14.8%)	65 (12.9%)	0.323
1-min Apgar score <7	21 (1.8%)	14 (2.8%)	0.194
5-min Apgar score <7	10 (0.8%)	5 (1.0%)	0.780
Neonatal intensive care unit admission	72 (6.1%)	30 (5.9%)	1.000
Fetal death	6 (0.5%)	5 (1.0%)	0.321
Neonatal death	1 (0.1%)	0	1.000
Congenital anomaly	11 (0.9%)	10 (2.0%)	0.092
Premature rupture of membranes	35 (2.9%)	13 (2.6%)	0.751
Meconium-stained fluid	104 (8.7%)	39 (7.7%)	0.505
Oligohydramnios	12 (1.0%)	5 (1.0%)	1.000
Polyhydramnios	9 (0.8%)	2 (0.4%)	0.522
Acute chorioamnionitis	5 (0.4%)	5 (1.0%)	0.176
Placental abruption	18 (1.5%)	5 (1.0%)	0.495
Placenta previa	34 (2.9%)	5 (1.0%)	0.020
Placenta accreta	6 (0.5%)	2 (0.4%)	1.000
Postpartum hemorrhage	20 (1.7%)	7 (1.4%)	0.833
Severe perineal injury	68 (5.7%)	46 (9.1%)	0.015

Table 2   Pregnancy	outcomes of the wome	n who did and who did n	ot undergo the postpart	um alvcemic screenina test

Data are presented as a number (%) or the mean  $\pm$  standard deviation. P-values are based on the  $\chi^2$ -test, Fisher's exact test or Student's t-test.

 Table 3 | Factors associated with undergoing the postpartum glycemic screening test in women with gestational diabetes mellitus

Variables	Adjusted OR (95% Cl)	Р
Operative vaginal delivery	1.87 (1.11–3.15)	0.018
Insulin therapy during pregnancy	1.63 (1.10–2.40)	0.015
Family history of diabetes mellitus	1.30 (1.05–1.61)	0.018
Male fetus	0.78 (0.63–0.97)	0.027
Preterm birth <37 weeks	0.65 (0.47-0.90)	0.009
Cesarean delivery	0.84 (0.67–1.06)	0.141
Placenta previa	0.46 (0.18–1.20)	0.112
Severe perineal injury	1.27 (0.83–1.93)	0.273

CI, confidence interval; OR, odds ratio.

diabetes. We further demonstrated different risk profiles between women with postpartum prediabetes and those with diabetes.

Similar to the results of a recent multicenter report from Korea<sup>32</sup>, the proportion of women with GDM who underwent a PGST in the present study was lower than those in most previous reports<sup>11,12</sup>. The difference in the rate of PGST can be explained by differences in the research design across different

studies. Active invitation of women in randomized clinical trials and prospective studies is more likely to have a positive effect on the PGST rate. Furthermore, a lower PGST rate in the present study might be attributed to reasons related to both physicians and patients. With regard to the physician-related factors, it is possible that some of the physicians in this hospital did not take PGST into account as part of their routine practice for the postpartum management for women with GDM during pregnancy, because they were unaware of or unfamiliar with this recommendation, forgot to order the test owing to heavy outpatient clinical load, or consciously ignored it, as they considered GDM to be a benign condition because most women with GDM have a favorable pregnancy outcome. With regard to the patient-related factors, the inconvenience of PGST and time utilization are the most commonly cited reasons for women with a history of GDM for not undergoing the PGST<sup>33</sup>. As nearly onethird of the women with GDM were noted to have abnormal PGST results, it is important to remind or educate obstetricians of the necessity to carry out this screening test to identify women with GDM at risk for metabolic disorders later in life. Furthermore, the use of a variety of proactive patient contact programs, such as phone calls, education programs or postal reminders, has been shown to increase the PGST rate<sup>34</sup>.

	Normal ( $n = 331$ )	Prediabetes ( $n = 135$ )	Diabetes ( $n = 27$ )	Р
Age (years)				
20–34	128 (38.7%)	51 (37.8%)	10 (37.0%)	0.974
>34	203 (61.3%)	84 (62.2%)	17 (63.0%)	0.974
Prepregnancy body mass index (kg/m <sup>2</sup> )				
<18.5	35 (10.6%)	11 (8.1%)	0	0.047
18.5–24.9	241 (72.9%)	83 (61.5%)	16 (59.3%)	0.032
>24.9	55 (16.6%)	41 (30.4%)**	11 (40.7%)**	< 0.001
Weight gain during pregnancy (kg)	$11.2 \pm 4.4$	10.2 ± 4.4**	$10.1 \pm 5.8$	0.064
Primiparity	188 (56.8%)	77 (57.0%)	12 (44.4%)	0.452
Cesarean delivery	128 (38.7%)	66 (48.9%)*	17 (63.0%)*	0.012
Operative vaginal delivery	24 (7.3%)	7 (5.2%)	1 (3.7%)	0.573
History of induced or spontaneous abortions	117 (35.3%)	35 (25.9%)	8 (29.6%)	0.130
History of fetal death	2 (0.6%)	5 (3.7%)*	1 (3.7%)	0.048
History of preterm birth	1 (0.3%)	2 (1.5%)	0	0.337
Conception through reproductive technology	17 (5.1%)	9 (6.7%)	2 (7.4%)	0.756
Cigarette smoking during pregnancy	1 (0.3%)	0 (0.0%)	0	0.671
Multiple gestation	11 (3.3%)	3 (2.2%)	0	0.364
Genetic amniocentesis	150 (45.3%)	67 (49.6%)	15 (55.6%)	0.187
Uterine fibroids	13 (3.9%)	8 (5.9%)	0	0.195
Group B streptococcal colonization	53 (16%)	29 (21.5%)	3 (11.1%)	0.252
Chronic hypertension	1 (0.3%)	3 (2.2%)	1 (3.7%)	0.085
Pre-eclampsia	8 (2.4%)	5 (3.7%)	2 (7.4%)	0.384
Hyperthyroidism	6 (1.8%)	1 (0.7%)	1 (3.7%)	0.488
Hypothyroidism	0	1 (0.7%)	0	0.273
Family history of diabetes mellitus	165 (50.0%)	66 (48.9%)	16 (59.3%)	0.610
History of gestational diabetes	16 (4.8%)	11 (8.1%)	1 (3.7%)	0.362
Insulin therapy during pregnancy	17 (5.2%)	17 (12.7%)**	14 (51.9%)***	< 0.001

Table 4 | Maternal characteristics of the women with normal and abnormal postpartum glycemic screening results

Data are presented as a number (%) or the mean  $\pm$  standard deviation. Prediabetes includes isolated impaired fasting glucose, isolated impaired glucose intolerance and impaired fasting glucose combined with impaired glucose intolerance. *P*-values are based on the logistic regression or Kruskal–Wallis test. \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001, compared with women with normal postpartum glycemic screening results.

It has been shown that the incidence of GDM increases with the adoption of a one-step approach and the IADPSG criteria than with other screening strategies and diagnostic criteria<sup>1,2</sup>. However, the effect of implementing the IADPSG criteria on the rate of abnormal glucose metabolism immediately in the postpartum period or several years after delivery remains unclear. In a recent meta-analysis of eight studies, published between 2003 and 2015, among Asian women with a history of GDM based on non-IADPSG criteria, the rates of diabetes and prediabetes diagnosed at 4-12 weeks postpartum were in the range of 8.2-20.6% (mean 13.9%) and 15.5-41.8% (mean 28.3%), respectively<sup>12</sup>. These results are higher than those in the present study. It is possible that our adoption of the IADPSG criteria identifies more women with mild disease than those with other GDM criteria. These women with mild GDM return to a euglycemic state either after delivery of the placenta or as a result of lifestyle modification, thereby reducing the rate of postpartum diabetes and prediabetes.

Furthermore, the risk factor profile for abnormal PGST results could be affected by the diagnostic criteria used for GDM. Previous studies using non-IADPSG criteria reported

that risk factors that are significantly associated with postpartum prediabetes and/or diabetes include a family history of diabetes, gestational age at diagnosis of GDM, insulin use during pregnancy and prepregnancy  $BMI^{12}$ . With the use of the IADPSG criteria for GDM, we found that women with GDM with a prepregnancy  $BMI > 24.9 \text{ kg/m}^2$  are more likely to have prediabetes, whereas women with GDM receiving insulin therapy during pregnancy, a fetal birthweight >4,000 g or preterm birth <37 weeks of gestation are more likely to be diagnosed with diabetes at 6–12 weeks postpartum. Further studies are required to clarify the effect of implementing the IADPSG criteria for GDM on the rate and risk profile of abnormal glucose metabolism in the immediate postpartum period or several years after delivery.

Isolated IFG, isolated IGT and IFG plus IGT are generally considered as intermediate states in glucose metabolism disorders that exist between normal glucose tolerance and overt diabetes. The present study shows the different risk factor profiles among women with GDM with different abnormal PGST results, suggesting that different metabolic abnormalities characterize these conditions<sup>17,35</sup>. Insulin resistance and impaired  $\beta$ -

Table 5	Pregnancy	outcomes of the v	women with normal	and abnormal	postpartum	glycemic screening resu	ults
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	Normal ( $n = 342$ )	Prediabetes ( $n = 138$ )	Diabetes ( $n = 27$ )	Р
Gestational age (weeks)	38.2 ± 1.7	37.7 ± 2.8	36.4 ± 4.8°	< 0.001
Birthweight (g)	3,107 ± 505	3,006 ± 645	3,162 ± 1,084	0.179
Male fetus	168 (49.1%)	67 (48.6%)	14 (51.9%)	0.952
Preterm birth <34 weeks	8 (2.3%)	7 (5.1%)	3 (11.1%)*	0.067
Preterm birth <37 weeks	40 (11.7%)	20 (14.5%)	9 (33.3%)**	0.018
Birthweight <1,500 g	1 (0.3%)	7 (5.1%)**	2 (7.4%)**	0.001
Birthweight <2,500 g	32 (9.4%)	18 (13.0%)	4 (14.8%)	0.396
Birthweight >4,000 g	13 (3.8%)	1 (0.7%)	5 (18.5%)**	0.001
Small-for-gestational age infants	19 (5.6%)	11 (8.1%)	2 (7.7%)	0.579
Large-for-gestational age infants	43 (12.6%)	13 (9.6%)	9 (34.6%)**	0.009
1-min Apgar score < 7	5 (1.5%)	7 (5.1%)*	2 (7.4%)	0.043
5-min Apgar score $< 7$	0	3 (2.2%)	2 (7.4%)	0.002
Neonatal intensive care unit admission	19 (5.6%)	9 (6.5%)	2 (7.4%)	0.874
Fetal death	0	3 (2.2%)	2 (7.4%)	0.002
Congenital anomaly	5 (1.5%)	4 (2.9%)	1 (3.7%)	0.503
Meconium-stained fluid	27 (7.9%)	9 (6.5%)	3 (11.1%)	0.707
Premature rupture of membranes	5 (1.5%)	7 (5.1%)*	1 (3.7%)	0.091
Oligohydramnios	3 (0.9%)	1 (0.7%)	1 (3.7%)	0.509
Polyhydramnios	1 (0.3%)	0	1 (3.7%)	0.141
Acute chorioamnionitis	3 (0.9%)	2 (1.4%)	0	0.656
Placental abruption	3 (0.9%)	2 (1.4%)	0	0.656
Placenta previa	4 (1.2%)	1 (0.7%)	0	0.686
Placenta accreta	2 (0.6%)	0	0	0.454
Postpartum hemorrhage	5 (1.5%)	1 (0.7%)	1 (3.7%)	0.528
Severe perineal injury	32 (9.4%)	11 (8.0%)	3 (11.1%)	0.830

Data are presented as the number (%) or the mean  $\pm$  standard deviation. Prediabetes includes isolated impaired fasting glucose, isolated impaired glucose intolerance and impaired fasting glucose combined with impaired glucose intolerance. *P*-values are based on the logistic regression or Kruskal–Wallis test. \**P* < 0.05; \*\**P* < 0.01; compared with women with normal postpartum glycemic screening results.

Table 6 | Risk factors for postpartum prediabetes

Variable	Model 1		Model 2	
	Adjusted OR (95% Cl)	Р	Adjusted OR (95% Cl)	Р
Prepregnancy body mass index >24.9 kg/m <sup>2</sup>	1.87 (1.17–2.98)	0.009	1.99 (1.24–3.21)	0.005
History of fetal death	3.37 (0.72–15.69)	0.122	3.73 (0.68–20.49)	0.129
Cesarean delivery	1.27 (0.84–1.91)	0.264	1.32 (0.86–2.02)	0.204
Insulin therapy during pregnancy	1.18 (0.61–2.28)	0.627	1.25 (0.63–2.50)	0.526
Birthweight >4,000 g	_		0.13 (0.02–1.07)	0.057
Preterm birth <37 weeks	_		0.60 (0.30–1.20)	0.149
Birthweight <1,500 g	_		5.26 (0.75–36.86)	0.095
Large-for-gestational age infants	_		0.87 (0.43–1.79)	0.708
1-min Apgar score <7	_		1.69 (0.40–7.20)	0.475

Cl, confidence interval; OR, odds ratio.

cell function are the primary defects that are observed in type 2 diabetes mellitus patients. Both isolated IFG and isolated IGT are insulin-resistant states, with a difference in the location of the insulin resistance<sup>36,37</sup>. Individuals with isolated IFG predominantly have hepatic insulin resistance and normal muscle insulin sensitivity, whereas those with isolated IGT have normal-to-slightly reduced hepatic insulin sensitivity and

moderate-to-severe muscle insulin resistance. Previous studies showed that the pattern of impaired insulin secretion differs between the aforementioned two groups<sup>36,37</sup>. Participants with isolated IFG manifest a decrease in basal insulin secretion and first-phase insulin release, whereas those with isolated IGT have severe impairment in both, first- and second-phase insulin responses to intravenous and oral glucose. Furthermore,

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Table 7	Risk factors	s for postpartu	m diabetes	mellitus

Variable	Model 1		Model 2	
	Adjusted OR (95% Cl)	Р	Adjusted OR (95% CI)	Р
Insulin therapy during pregnancy	10.86 (4.50–26.21)	<0.001	10.79 (4.07–28.58)	< 0.001
Prepregnancy body mass index >24.9 kg/m <sup>2</sup>	1.63 (0.68–3.93)	0.276	1.78 (0.71–4.49)	0.220
History of fetal death	1.57 (0.14–17.62)	0.716	0.73 (0.03–16.15)	0.843
Cesarean delivery	1.45 (0.61–3.47)	0.405	0.86 (0.32-2.32)	0.771
Birthweight >4,000 g	_		10.22 (1.74–59.89)	0.010
Preterm birth <37 weeks	_		3.33 (1.09–10.22)	0.036
Birthweight <1,500 g	_		0.66 (0.04–11.86)	0.781
Large-for-gestational age infants	_		1.25 (0.33-4.71)	0.745
1-min Apgar score <7	_		1.43 (0.11–17.90)	0.782

Cl, confidence interval; OR, odds ratio.

individuals with IFG plus IGT manifest severe liver and muscle insulin resistance, as well as markedly impaired insulin secretion. Understanding of the risk factors and pathophysiological abnormalities that characterize isolated IFG, isolated IGT and IFG plus IGT provides insights on interventions to slow or halt the progression to type 2 diabetes mellitus<sup>17,35</sup>.

The present study was rigorous with regard to the use of patient interviews, the extraction of data from medical records and the application of multivariable logistic regression analysis that was adjusted for potential confounders. Therefore, the association between various maternal and pregnancy outcome variables and abnormal PGST results was objectively investigated. However, the present study had several limitations that merit attention. A major limitation was the possibility of selection bias because of the retrospective and observational design. Indeed, there were differences in the rate of certain maternal characteristics and pregnancy outcomes between women who chose to or not to undergo the PGST. These include operative vaginal delivery, insulin therapy during pregnancy, family history of diabetes and delivery of a male fetus or before 37 weeks of gestation. Future prospective studies might help clarify whether differences of these variables have a major impact on the findings of the present study. Next, some important factors that might have an effect on the development of postpartum glucose intolerance were not examined, because this information was unavailable from our obstetric database. These factors include the frequency and intensity of breastfeeding<sup>38</sup>, and changes of bodyweight, physical activity and nutritional condition during the postpartum period. Furthermore, we did not measure the levels of glucose and insulin for homeostatic model assessments to assess  $\beta$ -cell function and insulin resistance in women with different abnormal postpartum glycemic metabolism disorders. Finally, the present study was carried out at a single tertiary care hospital in Taiwan, thereby limiting the generalizability of the conclusions.

In summary, the rate of PGST is suboptimal in the Taiwanese female post-pregnancy population. Future work should focus on reducing the barriers to screening for both healthcare providers and women with GDM. More research is required to elucidate the effects of implementing the IADPSG criteria for GDM on the rate and risk profile of abnormal glucose metabolism during postpartum or metabolic and cardiovascular diseases later in life.

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#### DISCLOSURE

The authors declare no conflict of interest.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Maternal characteristics of the women with normal and different categories of abnormal postpartum glycemic screening results.

Table S2 | Pregnancy outcome of the women with normal and different categories of abnormal postpartum glycemic screening results.