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The joint prediction model of pBMI and eFBG in predicting gestational diabetes mellitus

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Abstract

Objective: To explore the predictive value of prepregnancy body mass index (pBMI) and early gestational fasting blood glucose (eFBG) in gestational diabetes mellitus (GDM).

Methods: This case–control study enrolled pregnant women at 6 to 16 weeks of gestation. The pBMI, eFBG and glycosylated haemoglobin (HbA_{1c}) was recorded in the first trimester of pregnancy. Receiver-operating characteristic (ROC) curve analysis was used to measure the efficacy of factors that predict GDM.

Results: A total of 2119 pregnant women were enrolled in this study. Of these, 386 were diagnosed with GDM and 1733 did not have GDM. The age (odds ratio [OR] 1.16; 95% confidence interval [CI] 1.13, 1.20), pBMI (OR 1.12; 95% CI 1.07, 1.17) and eFBG (OR 5.37; 95% CI 3.93, 7.34) were independent risk factors for GDM occurrence. The areas under the ROC curve of eFBG, pBMI and eFBG + pBMI were 0.68 (95% credibility interval 0.65, 0.71), 0.66 (95% credibility interval 0.63, 0.69) and 0.71 (95% credibility interval 0.69, 0.74), respectively. The area under the curve of eFBG + pBMI was significantly higher than that of eFBG or pBMI alone.

Conclusion: The combination of eFBG and pBMI had a high predictive value for GDM.

Keywords

Gestational diabetes, fasting blood glucose, body mass index, predictive efficiency

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Introduction

In gestational diabetes mellitus (GDM), different levels of glucose metabolism occur during pregnancy, but blood sugar levels do not reach those of type 2 diabetes mellitus.[1] The incidence of GDM varies from

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2% to 25% of pregnant women, depending on demographic characteristics.[2,3] Recent studies have reported that the incidence of GDM is increasing annually.[3] Some studies have shown that GDM is associated with short- and long-term adverse events such as macrosomia, eclampsia, polyhydramnios and spontaneous abortion.[4] In addition, the risk of type 2 diabetes mellitus in pregnant women with GDM and their offspring also increases significantly.[5] During the early stage of pregnancy, women with a high risk of GDM are prescribed diet, exercise and medication that can significantly reduce the incidence of GDM and related undesirable outcomes.[6] This current study explored the predictive value of prepregnancy body mass index (pBMI) and early gestational fasting blood glucose (eFBG) for providing a theoretical basis for the early management of pregnant women at high risk for GDM. The aim is to find a model that can predict GDM in early pregnancy or before pregnancy.

Patients and methods

Patient population

This case–control study enrolled consecutive pregnant women, at 6 to 16 weeks of gestation, in the Department of Endocrinology, The Kunshan Hospital Affiliated with Jiangsu University, Suzhou, Jiangsu Province, China between January 2015 and March 2017. The inclusion criteria were as follows: (i) FBG and glycosylated haemoglobin (HbA_{1c}) values obtained at 6 to 16 weeks of gestation; (ii) oral glucose tolerance test (OGTT; 75 g glucose) performed at 24 to 28 weeks of gestation. Exclusion criteria were as follows: (i) history of type 1 or type 2 diabetes mellitus; (ii) twin or multiple pregnancy; (iii) FBG at the first antenatal care visit $\geq$7.0 mmol/l, FBG from OGTT $\geq$7.0 mmol/l or plasma glucose $\geq$11.1 mmol/l 2 h after a meal; (iv) diseases such as hypertension and hyperthyroidism; (v) incomplete medical history. According to the American Diabetes Association's criteria for screening and diagnosis of pregnant women who have not been diagnosed with diabetes mellitus, the 75-g OGTT can be used to screen for GDM at 24 to 28 weeks of pregnancy.[7] The diagnostic criteria were as follows: FBG $\geq$5.1 mmol/l, or plasma glucose $\geq$10.0 mmol/l 1 h after a meal, or plasma glucose $\geq$8.5 mmol/l 2 h after a meal. According to the diagnostic criteria, the patients were divided into a GDM group and a non-GDM group.

This study was approved by the Ethics Committee of The Kunshan Hospital Affiliated with Jiangsu University, Suzhou, Jiangsu Province, China (no. 2017-08-008-K01). Written informed consent was provided by the pregnant women at the first antenatal care visit.

Study methods

Demographic data including age, gestational age, parity, BMI, systolic blood pressure, diastolic blood pressure, past medical history, obstetric history, pregnancy follow-up data and pregnancy outcomes were retrospectively analysed using the Kunshan Maternal and Child Health Registration System. Height and weight were measured using an electronic measuring instrument and the mean values of the two measurements were obtained. The BMI was calculated using height and weight (BMI = weight/height; kg/m^2) measurements taken at 6–16 weeks of pregnancy and it was assumed that the weight of the pregnant women would be similar to that before pregnancy. HbA_{1c} and FBG were measured after an 8–10 h overnight fast. Pregnant women provided whole blood samples in hospital the day immediately after the first antenatal care visit. Nurses collected blood into a 1.5 mg/ml ethylenediaminetetraacetic acid K2 anticoagulant tube and a

nonanticoagulant tube. Whole blood was tested for HbA_{1c} immediately using an automated glycosylated haemoglobin analyser (Tosoh Automated Glycohemoglobin Analyzer HLC-723G8; Tosoh, Tokyo, Japan). Blood samples collected in the nonanticoagulant tube were used to produce serum and were tested for FBG immediately using a Roche E-170 automatic electrochemiluminescence detector (Roche, Shanghai, China) according to the manufacturer's instructions. At 24–28 weeks of gestation, the 75-g OGTT was performed to measure FBG, 1-h postprandial blood glucose and 2-h postprandial blood glucose.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp., Armonk, NY, USA). Data are presented as mean ± SD. An independent-sample *t*-test was used to compare the two groups. Logistic stepwise regression was used for univariate analysis. Significant variables ($P < 0.05$) were included in the regression model to analyse independent risk factors. Receiver-operating characteristic (ROC) curve analysis was used to measure the efficacy of factors that predict GDM. The area under the ROC curve was analysed by MedCalc version18.2.1 software (MedCalc Software, Ostend, Belgium). A *P*-value < 0.05 was considered statistically significant.

Results

A total of 2119 pregnant women, at 6 to 16 weeks gestation, were enrolled in this study. According to the diagnostic criteria, the patients were divided into a GDM group ($n = 386$) and a non-GDM group ($n = 1733$). As shown in Table 1, age, number of previous gestations, number of previous full-term pregnancies, pBMI, systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP) and eFBG in the GDM group were all significantly higher than those in the non-GDM group ($P < 0.05$ for all comparisons). No significant difference in the length of

Table 1. Clinical and demographic data of patients in the gestational diabetes mellitus group (GDM) and the non-GDM group that participated in a study to develop a model that can predict GDM in early pregnancy or before pregnancy.

Characteristic	GDM group $n = 386$	Non-GDM group $n = 1733$	*t*	Statistical significance[a]
Age, years	29.89 ± 4.32	26.63 ± 4.27	13.57	$P < 0.01$
Number of previous gestations	2.54 ± 1.32	2.23 ± 1.14	4.29	$P < 0.01$
Number of previous full-term pregnancies	1.68 ± 0.52	1.55 ± 0.53	4.33	$P < 0.01$
Length of pregnancy, days	81.08 ± 15.72	80.73 ± 16.26	0.39	NS
pBMI, kg/m^2	22.80 ± 3.11	21.16 ± 2.67	9.60	$P < 0.001$
Systolic blood pressure, mmHg	116.83 ± 10.78	113.22 ± 10.73	5.98	$P < 0.01$
Diastolic blood pressure, mmHg	72.85 ± 8.20	71.34 ± 7.89	3.39	$P < 0.01$
MAP, mmHg	87.51 ± 8.26	85.30 ± 7.93	4.92	$P < 0.01$
eFBG, mmol/l	4.92 ± 0.46	4.61 ± 0.40	12.40	$P < 0.01$
HbA_{1c}, %	5.17 ± 0.37	5.06 ± 1.07	1.94	NS

Data presented as mean ± SD.

[a]Between-group comparison; independent-sample *t*-test.

pBMI, prepregnancy body mass index; MAP, mean arterial pressure; eFBG, early gestational fasting blood glucose; HbA_{1c}, glycosylated haemoglobin; NS, no significant between-group difference ($P \geq 0.05$).

pregnancy or HbA_{1c} were found between the two groups.

Systolic and diastolic blood pressure values were excluded from the logistic regression analysis due to a significant correlation that was found between systolic blood pressure and MAP ($r = 0.85$, $P < 0.05$) and diastolic blood pressure and MAP ($r = 0.94$, $P < 0.05$). Age, number of previous gestations, number of previous full-term pregnancies, pBMI, MAP and eFBG were taken as independent variables to conduct multiple logistic regression analysis. The results showed that age (odds ratio [OR] 1.16; 95% confidence interval [CI] 1.13, 1.20), pBMI (OR 1.12; 95% CI 1.07, 1.17) and eFBG (OR 5.37; 95% CI 3.93, 7.34) were independent risk factors for GDM ($P < 0.01$ for each factor; Table 2).

The results of the ROC curve analysis showed that the areas under the ROC curve for eFBG, pBMI and eFBG + pBMI were 0.68 (95% credibility interval 0.65, 0.71), 0.66 (95% credibility interval 0.63, 0.69) and 0.71 (95% credibility interval 0.69, 0.74) ($P < 0.01$ for all analyses), respectively (Table 3). Sensitivity for eFBG, pBMI and eFBG + pBMI was 40.9%, 54.4% and 51.0%, respectively. Specificity for eFBG, pBMI and eFBG + pBMI was 87.3%, 69.6% and 81.0%, respectively. The cut-off value for eFBG, pBMI and eFBG + pBMI was 5.05 mmol/l, 22.25 kg/m^2 and 6.99, respectively. The combined prediction formula was eFBG (mmol/l) + pBMI (kg/m^2) *0.158/1.692. There was no significant difference in the area under the ROC curve for eFBG and pBMI, but the area under the

Table 2. Multiple-factor logistic regression analysis of predictive risk factors for gestational diabetes mellitus.

Covariant quantity	OR	95% CI		Statistical significance[a]
		Lower limit	Upper limit	
Age	1.16	1.13	1.20	$P < 0.01$
MAP	1.02	1.00	1.03	NS
Number of previous gestations	0.97	0.85	1.11	NS
Number of previous full-term pregnancies	0.84	0.61	1.14	NS
eFBG	5.37	3.93	7.34	$P < 0.01$
pBMI	1.12	1.07	1.17	$P < 0.01$

OR, odds ratio; CI, confidence interval; MAP, mean arterial pressure; eFBG, early gestational fasting blood glucose; pBMI, prepregnancy body mass index; NS, no significant association ($P \geq 0.05$).

Table 3. Receiver-operating characteristic (ROC) curve analysis of the efficacy of factors that predict gestational diabetes mellitus.

Variable	Area under the ROC curve	Credibility interval		Statistical significance	Sensitivity, %	Specificity, %
		Lower limit	Upper limit			
eFBG	0.68	0.65	0.71	$P < 0.01$	40.9	87.3
pBMI	0.66	0.63	0.69	$P < 0.01$	54.4	69.6
eFBG + pBMI	0.71	0.69	0.74	$P < 0.01$	51.0	81.0

eFBG, early gestational fasting blood glucose; pBMI, prepregnancy body mass index.

ROC curve for eFBG + pBMI was significantly higher than that of eFBG or pBMI alone ($P < 0.05$).

Discussion

The two-step method (50-g glucose tolerance test + 75-g glucose tolerance test) and the one-step method (75-g glucose tolerance test) are the most commonly used methods for the diagnosis of GDM. However, these methods are more complex, require more blood and are expensive, especially in economically underdeveloped areas. Thus, a simple and economical method of early diagnosis of GDM was the focus of the current study and the results confirmed that age, eFBG and pBMI were independent risk factors for GDM.

In this current study, the mean ± SD age of the women in the GDM group was 29.89 ± 4.32 years, which was significantly higher than that in the non-GDM group (26.63 ± 4.27 years; $P < 0.05$). Age was also an independent risk factor for GDM ($P < 0.05$), similar to previous research.[8] With an increase in age, the function of the pancreatic islets gradually declines, and insulin resistance progressively increases, thus increasing the likelihood of GDM.[8]

Previous research has shown that the incidence of GDM in pregnant women with high BMI before pregnancy is significantly increased,[9] which is consistent with the results of this present study. Obesity can be caused by hyperinsulinaemia;[10] and the dual influence of chronic insulin resistance in pregnant women with high BMI and physiological insulin resistance in late pregnancy is the cause of the increase in the incidence of GDM in pregnant women with high BMI.[11]

This study found that there was no significant difference in HbA_{1c} level between the GDM and non-GDM groups, so HbA_{1c} was not an independent predictor of GDM. A previous study reported that when the threshold of HbA_{1c} was 5.5%, the sensitivity was 82.1%.[12] Fifteen out of 90 women (16.7%) below the threshold were false negatives.[12] In high-risk pregnancies, when the threshold was 7.5%, the specificity of GDM was 95.8%.[12] Fifteen out of 21 patients (71.4%) were false positives.[12] Under any acceptable threshold of HbA_{1c}, the false positive rate is still high, and it is necessary to confirm OGTT for too many healthy women. Therefore, similar to the current results, HBA_{1c} levels in early pregnancy could not be used to screen for GDM.

This current study found the area under the combined ROC curve for eFBG + pBMI was significantly higher than that for eFBG or pBMI alone ($P < 0.05$), indicating that the pBMI + eFBG combined diagnosis had a higher predictive value for GDM as well as better specificity. A previous study found that the FBG level in pregnant women with GDM rises during early pregnancy, and when FBG is between 4.44 and 4.72 mmol/l, the sensitivity for predicting GDM is 75% to 55% and the specificity is 52% to 75%; whereas when BMI is between 25 and 28 kg/m^2, the sensitivity for predicting GDM is 60% to 40% and the specificity is 72% to 86%, and the area under the curve is similar.[13] These results were similar to the data in this current study.

This study had a number of limitations. A previous study found that the serum levels of sex hormone-binding globulin, homeostasis model assessment, low-density lipoprotein cholesterol and triglycerides in early pregnancy were important independent risk factors for GDM.[14] However, this current study did not include total cholesterol, low-density lipoprotein cholesterol and triglycerides in early pregnancy. Blood lipid assessment will be incorporated into future studies in order to improve the predictive model for GDM. In addition, future research will establish prediction models for high-risk and low-risk groups according

to BMI, family history of diabetes mellitus, history of hypertension, history of hyperlipidaemia and number of previous pregnancies.

In conclusion, age, pBMI and eFBG were independent risk factors for GDM; of which pBMI and eFBG were useful for GDM prediction. The combined prediction model, eFBG (mmol/l) + pBMI (kg/m^2) *0.158/1.692, had a higher predictive value than either pBMI or eFBG alone.

Author contributions

Y.P. and S.Z. conceived and designed the experiments. Y.P. conducted the experiments. Y.P. and S.Z. analysed the results. Y.P. and J.H drafted the manuscript. All authors participated in the discussion of the results and reviewed the manuscript.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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