Original Article

Maternal serum pentraxin 3 level in early pregnancy for prediction of gestational diabetes mellitus

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Background: Our study aimed to reveal the relationship of maternal pentraxin 3 (PTX3)'s serum concentrations in early pregnancy with gestational diabetes mellitus (GDM) and to explore its potential in the prediction of GDM.

Methods: Totally 824 pregnant women were enrolled and divided into a GDM group and a normal glucose tolerance (NGT) group, whose maternal fasting serum PTX3 levels, plasma glucose and insulin were collected. The beta cell function index and quantitative insulin sensitivity check index (QUICKI) was calculated and a homeostatic model assessment of insulin resistance (HOMA-IR) was used with SPSS 22 software used for statistical analysis.

Results: Of all subjects, 13.59% developed GDM. Compared to the NGT group, the PTX3 level was increased in the GDM group (1.48 *vs.* 1.52 ng/mL, P<0.05), and independently associated with the prediction of GDM (4.209, 95% CI, 1.756–10.091) (P=0.001). The area under receiver operating characteristic curve (AUROC) of the combined screening of PTX3 for GDM was incremented to 0.657 by the addition of maternal characteristics, and it reached a maximum of 0.743 in further combination with biochemical markers.

Conclusions: Serum PTX3 levels in early pregnancy may provide a useful approach for early prediction of GDM.

Keywords: Gestational diabetes mellitus (GDM); pentraxin 3 (PTX3); prediction

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Introduction

Gestational diabetes mellitus (GDM) is a disease, in which develops carbohydrate intolerance during pregnancy (1). Women with GDM will increase the risk of preeclampsia and a cesarean delivery, their offspring also have an increased risk of birth trauma macrosomia, and shoulder dystocia (2,3). Both mothers and their offspring have more likely developed cardiovascular disease, obesity, and type 2 diabetes mellitus (T2DM) (4-7).

Early intervention during pregnancy can significantly decrease the incidence of GDM, as well as less gestational weight gain and lower adverse outcomes of pregnancy, including hypertensive disorders, cesarean delivery and macrosomia (8-14). Sovio *et al.* indicated that before the diagnosis of GDM, there had already occurred accelerated fetal growth as early as 20 weeks of gestation (15). Furthermore, Logan *et al.* demonstrated that even mothers

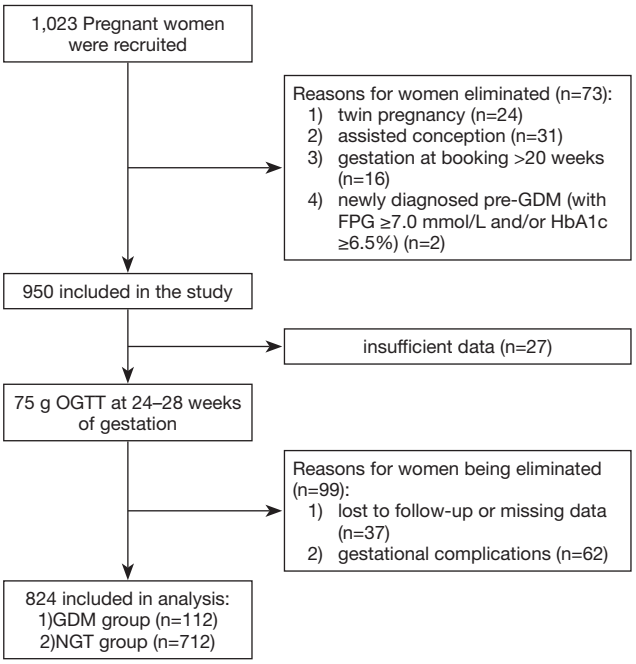

Figure 1 Flow diagram summarizing selection of patients.

with GDM had good glycemic control, their offspring also increased adiposity in early infancy (16). Early screening can improve glucose homeostasis and provide more time for intervention prior to term, so it is important to screen early in pregnancy to improve the outcome of GDM mothers and their fetus.

Recent evidence has suggested that the first trimester maternal serum levels of various biochemical factors are associated with GDM, including high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α (17), pregnancy-associated plasma protein A (18), placental growth factor (19), sex hormone-binding globulin, adiponectin and 1,5 anhydroglucitol (20), though not all were accurate as predictors.

In recent years, chronic subclinical inflammation is considered to have a potential role in the pathogenesis of hyperglycemia. Pentraxin 3 (PTX3), a recently identified multimeric inflammatory mediator, is correlated with the process of insulin resistance and its level is also increased in diabetes mellitus and diabetic nephropathy (21-23). Todoric *et al.* first observed that serum PTX3 concentrations are related to glucose levels in pregnant women with GDM and are negatively associated with insulin sensitivity, but their research focused on PTX3 serum concentrations at 24–28 weeks of gestation (24).

This study's first aim was to evaluate the relationship between the early maternal serum PTX3 and the occurrence of GDM at 24–28 weeks of gestation. The second goal was to measure the predictive value of PTX3 in early pregnancy in patients who developed GDM.

Methods

Patient population and data collection

A prospective cohort study was performed at Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, China between Oct 2015 and Dec 2015. We invited women with maternal age ≥18 years, singleton primipara pregnancy, nonsmokers, with confirmed gestation ≤20 weeks and spontaneous conception to participate our study. Women were excluded if they had multiple pregnancies, pre-GDM, hypertensive disorders, preterm delivery, cardiovascular disease, immunological disease, glucocorticoid therapy, or other severe illness. Women who were suffering from fetal abnormalities including chromosomally abnormal fetuses, structural defects or fetal growth restriction during pregnancy were also excluded.

On the first visit, held at ≤20 weeks of gestation, we recorded maternal characteristics and medical history and gestational age was confirmed. The levels of fasting serum PTX3 concentrations, fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c) and fasting plasma insulin (FINS) were tested at the first routine checkup. Additionally, during 24–28 weeks, all subjects accepted a 75 g OGTT. The study was approved by the Ethics Committee of our hospital (KS1535), and all participants signed the informed consent. The clinical trial registration number is NCT03563638.

A flow diagram describing the selection of women is shown in *Figure 1*. In total, 1,023 women with gestation ≤20 weeks were recruited. Excluded from the study were 199 women owing to twin pregnancy (n=24), assisted conception (n=31), gestation at booking >20 weeks (n=16), insufficient data (n=27), loss to follow-up or having missing data (n=37), gestational complications (n=62) or pre-GDM (n=2). The remaining 824 women were participated in the study.

GDM diagnostic criteria

GDM was verified in a one-step approach based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria (25). GDM is diagnosed when

any of the plasma glucose values are met or exceeded: FPG ≥5.1 mmol/L, 1h-PG ≥10.0 mmol/L or 2h-PG ≥8.5 mmol/L.

Laboratory measurements

We collected a venous blood sample from each participant at the first routine checkup. We separated the serum samples, and then stored them at –80 ℃ until we analyzed the levels of serum PTX3. At the same time, FPG, HbA1c and FINS were also tested.

Venous blood specimen collection of each woman was gathered at the first routine checkup, and the blood serum were then separated and stored at –80 ℃. The levels of PTX3, FPG, HbA1c and FINS from the samples were tested and analyzed subsequently. FPG was tested by G-6-PDH method, HbAlc was tested by HPLC method, and FINS was tested by Access Ultrasensitive Insulin method. The levels of serum PTX3 was tested by the same method of Akhter *et al.* (26). Serum PTX3 was analyzed using commercial sandwich ELISA kits (DY1826, R&D Systems, Minneapolis, MN, USA). The detection limit was 0.16 ng/mL. The intra-assay coefficient of variation (CV) was 10% and the inter-assay CV was 15% for the PTX3 assay.

Anthropometric measurements and data calculations

Pre-pregnant weight (in kg) was divided by height (in m) squared to count body mass index (BMI). After resting for five minutes in the sitting position, systolic blood pressure (SBP) and diastolic blood pressure (DBP) of each woman were measured on the right arm with an automated sphygmomanometer. [SBP (mmHg) +2× DBP (mmHg)]/3 was used to calculate mean arterial pressure (MAP). A HOMA2 calculator, released by the Diabetes Trials Unit affiliated to the University of Oxford, were employed to calculate homeostatic model assessment of insulin resistance (HOMA-IR) and HOMA-β data, which is available at: http://www.dtu.ox.ac.uk/homacalculator/index.php (updated January 8, 2013). Quantitative insulin sensitivity check index (QUICKI) used by the last equation, was calculated as 1/[log (FINS) + log (FPG)], as previously described by Katz *et al.* (27). The trapezoidal rule was applied to determine the AUCglu.

Statistical analyses

Continuous variables were summarized with mean ± standard deviation (mean ± SD) or median (inter-quartile range, IQR), while between-group comparisons were conducted by *t* tests or Wilcoxon rank tests according to assessments of normality and homogeneity of variance. Categorical variables were summarized with percentages, and two groups compared by the use of a chi-square test or Fisher's exact test as appropriate. Spearman correlation analyses were carried out to analyze relationships between PTX3 and other variables. Logistic regression analysis was fitted to analyze the contributions of variables including PTX3 and adjusted for potential factors. Specificity, sensitivity, positive and negative likelihood ratios, as well as positive and negative predictive values of PTX3 concentrations were calculated using tentative PTX3 thresholds to estimate the ability of PTX3 alone to serve as a predictor of GDM. Cut-off values of PTX3, HbA1c and FIN were determined by receiver operating characteristics (ROC) analysis using the Youden index. The predictive ability of each model was inferred using the area under the curve (AUROC). SPSS Statistics version 22.0 software was used to analyze all data. The difference was statistically significant when a P value <0.05. An AUROC >0.70 was defined as a significant discrimination.

Results

Clinical characteristics of the population

Of the 824 participants completing the study, 112 (13.59%) were diagnosed with GDM during 24–28 weeks of gestation. The median gestational weeks at the time of blood drawing for serum PTX3 test was 14.86 weeks (ranging from 10 to 20 weeks). Women who subsequently developed GDM, compared to those unaffected, were older (P=0.001), had higher HOMA-β (P=0.02), HbA1c (P=0.001), MAP (P=0.030), FINS and HOMA-IR levels (P=0.004), a lower QUICKI level (P<0.001), more often a first-degree relative history of diabetes (P=0.001), while the pre-pregnancy BMI ,FBG and the gestational weight gain up to the OGTT were similar between the outcome groups. Additionally, after adjustment for maternal age, MAP and family history of diabetes in a first-degree relative, the fasting PTX3 values in early pregnancy were statistically significantly higher in GDM subjects (P=0.011) (*Table 1*).

Relationship between PTX3 and relevant parameters in the 824 study participants

Spearman correlation analyses showed that PTX3 was

Table 1 Comparison of clinical characteristics between the two groups (n=824)

Characteristics	GDM group (N=112)	NGT group (n=712)	P value
Maternal age, years	29.79 (27.91–33.32)	28.84 (27.15–31.21)	0.001
Gravidity, n	1 [1–2]	1 [1–2]	0.139
First-degree relative history of diabetes, n (%)	17/112 (15.2%)	38/712 (5.3%)	0.001
History of PCOS, n (%)	1/112 (0.9%)	0/712 (0.0%)	0.136
Pre-pregnancy BMI, kg/m^2	20.44 (19.44–22.56)	20.28 (18.83–22.06)	0.061
MAP, mmHg	(86.73±8.56)	(84.96±7.85)	0.030
Gestation time at sampling for PTX3, weeks	14.71 (14.14–15.54)	14.86 (14.14–15.71)	0.334
HbA1c, %	5.00 (4.80–5.20)	4.90 (4.70–5.00)	0.001
FBG, mmol/L	4.40 (4.10–4.70)	4.30 (4.10–4.60)	0.079
FINS, uIU/mL	6.63 (4.35–9.07)	5.34 (3.77–7.44)	0.001
HOMA-IR	0.94 (0.43–1.45)	0.78 (0.23–1.33)	0.004
HOMA-β	116.43 (80.12–152.75)	106.74 (64.94–148.54)	0.02
QUICKI	0.37 (0.34–0.41)	0.39 (0.35–0.42)	0.000
PTX3, ng/mL	1.52	1.48	0.011
Gestation at OGTT, weeks	26.29 (25.29–27.00)	26.43 (25.43–27.00)	0.63
OGTT-0h-PG, mmol/L	4.45 (4.20–4.90)	4.30 (4.10–4.50)	0.001
OGTT-1h-PG, mmol/L	9.90 (8.83–10.58)	7.30 (6.40–8.28)	0.001
OGTT-2h-PG, mmol/L	8.70 (8.13–9.30)	6.50 (5.80–7.20)	0.001
OGTT-AUCglu, h*mmol/L	16.38 (15.45–17.05)	12.75 (11.55–13.85)	0.001
The gestational weight gain up to the OGTT	8.14 (4.39–11.89)	7.19 (0.59–13.79)	0.20

Data are expressed as median (IQR), number (%), or mean ± SE. Comparisons between outcome groups: Wilcoxon rank test or *t*-test for continuous variables, χ^2 test and Fisher's exact test for categorical variables. 0h-PG, fasting plasma glucose before glucose challenge; 1h-PG, 1 hour postprandial plasma glucose; 2h-PG, 2-hour postprandial plasma glucose; AUCglu, area under the curve of glucose during OGTT; BMI, body mass index; FBG, fasting blood glucose; FINS, fasting insulin; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment-insulin resistance index; HOMA-β, homeostasis model assessment beta cell function index; MAP, mean maternal pressure; OGTT, oral glucose tolerance test; PCOS, polycystic ovary syndrome; QUICKI, quantitative insulin sensitivity check index; GDM, gestational diabetes mellitus.

positively associated with FINS (r=0.132, P=0.001), 0h-PG (r=0.075, P=0.032), 1h-PG (r=0.086, P=0.014), and AUCglu (r=0.092, P=0.009) during OGTT, but negatively correlated with QUICKI (r=−0.133, P=0.001). After adjusting for maternal age, MAP and family history of diabetes, there was no statistically significant relationship between PTX3 levels with HbA1c, FPG or 2h-PG at the time of the OGTT (*Table 2*).

Evaluation of PTX3 for GDM

Hierarchical analysis was conducted for further assessment of PTX3 by percentile (*Table 3*). When the PTX3 level was below the 5th percentile (1.05 ng/mL) or the 10th percentile (1.12 ng/mL), the incidence of GDM was 0.00% and 1.20% respectively, the negative predictive rate was 100.0% and 98.8%, the false negative rate was 0.0% and 0.9%, and the negative likelihood ratio was 0.00 and 0.08, or <0.10 for both. When the PTX3 level was below the 15th percentile (1.18 ng/mL), a parallel result was obtained. At this cut-off point for PTX3 ($PTX3_{cutoff}$) of 1.21 ng/mL, the sensitivity of the prediction for GDM was 94.6%, the specificity was 20.2%, the negative predictive rate was 96.0%, and the negative likelihood ratio was 0.26 (*Table 4*).

Table 2 Association between PTX3 and clinical parameters in 824 study participants

Parameter	Spearman correlation coefficient	P value
HbA1c	–0.021	0.548
FBG	0.041	0.245
FINS	0.132	0.001
HOMA-IR	0.067	0.071
HOMA-β	0.054	0.143
QUICKI	–0.133	0.001
0h-PG at OGTT	0.075	0.032
1h-PG at OGTT	0.086	0.014
2h-PG at OGTT	0.067	0.055
AUCglu at OGTT	0.092	0.009

0h-PG, fasting plasma glucose before glucose challenge; 1h-PG, 1 hour postprandial plasma glucose; 2h-PG, 2-hour postprandial plasma glucose; AUCglu, area under the curve of glucose during OGTT; FBG, fasting blood glucose; FINS, fasting insulin; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment-insulin resistance index; HOMA-β, homeostasis model assessment beta cell function index; OGTT, oral glucose tolerance test; QUICKI, quantitative insulin sensitivity check index.

Compared to women with serum PTX3 <1.21 ng/mL ($PTX3_{cutoff}$), women with PTX3 ≥1.21 ng/mL in early pregnancy were 4.209 (95% CI, 1.756–10.091) times more likely to develop GDM (*Table 4*).

ROC analyses were performed to evaluate the usefulness of serum PTX3 levels for the prediction of GDM. The AUROC for prediction of GDM based on maternal characteristics incremented from 0.602 to 0.657 after the inclusion of PTX3, and reached a maximum of 0.743 after additional combination with biochemical markers including HbA1c and FINS (*Figure 2*).

Multivariate logistic regression analysis

We investigated the prediction GDM with the observed parameters using a multiple regression model (*Table 4*). According to the odds ratios, five variables were significantly and independently related to GDM including maternal age [adjusted odds ratio (AOR) for ≥35 years old, 4.235 (95% CI, 2.051–8.744); P<0.001], PTX3 [AOR for cutoff value, 4.209 (95% CI, 1.756–10.091); P=0.001], first-degree relative history of diabetes [AOR 3.604 (95% CI, 1.547–6.068); P=0.001], HbA1c [AOR for cutoff value, 2.833 (95% CI, 1.798–4.464); P<0.001], FINS [AOR for cutoff value, 1.919 (95% CI, 1.209–3.047); P=0.006]. There were no significant contributions from a history of polycystic ovary syndrome, pre-pregnancy BMI ≥24 kg/m^2 or FPG (cutoff value 4.65 mmol/L). All the cutoff values were based on the largest Youden index.

Discussion

The principal findings of this study were: (I) maternal serum levels of PTX3 in early pregnancy are significantly increased in pregnant women who develop GDM; (II) the AUROC for prediction of GDM based on PTX3 and other factors was 0.73; (III) PTX3 <1.21 pg/mL may be useful to rule out the diagnosis of GDM.

The prevalence of GDM in our study is 13.59%, and it was similar to other studies (28,29). PTX3 is produced in macrophages, granulocytes and endothelial cells, at inflammation's area. PTX3 together with the hs-CRP and other acute phase proteins, is an essential component of the humoral arm of innate immunity, and belong to the pentraxins' superfamily (30). PTX3 reflects tissue inflammation and damage under diverse clinical conditions (31). Syngelaki *et al.* showed that the levels of serum hs-CRP are not useful for first-trimester screening for GDM (17,20). A growing number of studies on the relationship between PTX3 and hyperglycemia associated with insulin resistance have been published that suggest potential involvement of PTX3 in diabetes mellitis pathology (21-24,32). PTX3 is a good predictor because its level in early pregnancy increases slightly but the change is limited (33). Furthermore, because PTX3 is related with the inflammation of vascular, PTX3 has been considered to associate with preeclampsia (34) and type 1 diabetes (35), and PTX3 levels are related to future cardiovascular disease risk (36). Therefore, we hypothesized that in the first trimester, the level of PTX3 as an inflammatory marker involved in pathogenesis of diabetes related comorbidities could be correlated with the development of GDM during pregnancy.

Our study shows that PTX3 level during pregnancy was significantly higher in GDM group. There was a significant positive correlation between serum glucose and PTX3, and a negative link with the QUICKI. These outcomes indicated that PTX3 may be associated with insulin resistance, which may have a role in the mechanism of development of GDM. PTX3 was negatively correlated

Table 3 Evaluation index of different PTX3 percentiles for GDM

PTX3 (ng/mL)	Incidence of GDM, %		Sensitivity, %	Specificity, %	Youden's index	FPR, %	FNR, %	PPV, %	NPV, %	+LR	–LR
	< Pn	≥ Pn									
P5 =1.05	0	14.3	100	5.6	0.06	94.4	0	14.3	100	1.06	0
P10 =1.12	1.2	15	99.1	11.4	0.1	88.6	0.9	15	98.8	1.12	0.08
P15 =1.18	4.1	15.3	95.5	16.6	0.12	83.4	4.5	15.3	95.9	1.15	0.27
P_{cutoff} =1.21	4.0	15.7	94.6	20.2	0.15	79.8	5.4	15.7	96	1.19	0.26
P20 =1.23	6.1	15.5	91.1	21.8	0.13	78.2	8.9	15.5	93.9	1.16	0.41
P25 =1.27	8.3	15.4	84.8	26.5	0.11	73.5	15.2	15.4	91.7	1.16	0.57
P30 =1.32	9.7	15.3	78.6	31.3	0.1	68.7	21.4	15.3	90.3	1.14	0.68
P35 =1.35	10.4	15.3	73.2	36.2	0.09	63.8	26.8	13.6	89.6	1.15	0.73
P40 =1.39	10.3	15.8	69.6	41.43	0.11	58.6	30.4	15.8	89.7	1.19	0.73
P45 =1.44	10.2	16.3	66.1	46.8	0.13	53.2	33.9	16.3	89.8	1.24	0.79
P50 =1.49	11.7	15.5	57.1	51.1	0.08	48.9	42.9	15.5	88.3	1.17	0.84
P55 =1.53	12.6	14.8	49.1	55.6	0.05	44.4	50.9	14.8	87.4	1.11	0.92
P75 =1.79	12.8	16.0	29.5	75.7	0.05	24.3	70.5	16.0	87.2	1.21	0.93
P85 =1.95	12.7	18.7	20.5	86.0	0.06	14.0	79.5	18.7	87.3	1.46	0.92
P95 =1.44	13.3	19.5	7.1	95.4	0.03	4.6	92.9	19.5	86.7	1.54	0.97

+LR, positive likelihood ratio; –LR, negative likelihood ratio; FNR, false negative rate, FPR, false positive rate, NPV, negative predictive rate, PPV, positive predictive rate; GDM, gestational diabetes mellitus.

Table 4 Multivariate logistic regression analysis for the prediction of GDM by all parameters

Values	B	S.E.	Wald	df	P	AOR	95% CI
Maternal age, 35 years old	1.443	0.370	15.226	1	<0.001	4.235	2.051–8.744
First-degree relative history of diabetes	1.120	0.349	10.314	1	0.001	3.064	1.547–6.068
History of PCOS	22.719	NA	0.000	1	1.000	NA	NA
Gravidity	–0.115	0.156	0.544	1	0.461	0.891	0.656–1.210
Parity	0.070	0.365	0.037	1	0.847	1.073	0.525–2.192
Pre-pregnancy BMI ≥24 kg/m^2	–0.203	0.334	0.369	1	0.544	0.816	0.424–1.571
MAP, mmHg	0.008	0.014	0.317	1	0.574	1.008	0.980–1.037
Gestation at sampling, weeks	–0.141	0.084	2.820	1	0.093	0.869	0.737–1.024
Gestation at OGTT, weeks	0.016	0.103	0.025	1	0.875	1.016	0.831–1.243
$PTX3_{cutoff}$*	1.437	0.446	10.378	1	0.001	4.209	1.756–10.091
FBG_{cutoff}	0.334	0.257	1.693	1	0.193	1.397	0.844–2.312
$HbA1c_{cutoff}$	1.041	0.232	20.151	1	<0.001	2.833	1.798–4.464
$FINS_{cutoff}$	0.652	0.236	7.644	1	0.006	1.919	1.209–3.047

Overweight was defined as BMI ≥24.0 kg/m^2; *, $PTX3_{cutoff}$ =1.21 ng/mL. BMI, body mass index; HbA1c, glycated hemoglobin; FPG, fasting plasma glucose; FINS, fasting insulin; MAP, mean maternal pressure; NA, not available; OGTT, oral glucose tolerance test; PCOS, polycystic ovary syndrome. GDM, gestational diabetes mellitus.

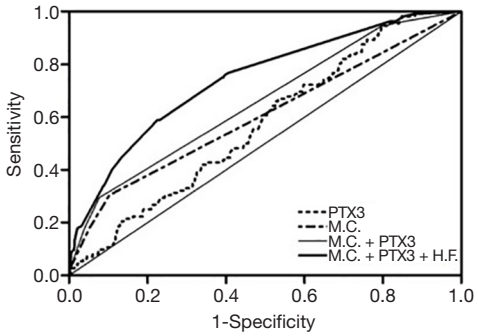

Figure 2 ROC curves of different combination screening for GDM. H.F., HbA1c and FINS; M.C., maternal characteristics (maternal age ≥35 years old, first-degree relative history of diabetes). PTX3, pentraxin 3; GDM, gestational diabetes mellitus.

with QUICKI, which showed that a higher level of PTX3 is related to lower insulin sensitivity, but more studies are needed to determine the mechanism. The present finding is in line with other recent studies (24,37).

Publications in the literature have reported that potential predictors of GDM, when used alone for screening, have some shortcomings, such as a low detection rate and high false positive rate. To make up for the limitations of single screenings, a variety of blood indicators have been used in combined screening for GDM (38,39). Our multiple logistic regression analysis on risk factor assessment of GDM revealed that five variables remained statistically significant among all the parameters (age of women, family history of diabetes in first-degree relatives, PTX3, HbA1c and FINS, $P<0.05$). Further, the AUROC for prediction of GDM based on maternal characteristics was improved after combination with PTX3, and reached a maximum of 0.743 with combination of other biochemical markers and characteristics of the mother. Such an elevation of AUROC after combining it with several clinical parameters is also consistent with reports in the literature (38,39).

One study reported different results from others. Lekva *et al.* (36) reported that PTX3 levels was significantly lower in women with GDM than those without GDM, not only at pregnancy but also at a 5-year follow-up by using the WHO criteria. This discrepancy could be due to fewer patients with GDM, the different GDM diagnostic criteria (WHO and IADPSG), and the screening time of OGTT at 30–32 weeks. The study also included preeclampsia, while our study excluded this disease.

An important strength of our study is that it was the first to examine PTX3 for the early prediction of GDM, and detected a significant increase of fasting serum PTX3 concentration in pregnant women who develop GDM, which may contribute to the early prediction of GDM. In addition, unlike other studies, we have identified a predictor; serum PTX3 <1.21 pg/mL may be useful to rule out the diagnosis of GDM. Therefore, if this finding is corroborated in future studies with more participants, women with lower levels will not need any further procedures to rule out GDM.

There are some limitations of this study. Its major shortcoming is that we have not examined the level of hs-CRP at the same time in different participants. Hs-CRP is also a classical inflammatory marker, and some research in the first trimester has suggested that hs-CRP might be a marker for prediction of GDM (40). Second, our study was not a sequential cohort study; we only collected values for different women at their first visit in different weeks of gestation, not throughout their entire pregnancy or after long-term follow-up. Third, further studies are required to investigate whether our results are reproducible at larger sample sizes.

Conclusions

We first demonstrated that serum PTX3 levels are an early predictor of GDM, and unlike other studies, lower serum PTX3 levels (<1.21 pg/mL) may be useful to rule out a diagnosis of GDM.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of our hospital (KS1535), and all participants signed the informed consent.

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