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POLISH GYNECOLOGY
GINEKOLOGIA POLSKA
ORGAN POLSKIEGO TOWARZYSTWA GINEKOLOGICZNEGO
THE OFFICIAL JOURNAL OF THE POLISH GYNECOLOGICAL SOCIETY

ISSN: 0017-0011

e-ISSN: 2543-6767

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DOI: 10.5603/GP.a2022.0007

Article type: Research paper

Submitted: 2021-11-23

Accepted: 2022-02-21

Published online: 2022-03-28

ORIGINAL PAPER/GYNECOLOGY

Risk factors for recurrence of gestational diabetes mellitus in southern Chinese awomen: a retrospective study

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Running title: Recurrent gestational diabetes mellitus

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ABSTRACT

Objectives: Predictors of gestational diabetes mellitus (GDM) recurrence (GDMR) was determined in southern Chinese women.

Material and methods: A total of 376 women with GDM who had two consecutive singleton deliveries at our hospital between January 2014 and October 2020 were enrolled in the current study. We retrospectively compared the clinical characteristics, fasting plasma glucose level (FPG-1), and oral glucose tolerance test-1h-1 and -2h-1 (OGTT 1hr-1: 1-h post-load glucose level during the first pregnancy and OGTT 2hr-1: 2-h post-load glucose level during the first pregnancy) for the first pregnancy between patients in the GDMR group (n = 166) and the non-GDMR group (n = 210).

Results: The incidence of GDMR in the study population was 44.15%. During the first pregnancy, women in the GDMR group had significantly higher OGTT 1h-1, OGTT 2h-1, and FPG-1 + OGTT 1h + 2h-1 compared to the non-GDMR group. When the threshold of the FPG-1 + OGTT 1h + 2h-1 level in the first pregnancy was > 23.6 mmol/L, the specificity for predicting GDMR was 0.85, the sensitivity was 0.45, and the area under the receiver operating characteristic curve (ROC-AUC) was 0.70, indicating a 70% probability of predicting GDMR in the next pregnancy. Logistic regression analysis showed that patients with a combined abnormal FPG-1 + OGTT 1h + 2 h-1 level had a 10-fold increased risk for GDMR in subsequent pregnancies than patients with normal indicators (OR: 10.542, 95% CI: 3.097–35.881; $p < 0.0001$).

Conclusions: The OGTT 1h-1 and OGTT 2h-1 are independent risk factors for GDMR in southern Chinese women. Women with an FPG-1 + OGTT 1h + 2h-1 threshold level > 23.6 mmol/L in the first pregnancy had a 10-fold greater probability of developing GDMR in the second pregnancy than women in the non-GDMR group.

Key words: recurrence; gestational diabetes mellitus; risk factor; OGTT

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most universal complications of pregnancy. GDM affects between 5% and 14% of pregnancies [1-4]. The American Diabetes Association defines GDM as DM diagnosed during pregnancy [5, 6] and this standard is widely used in China. Gestational diabetes mellitus recurrence (GDMR) is defined as a history of one or more episodes of GDM and the occurrence of glucose metabolism abnormalities in the current pregnancy that meet the diagnostic criteria for GDM[5-6]. In most women with GDM, the postpartum blood glucose returns to normal, but the risk of developing diabetes is much higher than women without GDM[7]. In southeast Asia, 57.7% of parturients with GDM develop DM or prediabetes [7].

Between 35% and 50% of women with GDM may have GDMR in subsequent

pregnancies [8]. In China, the GDMR rate is gradually increasing with the opening of the two-child policy [9]. GDMR associated with adverse maternal and neonatal outcomes, such as premature delivery and macrosomia [10].

It is essential to predict the risk of GDMR in advance and develop reasonable prevention methods for high-risk groups. Some risk factors may help us predict GDMR. Indeed, ethnicity, maternal age, oral glucose tolerance test (OGTT) levels, the interval between pregnancies, pre-pregnancy body mass index (BMI), and weight gain during two pregnancies have been recently reported as risk factors [10]; however, data on GDMR in the southern Chinese population are limited.

Objectives

The purpose of this retrospective study was to determine unique risk factors for local women with GDMR.

MATERIAL AND METHODS

This was a retrospective study. This protocol was approved by Institutional Review Boards from our hospital (PYRC-2021-038). All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki). All participants have given their oral consent for this study. The inclusion criteria for participants were as follows: 1. women with first and second pregnancies with singleton deliveries between January 2014 and October 2020 at our hospital; 2. diagnosed with GDMR during the second pregnancy. The exclusion criteria were as follows: 1. known pregestational diabetes; 2. incomplete OGTT during the first and second pregnancies. The subjects were divided into GDMR and non-GDMR groups based on OGTT results during the second pregnancy.

Diagnosis of GDM

We used the one-step 75-g OGTT and the latest diagnostic criteria established by the American Diabetes Association in 2015 [6]. All pregnant women without preexisting diabetes underwent a 75-g OGTT at 24–28 weeks gestation. A diagnosis

of GDM was made based on an OGTT fasting plasma glucose (FPG) level ≥ 5.1 mmol/L, 1-h glucose level ≥ 10.0 mmol/L, and 2-h glucose level ≥ 8.5 mmol/L [11].

Patient information

We retrieved the following data from the medical record system: maternal age; mode of delivery; infant birth weight; maternal complications; gestational interval; and the first pregnancy fasting plasma glucose (FPG-1), 1-h post-load glucose level (OGTT 1h-1), and 2-h post-load glucose level (OGTT 2h-1).

Statistical analysis

The data were evaluated using SPSS (IBM SPSS Statistics for Windows, version 21, IBM Corp., Armonk, N.Y., USA). Continuous variables with a normal distribution are expressed as the mean ± standard deviation (SD) and categorical variables are reported as numbers and percentages. We analyzed the mean of two continuous variables with an independent samples t-test and analyzed categorical variables with the Pearson's chi-square test and Fisher's exact test. Analysis of covariance (ANCOVA) was used to detect differences in the OGTT results between the two pregnancies. The odds ratio (OR) and 95% confidence interval (CI) were calculated using a binary logistic regression model to analyze the characteristics of GDM patients during the first pregnancy and to identify risk factors for GDMR in the subsequent pregnancy. A $P < 0.05$ was considered significant.

RESULTS

Three hundred seventy-six women were enrolled in the study, including 166 women with GDMR (44.15%) and 210 (55.85%) without GDMR. The general characteristics of the participants are shown in Table 1. The mean age and the proportion of women ≥ 35 years of age were significantly different between the two groups (Tab. 1). There were no significant changes between groups in gestational interval, gravidity, and parity.

Table 2 shows the glucose biomarker levels for the two groups. The GDMR

group OGTT 1h-1 (9.87 ± 1.58 mmol/L vs 8.93 ± 1.54 mmol/L), OGTT 2h-1 (8.76 ± 1.49 mmol/L vs 7.82 ± 1.44 mmol/L), FPG-1 + OGTT 1h-1 (14.83 ± 1.78 mmol/L vs 13.79 ± 1.41 mmol/L), FPG-1 + OGTT 2h-1 (13. 72 ± 1.64 mmol/L vs 12.65 ± 1.44 mmol/L), OGTT 1h + 2h-1 (18.62 ± 2.66 mmol/L vs 16.72 ± 2.10 mmol/L), and FPG-1 + OGTT 1h + 2h-1 levels (23.59 ± 2.78 mmol/L vs 21.58 ± 2.34 mmol/L) were significantly higher than the non-GDMR group (all p values < 0.0001), but the FPG-1 level did not differ between the 2 groups (4.96 ± 0.69 mmol/L vs 4.86 ± 0.50 mmol/L, p = 0.69).

The number of biomarker abnormalities was significantly higher in the GDMR group than the non-GDMR group, as follows: OGTT 1h-1 (53.61% vs 32.38%, p < 0.0001), OGTT 2h-1 (61.45% vs 42.85%, p < 0.0001), FPG-1 + OGTT 1h-1 (18.07% vs 5.71%, p < 0.0001), FPG-1 + OGTT 2h-1 (18.07% vs 3.33%, p < 0.0001), OGTT 1h + 2h-1 (35.54% vs 12.86%, p < 0.0001), and FPG-1 + OGTT 1h + 2h-1 levels (13.25% vs 1.43%, p < 0.0001); however, the FPG-1 level (42.77% vs 43.81, p = 0.840) was not statistically different between the groups (Fig. 1).

ANCOVA (Tab. 3) showed significant changes in the OGTT 2 h-1 (p = 0.04) and FPG-1 + OGTT 2 h-1 levels (p = 0.02) in the GDMR group compared to the non-GDMR group during the first and subsequent pregnancies.

The receiver operating characteristic (ROC) curve analysis (Fig. 2 and 3; Tab. 4) showed that the FPG-1 + OGTT 1h + 2 h-1 level was the best predictor of GDMR with an area under the receiver operating characteristic curve (ROC-AUC), sensitivity, and specificity of 0.70, 0.45, and 0.85, respectively. Binary logistic regression analysis (Tab. 5) showed that the risk factors for GDMR were (in descending order) the FPG-1 + OGTT 1h + 2 h-1 level (OR, 10.542; 95% CI, 3.097–35.881; p < 0.0001), followed by the FPG-1 + OGTT 1h-1 (OR, 6.640; 95% CI, 1.088–7.360; p < 0.0001), FPG-1 + OGTT 2h-1 (OR, 6.397; 95% CI, 2.732–14.980; p < 0.0001), OGTT 1h + 2h-1 (OR, 3.737; 95% CI, 2.235–6.249; p < 0.0001), OGTT 1h-1 (OR, 2.414; 95% CI, 1.586–3.674; p < 0.0001), and OGTT 2h-1 (OR, 2.215, 95% CI, 1.403–3.219; p < 0.0001).

DISCUSSION

The 75-g OGTT involves the administration of glucose in a controlled environment to determine the rate of glucose clearance from the blood and can be used to diagnose type 1, type 2, and gestational DM [12]. Antibodies are triggered in an autoimmune response, resulting in beta cell dysfunction in the pancreas of patients with type 1 DM[13]. The cells in the liver become resistant to insulin, resulting in decreased uptake of glucose in the blood in patients with type 2 DM. GDM is also a disease of insulin resistance, symptoms of which usually appear around the second trimester of pregnancy. GDM often resolves at the end of the pregnancy, but the parturient does bear the risk that type 2 DM may develop later in life [13].

Age is strongly associated with the risk of GDM. Women 35–39 years and > 40 years of age have 4- and 6-fold higher probability of GDM compared with women 20–24 years of age [14]. Our study comfirmed that women > 35 years of age had a higher GDMR rate. The interpregnancy interval, gravidity, and parity were not related to the occurrence of GDMR in the subsequent pregnancy. The risk of GDMR during pregnancy has not been established, but a study has confirmed that the risk of GDMR during pregnancy is > 50%, independent of the interval between deliveries [15]. Gravidity and parity are not significantly related to GDM and had no effect on GDMR [16]. A study of pregnant women in the Arab region showed that multiparas were 8.29-fold more likely to have GDM than nulliparas; however, after adjusting for maternal age and history of pregnancy loss, nulliparas were 2.95-fold more likely to progress to GDM than parous women[17]. Therefore, maternal age cannot be ruled out as a cause of the high rate of GDM among grand multiparas [17].

Using the plasma glucose levels as biomarkers, including FPG-1, OGTT 1h-1, OGTT 2h-1, FPG-1 + OGTT 1h-1, FPG-1 + OGTT 2h-1, OGTT 1h + 2h-1, and FPG-1OGTT 1h + 2h-1, women in the GDMR group had significantly higher levels during the first pregnancy, whereas the FPG concentration was not a useful maker to predict GDMR in the following pregnancy. The sensitivity of OGTT is between 81% and

93%, which is superior to the FGP level with a sensitivity between 45% and 54% [18].

The changes in blood glucose biomarker levels during the two pregnancies between the GDMR and non-GDMR groups were compared using ANCOVA. The difference between the OGTT 2h-1 and FPG-1 + OGTT 2h-1 level in the GDMR group in the first and subsequent pregnancy was prominent, thus an abnormal (cut-off > 23.6 mmol/L) OGTT 2h-1 level is an important biomarker for predicting GDMR. Compared with impaired FPG (IFPG), an increase in the blood glucose level in the OGTT 2h indicates more severe insulin resistance and β-cell dysfunction in patients with impaired glucose tolerance. These results indicate β-cell defects in patients with IFPG and impaired glucose tolerance [19]. High OGTT 2h levels indicate not only an impaired β-cell response to hyperglycemia, but also a defect in incretin action and inhibition of glucagon levels [20].

According to the data in Figure 1, among southern Chinese women, 61.45% with GDMR have OGTT 2h-1 levels significantly higher than normal (8.5 mmol/L). The GDMR rate is variable between studies[21–23]. A meta-analysis by Schwartz [21], including studies from 1973–2014, indicated that the rate varied in ethnic groups between 30% and 80%. Non-Hispanic white populations have a lower GDMR of 30%, while Latinas and Hispanics have GDMR > 50% [22]. In our study, the population consisted of Han Chinese without immigration and the GDMR rate was 44.15%, which was similar to the GDMR in Korean women, as reported by Kwak et al. [23]. The variations were affected by differences in susceptibility to GDM between ethnic groups and the testing criteria for GDM. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) standards may facilitate the diagnosis of women with GDM more easily [24]; however, the ROC data showed that the AUC of the OGTT 2h-1 level was lower than the FPG-1 + OGTT 1h + 2h-1 level, which means that the OGTT 1h-1 level should be observed when predicting GDMR.

It has been reported that the OGTT 1h level can be used as a new biomarker, which can detect abnormal blood glucose levels earlier than the currently

recommended screening criteria for glucose disorders [25]. An abundance of evidence shows that a plasma glucose value ≥ 8.6 mmol/L 1 h after loading indicates an immediate loss of insulin response after eating [25]. The clinical manifestations of diabetic hyperglycemia can be caused by progressive β-cell failure, peripheral insulin resistance, and decreased availability of insulin, GLP-1, and amylin [26]. Individuals with reduced β-cell function can be identified before progressing to prediabetes and DM, and the predictive ability of individuals who may progress to DM is higher than the HbA1c or OGTT 2h levels [25–27]. In women between 24 and 28 weeks gestation, if the OGTT 1h level is consistent with impaired or abnormal glucose tolerance, then a OGTT-2h is required to confirm the diagnosis of DM [12]. OGTT detects whether there is a delayed response of the pancreas to excrete insulin or a delayed uptake of glucose by the liver [12].

In recent years, it has been suggested that non-diabetic patients with an OGTT 1h level > 8.6 mmol/L + ATP III are classified as low-moderate-high risk for diabetes according to the metabolic syndrome criteria of the Botnia study [28]. It has also been reported that patients with an OGTT 1h level ≥ mmol/L are at greater risk of DM than patients with IFPG [29]. A higher antepartum blood glucose level is associated with more severe insulin resistance and decreased pancreatic β cell function[30]. Recent evidence indicates that women with an OGTT 1h level ≥ 8.6 mmol/L are more likely to develop impaired glucose tolerance after delivery than women without GDM [30]. Even if the OGTT blood glucose level is normal in the puerperium there is a possibility of insulin resistance and impaired β cell function. In addition, parturients with abnormal glucose metabolism suffer more significantly [30].

The higher the postprandial blood glucose level, the more likely GDM will recur. Abnormal post-load hyperglycemia during pregnancy is considered a risk factor for DM [31]. A study demonstrated that elevated OGTT 1h and 2h values increase the risk for developing type 2 DM [31]. GDM is considered to lead to prediabetes. Women with GDM with elevated OGTT 1h and 2h blood glucose levels should actively change their lifestyle.

A study conducted by Wang [32] reported that elevated OGTT 1h and lower FPG levels in the first trimester predicts a higher risk of GDM recurrence [32]. A meta-analysis showed that the FPG level in the antepartum OGTT was a significant predictor of type 2 DM [33]. The metabolic determinants of the FPG and OGTT 2h glucose values are different [33, 34]. The fasting glucose level depends on hepatic insulin resistance, while an elevated 2-h plasma glucose level is associated with muscle insulin resistance [35]. Festa showed that isolated IGT tends to have higher peak insulin concentrations and lower proinsulin content than isolated IFPG [36]. IGT is associated with more severe insulin resistance than IFPG[36]. We speculate that an elevated FPG level in the OGTT, without increasing the postprandial glucose level, has lower insulin resistance. An isolated elevated FPG level in the OGTT in women diagnosed with GDM is a protective factor for the recurrence of GDM in the subsequent pregnancy.

Furthermore, the FPG-1 + 1h + 2hr-1were of higher risk of GDMR than one elevated glucose value. It is concerned with more severe damage to pancreatic islet β-cell function. In our case, it is easy to speculate that pronounced insulin resistance was associated with more GDMR.

When the threshold of the FPG-1 + OGTT 1h + 2h-1 level in the first pregnancy was > 23.6 mmol/L, women had a 10-fold higher risk of developing GDMR in the second pregnancy than women in the non-GDMR group.

In addition, high OGTT 1h-1 or 2h-1 levels were also related to GDMR. A meta-analysis showed that the antepartum OGTT glucose level predicts the risk of incident type 2 DM (OR range: 3.64–15; RH = 2.13) [37], which is related to the severity of maternal hyperglycemia. Age > 35 years was a week predictor of GDMR (OR, 1.880; 95% CI, 1.001–3.553; p = 0.050) and had no significant interaction with any biomarkers based on binary logistic regression analysis.

There were a few limitations in this study. First, BMI information before pregnancy and weight gain during pregnancy were not available, both of which may have a significant effect on GDMR. Second, the postpartum OGTT results of the

women following the first delivery were not available. Most women thought their likelihood of developing type 2 DM was low, and there was no need to undergo a postpartum OGTT [38]. Furthermore, information about diet control and physical activity following the first pregnancy was difficult to collect, although dietary and exercise therapy improves insulin resistance. This depends on more effective education on GDM and increasing awareness of postnatal follow-up in the future.

CONCLUSIONS

In summary, the current study showed that the OGTT 1h-1 and 2h-1 levels are independent risk factors for GDMR in southern Chinese women. When the threshold for the FPG-1 + OGTT 1h + 2h-1 level in the first pregnancy was >23.6 mmol/L, the women had a 10-fold higher risk of developing GDMR in the second pregnancy than women in the non-GDMR group.

Funding

This study was supported by Science and Technology Plan Project of Panyu District, Guangzhou (No.2019-Z04-55 and No.2020-Z04-109).

Author Contributions

Y. Liang conceived the study and design. J. Gong, X. Chen, G. Li, X. Lin facilitated acquisition of the data. J. He, Y. Chen, R. Wang analyzed the data. Y. Liang interpreted the data and drafted the manuscript. All the authors provided critical review and made major revisions on the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by Science and Technology Plan Project of Panyu District,

Guangzhou (No.2019-Z04-55 and No.2020-Z04-109).

Conflict of Interest

The authors declare that they have no competing interests.

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Table 1. Maternal characteristics in the first and subsequent pregnancies

Variables	**GDMR group N = 166**	**Non-GDMR group N = 210**	**t or χ^2**	**p**
Age[a]	28.13 ± 3.67	27.13 ± 3.26	2.79	= 0.006
Age[b]	30.66 ± 3.82	29.67 ± 3.37	2.67	= 0.008
≥ 35 years[a]	9□5.42%□	3□1.45%□	4.79	= 0.029
≥ 35 years[b]	26□15.76%□	19□9.05%□	3.86	= 0.05
Interpregnancy interval [years][c]	30.36 ± 12.23	30.46 ± 12.37	-0.075	= 0.940
Gravidity	1.61 ± 0.90	1.53 ± 0.81	0.89	= 0.37

Parity	1.07 ± 0.28	1.83 ± 0.36	-0.38	= 0.70

[a] represents the first pregnancy; [b] represents the second pregnancy; [c] refers to the months between delivery of the first pregnancy and the date of the last menstrual period in the subsequent pregnancy; GDMR — gestational diabetes mellitus recurrence

Table 2. Characteristics of the 75-g OGTT in the first pregnancy

Glucose biomarkers	**GDMR group N = 166**	**Non-GDMR group N = 210**	**t**	**p**
FPG-1	4.96 ± 0.69	4.86 ± 0.50	1.70	= 0.69
OGTT 1h-1	9.87 ± 1.58	8.93 ± 1.54	5.78	< 0.0001
OGTT 2h-1	8.76 ± 1.49	7.82 ± 1.44	6.13	< 0.0001
FPG-1 + OGTT 1h-1	14.83 ± 1.78	13.79 ± 1.41	6.32	< 0.0001
FPG-1 + 2h-1	13.72 ± 1.64	12.65 ± 1.44	6.74	< 0.0001
OGTT 1h + 2h-1	18.62 ± 2.66	16.72 ± 2.54	7.07	< 0.0001
FPG-1 + OGTT 1h + 2h-1	23.59 ± 2.78	21.58 ± 2.34	7.58	< 0.0001

GDMR — gestational diabetes mellitus recurrence; FPG-1 — fasting plasma glucose during the first pregnancy; OGTT 1h-1 — 1-h post-load glucose level during the first pregnancy; OGTT 2h-1 — 2-h post-load glucose level during the first pregnancy; FPG-1 + OGTT 1h-1 — the sum of FPG-1 and OGTT 1h-1; FPG-1 + OGTT 2h-1 — the sum of FPG-1 and OGTT 2h-1; OGTT 1h + 2h-1 — the sum of OGTT 1h and 2h-1; FPG-1 + OGTT 1h + 2h-1 — the sum of FPG-1 + OGTT 1h and 2h-1

Table 3. ANCOVA data for the OGTT between the first and subsequent pregnancies

Glucose biomarkers	GDMR group 1 (n = 166)*	GDMR group 2 (n = 166)**	Non-GDMR group 1 (n = 210)*	Non-GDMR group 2 (n = 210)**	F	p
FPG-1	4.96 ± 0.69	4.89 ± 0.72	4.86 ± 0.50	4.53 ± 0.34	0.90	= 0.34
OGTT 1h-1	9.87 ± 1.58	10.20 ± 1.73	8.93 ± 1.54	7.98 ± 1.25	1.25	= 0.26
OGTT 2h-1	8.76 ± 1.49	8.84 ± 1.81	7.82 ± 1.44	6.88 ± 1.02	4.82	= 0.04
FPG-1 + OGTT 1h-1	14.83 ± 1.78	15.10 ± 2.01	13.79 ± 1.41	12.51 ± 1.29	1.08	= 0.30
FPG-1 + OGTT 2h-1	13.72 ± 1.64	13.74 ± 2.04	12.65 ± 1.44	11.41 ± 1.09	5.24	= 0.02
OGTT 1h + 2h-1	18.62 ± 2.66	19.05 ± 3.13	16.72 ± 2.54	14.86 ± 1.96	1.57	= 0.21
FPG-1 + OGTT 1h + 2h-1	23.59 ± 2.78	23.94 ± 3.35	21.58 ± 2.34	19.38 ± 1.99	1.82	= 0.18

GDMR — gestational diabetes mellitus recurrence; ANCOVA — analysis of covariance; * — first pregnancy; ** — subsequent pregnancy; FPG-1 — fasting plasma glucose during the first pregnancy; OGTT 1h-1 — 1-h post-load glucose level during the first pregnancy; OGTT 2h-1 — 2-h post-load glucose level during the first pregnancy; FPG-1 + OGTT 1h-1 — the sum of FPG-1 and OGTT 1h-1; FPG-1 + OGTT 2h-1 — the sum of FPG-1 and OGTT 2h-1; OGTT 1h + 2h-1 — the sum of OGTT 1h and 2h-1; FPG-1 + OGTT 1h + 2h-1 — the sum of FPG-1, OGTT 1h and 2h-1

Table 4. The area under the receiver operating characteristic curve of glucose biomarkers

Glucose biomarkers	AUC	Cut-off > (mmol/L)	Sensitivity	Specificity

FPG-1	0.54	5.46	0.22	0.90
OGTT 1h-1	0.66	9.10	0.72	0.51
OGTT 2h-1	0.67	7.42	0.85	0.71
FPG-1 + OGTT 1h-1	0.67	14.1	0.70	0.56
FPG-1 OGTT 2h-1	0.69	12.9	0.75	0.54
OGTT 1h + 2h-1	0.69	18.3	0.55	0.72
FPG-1 + OGTT 1h + 2h-1	0.70	23.6	0.45	0.85

AUC — the area under the receiver operating characteristic curve; FPG-1 — fasting plasma glucose during the first pregnancy; OGTT 1h-1 — 1-h post-load glucose level during the first pregnancy; OGTT 2h-1 — 2-h post-load glucose level during the first pregnancy; FPG-1 + OGTT 1h-1 — the sum of FPG-1 and OGTT 1h-1; FPG-1 + OGTT 2h-1 — the sum of FPG-1 and OGTT 2h-1; OGTT 1h + 2h-1 — the sum of OGTT 1h and 2h-1; FPG-1 + OGTT 1h + 2h-1 — the sum of FPG-1 + OGTT 1h and 2h-1

Table 5. Select characteristics of glucose biomarkers associated with the risk for gestational diabetes mellitus recurrence

Variables	**OR (95% CI)**	**P**
FPG-1	0.959 (0.636-1.446)	= 0.840
OGTT 1h-1	2.414 (1.586-3.674)	< 0.0001
OGTT 2h-1	2.215 (1.403-3.219)	< 0.0001
FPG-1 + OGTT 1h-1	6.640 (1.088-7.360)	< 0.0001
FPG-1 + OGTT 2h-1	6.397 (2.732-14.980)	< 0.0001

OGTT 1h + 2h-1	3.737- (2.235-6.249)	< 0.0001
FPG-1 + OGTT 1h + 2h-1	10.542(3.097-35.881)	< 0.0001
Age (> 35 y)	1.880 (1.001-3.553)	= 0.050

FPG-1 — fasting plasma glucose during the first pregnancy; OGTT 1h-1 — 1-h post-load glucose level during the first pregnancy; OGTT 2h-1 — 2-h post-load glucose level during the first pregnancy; FPG-1 + OGTT 1h-1 — the sum of FPG-1 and OGTT 1h-1; FPG-1 + OGTT 2h-1 — the sum of FPG-1 and OGTT 2h-1; OGTT 1h + 2h-1 — the sum of OGTT 1h and 2h-1; FPG-1 + OGTT 1h + 2h-1 — the sum of FPG-1 + OGTT 1h and 2h-1

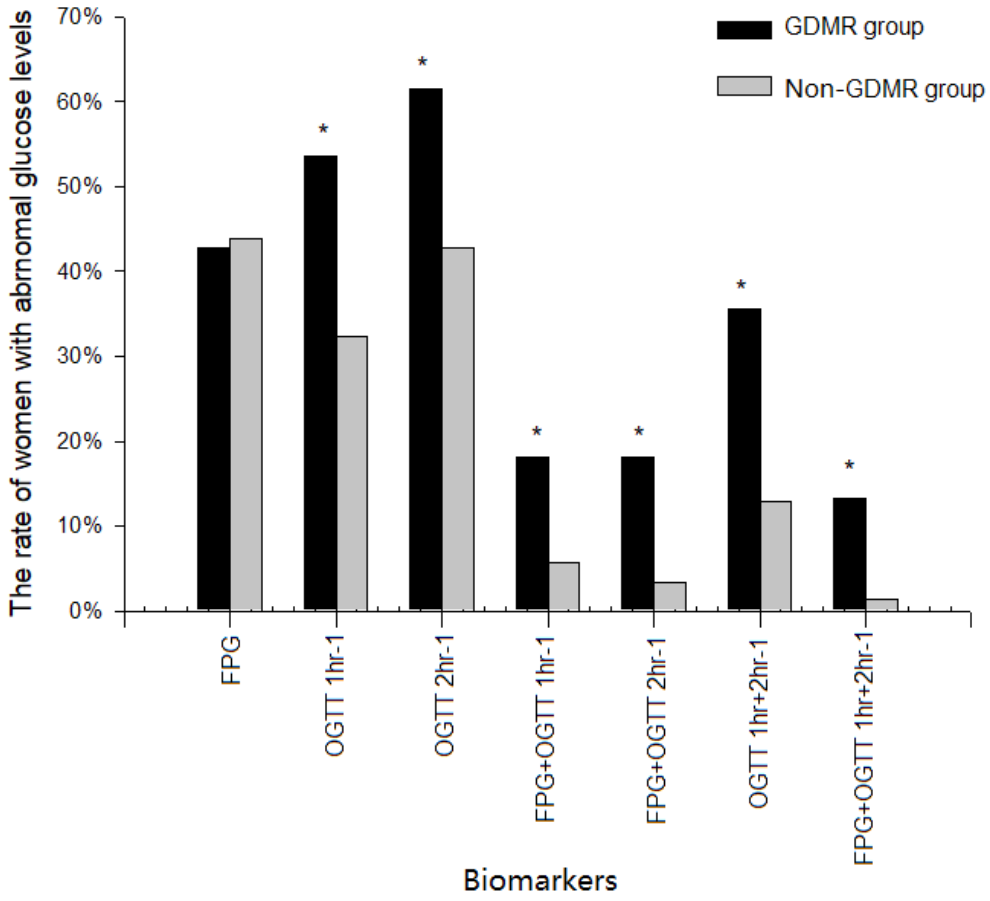

Figure 1. Comparison of the number of biomarker abnormalities (%) of women in the gestational diabetes mellitus recurrence (GDMR) and non-GDMR groups; * $p < 0.05$, GDMR group compared to the non-GDMR group

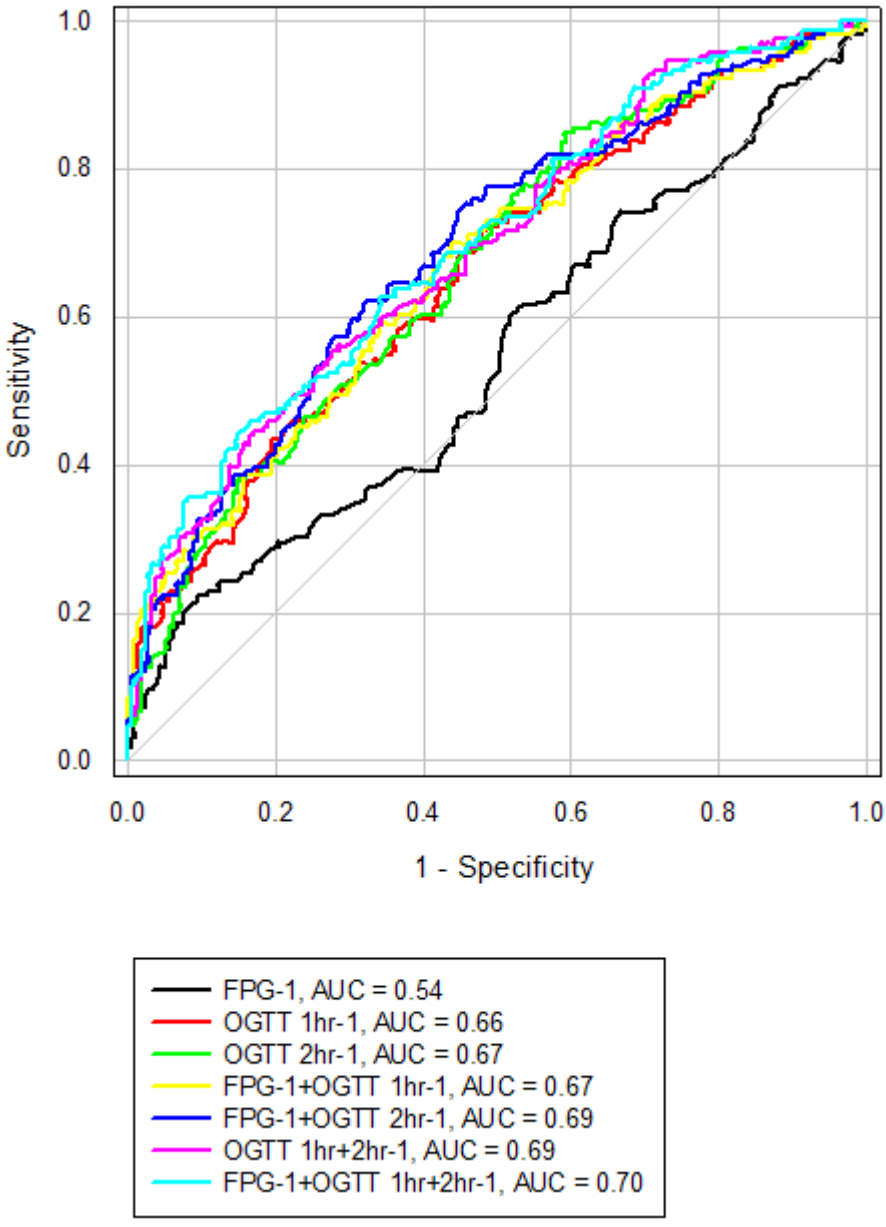

Figure 2. Receiver operating characteristic (ROC) curve analysis of blood glucose biomarkers in the GDMR and non-GDMR groups, FPG-1, fasting plasma glucose during the first pregnancy; OGTT 1h-1 — 1-h post-load glucose level during the first pregnancy; OGTT 2h-1 — 2-h post-load glucose level during the first pregnancy;

FPG-1 + OGTT 1h-1 — the sum of FPG-1 and OGTT 1h-1; FPG-1 + OGTT 2h-1 — the sum of FPG-1 and OGTT 2h-1; OGTT 1h + 2h-1 — the sum of OGTT 1h and 2h-1; FPG-1 + OGTT 1h + 2h-1 — the sum of FPG-1 + OGTT 1h and 2h-1

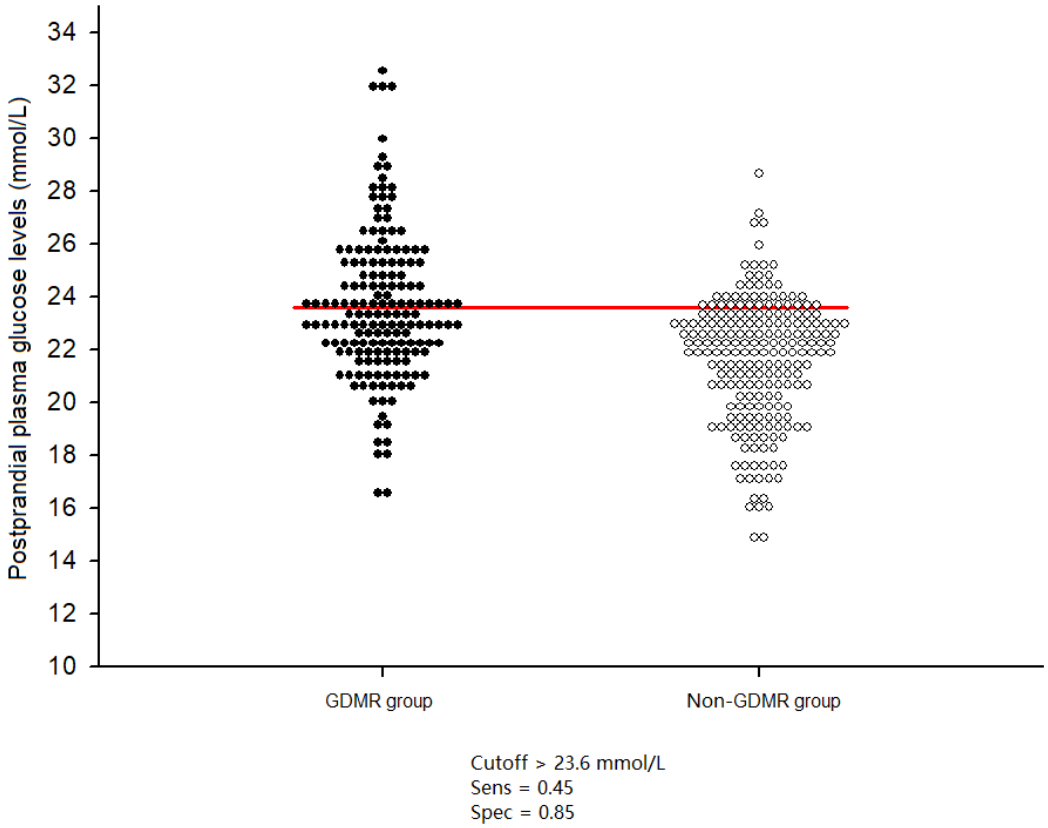

Figure 3. Dot histogram showing the area under the receiver operating characteristic curve (AUC), sensitivity, and specificity of FPG-1 + OGTT 1h and 2h-1