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Comparative analysis of perinatal outcomes in pregnant women with pregestational diabetes mellitus based on diagnostic timing

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Diabetes is a major concern in healthcare worldwide and is detrimental to mothers and fetuses during pregnancy. However, half of the women were unaware of hyperglycemia before pregnancy, and there is no consensus on their identification during pregnancy. We aim to understand the role that diagnostic timing plays in perinatal outcomes. This was a multicenter retrospective study of all pregestational diabetes mellitus (PGDM) women who delivered from January 2021 to June 2023. Diagnoses were made before or during gestation. Characteristics and outcomes were compared among stages, and logistic regression was performed to explore the relationship between adverse outcomes and the diagnostic timing. This study included 2,818 women; 1188 (42.2%) were self-aware before pregnancy, and 286 (10.1%), 1208 (42.9%), and 136 (4.8%) were diagnosed in the first, second, and third trimesters, respectively. Maternal body mass index, hypertensive disorders during pregnancy, glucose profile, large-for-gestational-age (LGA), etc., differed among stages (all P < 0.05). Logistic regression revealed that PGDM diagnosed during any trimester was significantly associated with an increased risk of macrosomia (aOR = 2.632, 1.502, 2.314; all P < 0.05). However, the risk of LGA decreased if the diagnosis was based on the 2 h value of the oral glucose tolerance test (OGTT) alone in the second trimester (aOR = 0.608, 95% CI: 0.444–0.831). No relationship existed between diagnostic timing and neonatal birth defects or hypoglycemia (both P > 0.05). PGDM identified during pregnancy was significantly associated with an increased risk of fetal overgrowth. The role of the 2 h-OGTT alone in diagnosis warrants further exploration. PGDM screening is essential for the entire gestational period.

Keywords Pregestational diabetes mellitus, Fetal overgrowth, Diagnostic timing, Large for gestational age, Macrosomia, Oral glucose tolerance test

Diabetes is one of the fastest-growing health issues worldwide and is the leading cause of a variety of life-threatening diseases. It is estimated that by 2045, the number of patients will reach 783 million worldwide[1]. In recent years, with rapid socioeconomic development, the prevalence has also risen sharply in China[2]. Moreover, the onset of diabetes tends toward reproductive-aged women[3], which puts them at greater risk during pregnancy, namely, embryo loss, fetal congenital anomalies, fetal overgrowth, etc[4]. , and may also impair the metabolic and cardiovascular development of offspring in the long term[5,6]. The situation became more serious after the full implementation of the third-child policy.

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Diabetes that occurs before pregnancy is referred to as pregestational diabetes mellitus (PGDM), but more than half of reproductive-aged women are unaware of hyperglycemia before pregnancy[7]. Moreover, due to maternal physiological glycemic changes during pregnancy (usually characterized by a mild decrease in fasting and a slight increase postprandial[8–10]), it is even more difficult to identify PGDM precisely during gestation. In light of this, PGDM which was first identified during pregnancy is often referred to as overt diabetes[11]or diabetes in pregnancy[12]. Even if the diagnostic criteria for pregnant patients are the same, the appropriate timing of diagnosis remains controversial[13]. Evidence is scarce regarding whether the PGDM newly diagnosed during pregnancy is as severe as it was identified before pregnancy[14,15], which is essential to their glycemic management.

In this study, we compared the maternal characteristics and perinatal outcomes between PGDM patients who were aware of their condition before pregnancy and those diagnosed at different stages of gestation. Our aim was to understand the significant impact of diagnostic timing on maternal and fetal outcomes.

Results

Characteristics and perinatal outcomes

In total, 2,818 pregnant women with PGDM were included in the study. There were 51 (1.81%) patients with type 1 diabetes, 2540 (90.13%) with type 2 diabetes and 227 (9.83%) with missing data. Among the entire study population, 1188 (42.2%) were self-aware before pregnancy, and 286 (10.1%), 1208 (42.9%), and 136 (4.8%) were newly diagnosed in the first, second, and third trimesters, respectively. Significant differences were observed among the four groups in maternal BMI, family history of diabetes, polycystic ovary syndrome, and HDPs. Specifically, women diagnosed in the second trimester had a higher proportion of nonoverweight/obese individuals and fewer HDPs (all $P<0.001$). During pregnancy, excessive GWG was most common in those diagnosed in the third trimester, while those diagnosed in the second trimester had the lowest FPG, medication usage, and the highest rate of third trimester HbA1c < 6% (all $P<0.001$). Perinatal outcomes, including fetal loss, birth defects, fetal overgrowth, PTB, mode of delivery, and neonatal hypoglycemia, also varied significantly. Notably, the rates of Cesarean delivery (CD) and LGA were lowest in the second trimester diagnosis group (all $P<0.001$) (Table 1).

	Valid cases ($N=2818$)	Self-reported diabetes ($N=1188$)	Diagnosed in the 1st trimester ($N=286$)	Diagnosed in the 2nd trimester ($N=1208$)	Diagnosed in the 3rd trimester ($N=136$)	*P* value
Age $\bar{x}\pm s$	2816	32.90 ± 0.18	33.53 ± 0.37	33.33 ± 0.18	32.95 ± 0.57	0.262
BMI < 24 kg/m^2 [n, (%)]	2427	336(37.8%)	53(23.2%)	557(51.0%)	32(28.3%)	<0.001*
24 ≤ BMI < 28 kg/m^2 [n, (%)]		329(33.1%)	81(35.5%)	337(30.9%)	39(34.5%)	
BMI ≥ 28 kg/m^2 [n, (%)]		289(29.1%)	94(41.2%)	198(18.1%)	42(37.2%)	
Family history of diabetes	2777	337(29.0%)	63(22.6%)	163(13.6%)	21(15.4%)	<0.001
Polycystic ovary syndrome	2574	87(8.0%)	6(2.3%)	41(3.7%)	9(6.8%)	<0.001
Hypertensive disorders of pregnancy	2646	371(33.0%)	86(31.5%)	206(18.4%)	50(38.8%)	<0.001*
Adequate GWG [n, (%)]	2417	386(39.5%)	86(37.4%)	472(44.0%)	33(29.5%)	<0.001&
Insufficient GWG [n, (%)]		226(23.1%)	75(32.6%)	315(29.4%)	16(15.2%)	
Excessive GWG [n, (%)]		365(37.4%)	69(30.0%)	285(26.6%)	62(55.4%)	
Medication usage in pregnancy	2661	885(77.7%)	222(80.1%)	424(38.0%)	68(52.3%)	<0.001*
HbA1c in the 3rd trimester	1899	5.80(5.40,6.30)	6.10(5.60,6.60)	5.70(5.32,6.10)	6.60(6.10,7.10)	<0.001
3rd trimester HbA1c < 6% [n, (%)]		464(58.6%)	85(43.4%)	524(65.8%)	15(13.0%)	<0.001*
Fasting glucose in the 3rd trimester	2280	5.17(4.54,6.07)	5.49(4.82,6.41)	4.85(4.31,5.60)	7.04(5.35,7.57)	<0.001*
Fetal loss	2818	28(2.4%)	5(1.7%)	5(0.4%)	2(1.5%)	<0.001
Birth defect##	2893	63(5.3%)	14(4.9%)	44(3.5%)	1(0.7%)	0.022
Preterm birth#	2818	226(19.5%)	62(22.1%)	211(17.5%)	46(34.3%)	<0.001
Cesarean Delivery# [n, (%)]	2777	853(73.5%)	218(77.6%)	741(61.6%)	106(79.1%)	<0.001*
Postpartum hemorrhage# [n, (%)]	2715	39(3.4%)	10(3.6%)	46(4.0%)	6(4.5%)	0.868
Birth weight## (g, $\bar{x}\pm s$)	2885	3162.10 ± 22.44	3276.09 ± 46.28	3154.27 ± 19.72	3207.39 ± 75.74	0.083
Small for gestational age## [n, (%)]	2875	84(7.0%)	21(7.4%)	77(6.1%)	6(4.3%)	0.519
Large for gestational age## [n, (%)]	2875	364(30.5%)	110(38.6%)	303(24.1%)	68(49.3%)	<0.001*
Macrosomia## [n, (%)]	2885	113(9.4%)	46(16.1%)	118(9.4%)	25(18.1%)	<0.001
Neonatal hypoglycemia## [n, (%)]	2546	56(5.4%)	20(8.4%)	49(4.6%)	17(14.0%)	<0.001

Table 1. Maternal characteristics and perinatal outcomes of patients diagnosed at different gestational stages. PGDM: pregestational diabetes mellitus, BMI: body mass index, GWG: gestational weight gain, HbA1c: glycosylated hemoglobin *Indicates significant statistical difference in the group diagnosed in the 2nd trimester compared to other 3 groups (multiple comparison, $P<0.0083$) &Indicates significant statistical difference in the group diagnosed in the 3rd trimester compared to other 3 groups (multiple comparison, $P<0.0083$) # Comparison was performed excluding fetal loss, ##comparison was performed among all the live neonates ($N=2885$).

Outcome	Adjusted Odds Ratio (95% Confidence Interval)		
	Diagnosed in the 1st trimester	Diagnosed in the 2nd trimester	Diagnosed in the 3rd trimester
Birth defect	1.195(0.598–2.387)	0.801(0.510–1.259)	0.223(0.030–1.659)
Large for gestational age	1.724(1.244–2.391)*	0.906(0.732–1.122)	1.672(1.089–2.566)*
Macrosomia	2.632(1.665–4.161)*	1.502(1.072–2.102)*	2.314(1.282–4.177)*
Neonatal hypoglycemia	1.304(0.681–2.499)	1.090(0.694–1.710)	1.608(0.743–3.481)

Table 2. Relationships between the diagnostic timing and the adverse perinatal outcomes. *Indicates significant statistical difference ($P < 0.05$). The reference group was self-reported diabetes before pregnancy. All the data of the live neonates were used. All models were adjusted for maternal age, hospital, maternal pre-pregnancy body mass index and family history of diabetes. In the analysis of large for gestational age, the model was further adjusted for gestational weight gain, and in the analysis of macrosomia and neonatal hypoglycemia, the models were adjusted for neonatal sex and gestational age at delivery as well.

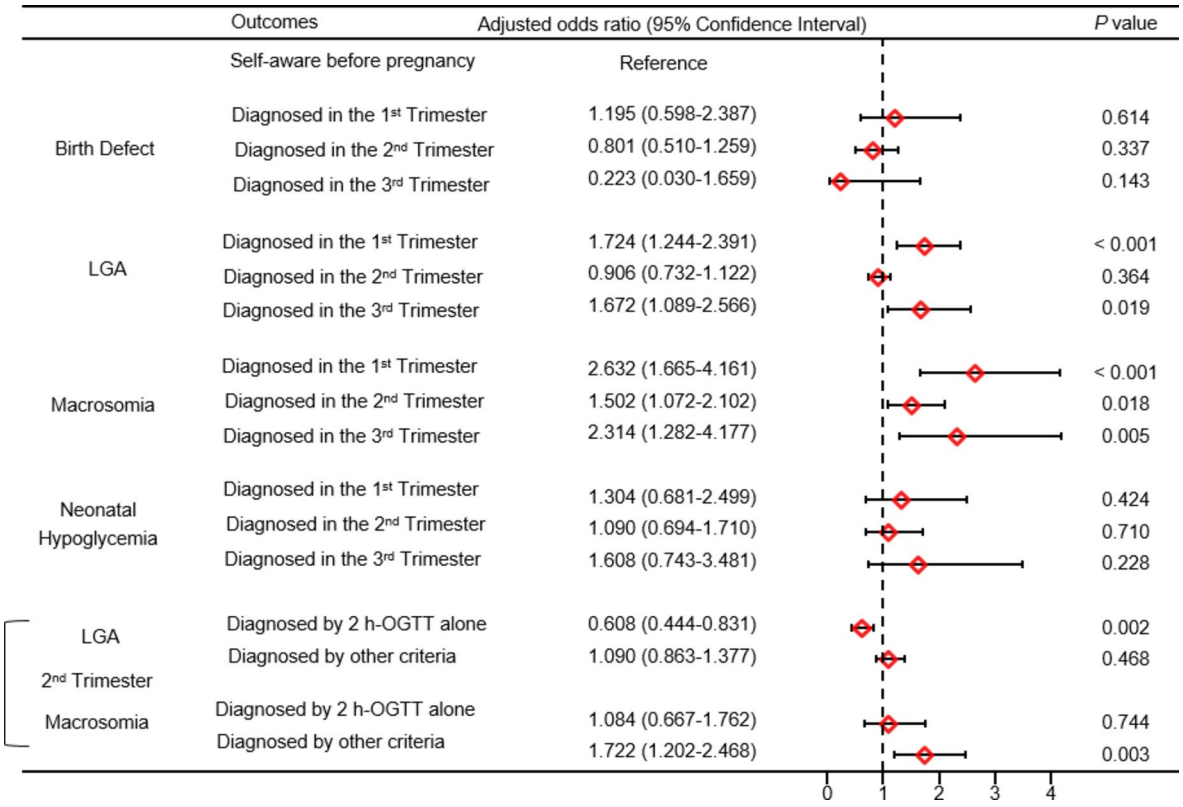

Fig. 1. Relationships between diagnostic timing of PGDM and the adverse perinatal outcomes. PGDM: pregestational diabetes mellitus, LGA: large for gestational age. OGTT: oral glucose tolerance test. Compared to the self-aware diabetes before pregnancy, PGDM diagnosed in any stages of pregnancy significantly increased the risk of macrosomia, and it increased the risk of LGA in both the first and third trimester as well. In the second trimester, the risk of macrosomia was only increased if the diagnosis was not based solely on the result of 2 h-OGTT.

Diagnostic timing and adverse perinatal outcomes

PGDM, which is newly identified during pregnancy, is strongly related to fetal overgrowth (Table 2). Multivariate logistic regression analysis revealed that, compared with women diagnosed before pregnancy, those diagnosed in the first trimester had a 70% higher risk of LGA (aOR = 1.724, 95% CI: 1.244–2.391) and a 160% higher risk of macrosomia (aOR = 2.632, 95% CI: 1.665–4.161). Diagnosis in the second trimester was associated with a 50% increased risk of macrosomia (aOR = 1.502, 95% CI: 1.072–2.102) but not the with risk of LGA (aOR = 0.906, 95% CI: 0.732–1.122). Those diagnosed in the third trimester had a significantly increased risk of both LGA (aOR = 1.672, 95% CI: 1.089–2.566) and macrosomia (aOR = 2.314, 95% CI: 1.282–4.177). However, no significant relationships were detected between diagnostic timing and birth defects or neonatal hypoglycemia (all $P > 0.05$). The associations between adverse perinatal outcomes and different timings of diagnosis are illustrated in Fig. 1.

Outcome	Adjusted Odds Ratio (95% Confidence Interval)	
	Diagnosed only by 2 h-OGTT	Diagnosed by other criteria other than 2 h-OGTT
Large for gestational age	0.608(0.444–0.831)*	1.090(0.863–1.377)
Macrosomia	1.084(0.667–1.762)	1.722(1.202–2.468)*

Table 3. The relationship between 2 h-OGTT or other diagnostic criteria and fetal overgrowth in the second trimester. OGTT: oral glucose tolerance test, *Indicates significant statistical difference ($P < 0.05$). The reference group was self-reported diabetes before pregnancy. All the data of the live neonates were used. Both models were adjusted for maternal age, hospital, maternal pre-pregnancy body mass index and family history of diabetes and gestational weight gain. In the analysis of macrosomia, the model was further adjusted for neonatal sex and gestational age at delivery.

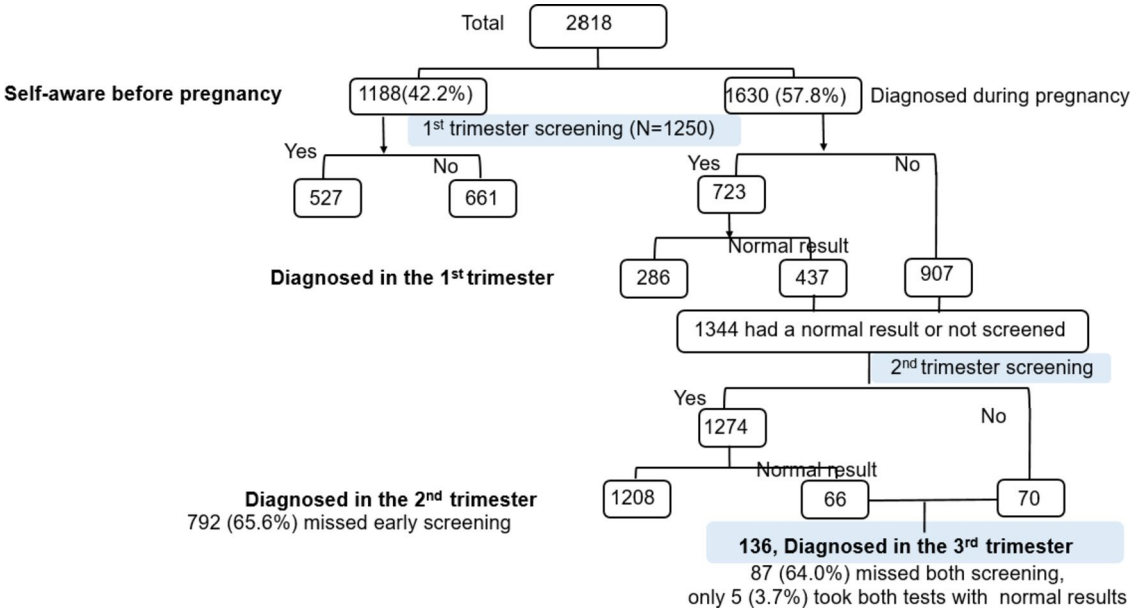

Fig. 2. The screening and classification of pregestational diabetes mellitus patients.

2 h-OGTT and fetal overgrowth

Subgroup analysis was further performed to explore the relationship between using the 2 h-OGTT alone for diagnosis or other criteria and fetal overgrowth in the second trimester (Table 3). Among the 1208 women, 446 were diagnosed by the 2 h-OGTT alone, and other criteria diagnosed 762. The results revealed that, compared with women diagnosed before pregnancy, using the 2 h-OGTT alone was not significantly correlated with macrosomia but was associated with a decreased risk of LGA by almost 40% (aOR = 0.608, 95% CI: 0.444–0.831). In contrast, diagnosis based on the other three criteria was significantly associated with an increased risk of macrosomia (aOR = 1.722, 95% CI: 1.202–2.468) but not with the risk of LGA (aOR = 1.090, 95% CI: 0.863–1.377). Moreover, when the diagnosis relied exclusively on the FPG, a significant correlation remained between elevated FPG levels and the occurrence of LGA or macrosomia, with ORs of 1.896 and 2.436 respectively (both $P < 0.05$, Supplementary Table 1).

The absence of screening in each stage

As shown in Fig. 2, of the 2818 PGDM patients, 1250 (44.4%) received early glucose screening, and 286 women were newly identified as having PGDM in the first trimester. Among the remaining 1344 (2818-1188-286) women who were not screened or had a normal result during the early screening, 1274 (94.8%) underwent an OGTT in the second trimester, and 1208 (74.1%) were additionally diagnosed; among these people, 792 (65.6%) did not undergo early glucose screening. The remaining 136 (1344 – 1208) patients were identified in the third trimester. However, 87 (64.0%) missed early screening and OGTT, and only 5 (3.7%) took both tests with normal glucose results.

Sensitivity analysis among singleton pregnancies with type 2 diabetes

A sensitivity analysis was performed among singleton pregnancies with type 2 diabetes in the study population ($N = 2444$), and we obtained similar results. As shown in Supplementary Tables 2 and 3, PGDM diagnosed in the first and third trimesters was significantly associated with LGA and macrosomia (all $P < 0.05$), whereas PGDM diagnosed in the second trimester was not significantly associated with either outcome (both $P > 0.05$).

Additionally, when diagnosis in the second trimester was based solely on the 2 h-OGTT, the risk of LGA decreased (aOR = 0.696, 95% CI: 0.495–0.980), while the risk of macrosomia increased if the diagnosis was based on other criteria (aOR = 1.648, 95% CI: 1.119–2.426).

Discussion

In this study, we found that the prevalence of self-reported diabetes before pregnancy was 42.2% among eight tertiary hospitals in urban China. The maternal characteristics, gestational glucose profile and perinatal outcomes differed among the diagnostic stages. While identification during pregnancy significantly increases the risk of fetal overgrowth, the value of a 2 h-OGTT alone in diagnosis requires further exploration. PGDM screening is crucial throughout the entire gestational period.

Several studies have compared PGDM diagnosed during pregnancy with other hyperglycemic categories and revealed a greater incidence of adverse perinatal outcomes (maternal retinopathy, pregnancy-induced hypertension, fetal malformation, macrosomia, neonatal jaundice, etc.) than prediabetes or gestational diabetes mellitus (GDM)[14,16–19]. Oppermann et al.[15] analyzed the data of 414 PGDM patients diagnosed before pregnancy and 204 patients diagnosed during pregnancy and found similar levels of maternal pre-pregnancy BMI, preeclampsia (PE), HbA1c (≥ 28 weeks), fetal congenital anomaly, neonatal birth weight, hypoglycemia, etc. (all $P > 0.05$) between the two groups, and he further stressed the importance of pre-pregnancy glycemic screening based on their glucose control level. In our study, if we combined all three groups that were diagnosed during pregnancy as a whole, we would find that the levels of maternal third trimester HbA1c, birth weight and LGA, neonatal hypoglycemia, etc., were comparable to those of the self-reported group (all $P > 0.05$, data not shown). However, considering the lack of hyperglycemic screening, maternal glucose variations, and diagnostic criteria, PGDM patients diagnosed at different stages exhibited distinct characteristics. Notably, those diagnosed in the second trimester, particularly by the 2 h-OGTT alone, may have the mildest hyperglycemic severity. Regnault et al.[20] reported that GDM patients diagnosed outside the 22–30 week (either < 22 weeks or > 30 weeks) had a higher risk of LGA (aOR = 1.55 and 1.44, respectively; both $P < 0.05$). This finding aligns with ours, possibly due to the lack of timely glycemic screening. However, even with sufficient screening, Cosson et al.[21] proved that only late-diagnosed PGDM (> 22 weeks) was significantly associated with maternal gestational hypertension and/or PE (aOR = 3.48, 95% CI: 1.26–9.57) but not early-diagnosed PGDM (< 22 weeks, $P > 0.05$). In their study, all the late-diagnosed PGDM patients had a normal FPG (< 5.1 mmol/L) at early screening, which indicated that maternal gestational glucose varied with gestation. Meanwhile, Skajaa et al.[22] and Dori-Dayan et al.[23] also reported that the insulin requirement varied in type 1 diabetic patients during pregnancy, with a sharp increase in the second trimester followed by a mild decrease near term.

To date, discrepancies still exist over the optimal timing and criteria of PGDM diagnosis during pregnancy. While a consensus has been reached over the significance of early screening before the late second trimester, evidence is missing on the later period[7,13,24,25]. Gupta et al.[26]. followed the OGTT results of 92 PGDM women diagnosed during pregnancy for more than three years and reported that the progression of diabetes was more common in those who were diagnosed in the first trimester than in those diagnosed in the second trimester (93.1% vs. 61.4%, $P = 0.005$). Regarding the diagnostic criteria, this study questions the adequacy of using the 2 h-OGTT alone. This is consistent with our previous findings: Women diagnosed only by the 2 h-OGTT had the lowest rates of cesarean delivery (CD) and preeclampsia (PE)[27], and only 10% progressed to diabetes within one year after delivery[28]. This theory was also supported by the finding that the 2 h-OGTT had the poorest diagnostic performance in predicting diabetes at 6–8 weeks after delivery[14], its area under the curve was only 0.476, whereas it was 0.611 for HbA1c and 0.726 for FPG[26]. Furthermore, Gupta et al.[26]. reported that the use of HbA1c and FPG before 15 weeks was estimated to be associated with 95% and 85.4% postpartum diabetes, respectively, whereas 58.9% of the participants were diagnosed with 2 h-OGTT. The higher proportion in their study compared to others is due to the increased rate with longer follow-up, rising from 47.4% in the first year to 86.8% after three years among PGDM women diagnosed during pregnancy. Given that maternal postprandial hyperglycemia during gestation is considered a protective anabolism for fetal development[29], the value of using the 2 h-OGTT alone for PGDM diagnosis remains uncertain in both short- and long-term contexts.

With the current data, we are delighted to see that the prevalence of self-reported diabetes has greatly improved in China over the past decade. According to our previous findings, this rate was only 1.20% according to a national survey of FPG in reproductive-aged women between 2010 and 2016[30]. Although the populations were different, progress can still be seen with such a significant gap. The current level was similar to the Chinese average rate of self-aware diabetes, which was reported to be 43.3% based on a cross-sectional survey[2]. However, in the current study, 65.6% of the women diagnosed in the second trimester missed early screening, only 3.7% of the patients diagnosed in the third trimester underwent both early screening and OGTT, and a delay in diagnosis was significantly associated with fetal overgrowth. These findings emphasize the importance of early PGDM screening as a priority in clinical practice[31].

To our knowledge, this is the first study that specifically compared the characteristics and outcomes of patients with PGDM diagnosed within trimesters. We have shown that variances exist among diagnostic stages and that identifying PGDM before pregnancy is essential. Our limitations include the following: first, without a postpartum glycemic profile, even though we have proven that the timing of diagnosis is significantly associated with fetal overgrowth, how it affects the occurrence and severity of maternal and neonatal metabolism in the long term remains unknown. Second, owing to the retrospective nature of the study, we could include only hospitalized patients, and those who experienced fetal loss in an earlier stage (whether screened or not) were overlooked. Moreover, the heterogeneity in hyperglycemic management among hospitals may influence the study results, even if we adjusted for hyperglycemic management as a confounder in the multi-regression analysis. Finally, although type 1, 2 or other specific diabetes has a unique etiology and glucose profile during pregnancy[32], considering the lower prevalence of type 1 and other specific types in China[2] and the missing medical records,

we did not differentiate them during the analysis. However, we showed that the same conclusion was reached for most (type 2) of the diabetic population. Prospective studies are essential to further validate the significance of the 2 h - OGTT alone in diagnosis, with a focus on both short - and long - term outcomes. Subsequently, clinical trials tailored to different glycemic control strategies should be conducted based on the results obtained.

In summary, compared with the self-reported diabetes before pregnancy, PGDM identified during pregnancy is strongly associated with an increased risk of fetal overgrowth, and the value of 2 h-OGTT alone in PGDM diagnosis warrants further exploration. Given the current situation, it is necessary to perform PGDM screening for the entire gestational period.

Methods

Study design and PGDM diagnosis

A multicenter retrospective cohort study was conducted among pregnant women diagnosed with PGDM either before or during gestation and delivered from January 1, 2021, to June 30, 2023, at eight hospitals in eight different regions in China. Information such as maternal age, pre-pregnancy weight, family history of diabetes and gestational complications, weight gain, PGDM treatment and perinatal outcomes, including neonatal birth weight and hypoglycemia, were extracted from the hospitals' inpatient medical records. The protocol and procedure of the study were reviewed and approved by the Institutional Review Board (IRB) of Peking University First Hospital, Beijing, China (identification number 2023-521-003), and the study was conducted in accordance with the World Medical Association's Declaration of Helsinki, with the need for informed consent to the participant waived by the hospital's IRB.

Self-reported PGDM refers to women who were known to have diabetes (determined by a health care professional) before pregnancy. PGDM was diagnosed during pregnancy was based on the criteria of the Chinese Guidelines for Pregnancy with Diabetes[33], including (1) fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L), (2) a 2-hour value of the oral glucose tolerance test (75 g OGTT) ≥ 200 mg/dL (11.1 mmol/L), (3) classic symptoms of hyperglycemia or hyperglycemic crisis with random plasma glucose ≥ 200 mg/dL (11.1 mmol/L), or (4) glycosylated hemoglobin ≥ 6.5% (48 mmol/mol). A diagnosis was made when any of the values met or exceeded the above criteria. In clinical practice, OGTT is recommended for all individuals between 24 and 28 weeks of gestation, FPG is widely used for hyperglycemic screening in the early and late gestational periods, and HbA1c is further implemented when a high-risk (family history of diabetes, accelerated maternal weight gain or fetal growth, etc.) for hyperglycemia exists.

Definitions

The first trimester was defined as a gestational week less than 14 weeks, the second trimester as a gestational age between 14 and 28 weeks, and the third trimester as a gestational age over 28 weeks. The pre-pregnancy body mass index (BMI) was classified into nonoverweight/obese (< 24 kg/m^2), overweight (24–28 kg/m^2) and obese (≥ 28 kg/m^2) groups according to the standards of the Chinese Health Ministry[34]. Adequate, insufficient and excessive gestational weight gain (GWG) were defined according to the BMI-based recommendation for the Chinese population, and we used separate standards for singleton and twin pregnancies[35,36]. Hypertensive disorders of pregnancies (HDPs) refer to a group of hypertensive disorders that occur during gestation, including gestational hypertension, preeclampsia-eclampsia, chronic hypertension and chronic hypertension with superimposed preeclampsia[37]. Birth defects are structural abnormalities present at birth. Preterm birth was defined as delivery at less than 37 gestational weeks. LGA was defined as a birth weight higher than the 90th percentile of gestational age based on the Chinese reference for singleton and twin pregnancies[38,39]. Macrosomia was defined as a neonatal birth weight not less than 4000 g. Neonatal hypoglycemia was defined as neonatal peripheral blood glucose < 2.2 mmol/L[40].

Statistical analyses

Continuous variables are presented as the means ± standard deviations (SDs) if normally distributed and median values (25th, 75th percentiles) if skewed. Categorical variables are summarized as numbers (percentages). Comparisons were performed among the four groups by ANOVA, the Kruskal–Wallis test and the chi-square test (or Fisher's exact test) according to the variance type, and the Bonferroni correction was further used for multiple comparisons. Logistic regression was performed to analyze the associations between adverse perinatal outcomes (binary) and the timing of diagnosis, and the results are presented as odds ratios (ORs) and 95% confidence intervals (95% CIs). PGDM patients who were diagnosed before pregnancy constituted the reference group. The models were adjusted for maternal age, hospital, pre-pregnancy BMI, family history of diabetes, GWG, neonatal sex and gestational age at delivery. All the statistical analyses were performed with SPSS 25.0 software. *P* values were two-sided, the statistical significance was set as 0.05, and in the multiple comparisons, this value was set as 0.0083 (0.05/6).

Data availability

All the data in this study will be shared by the corresponding author upon reasonable request.

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References

1. Magliano, D. J. & Boyko, E. J. *IDF DIABETES ATLAS* (Brussels, 2021).

2. Li, Y. et al. Prevalence of diabetes recorded in Mainland China using 2018 diagnostic criteria from the American diabetes association: National cross sectional study. *BMJ* **369**, m997 (2020).
3. Wang, Z. et al. Trends in prevalence and incidence of type 2 diabetes among adults in Beijing, China, from 2008 to 2017. *Diabet. Med.* **38** (9), e14487 (2021).
4. Macintosh, M. C. et al. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. *BMJ* **333** (7560), 177 (2006).
5. Higa, R., Leonardi, M. L. & Jawerbaum, A. Intrauterine programming of cardiovascular diseases in maternal diabetes. *Front. Physiol.* **12**, 760251 (2021).
6. Chen, S., Wang, X., Lee, B. K. & Gardner, R. M. Associations between maternal metabolic conditions and neurodevelopmental conditions in offspring: the mediating effects of obstetric and neonatal complications. *BMC Med.* **21** (1), 422 (2023).
7. Coetzee, A., Sadhai, N., Mason, D., Hall, D. R. & Conradie, M. Evidence to support the classification of hyperglycemia first detected in pregnancy to predict diabetes 6–12 weeks postpartum: A single center cohort study. *Diabetes Res. Clin. Pract.* **169**, 108421 (2020).
8. Zhu, W. W. et al. Evaluation of the value of fasting plasma glucose in the first prenatal visit to diagnose gestational diabetes mellitus in China. *Diabetes Care*. **36** (3), 586–590 (2013).
9. Di Cianni, G., Miccoli, R., Volpe, L., Lencioni, C. & Del Prato, S. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab. Res. Rev.* **19** (4), 259–270 (2003).
10. Lain, K. Y. & Catalano, P. M. Metabolic changes in pregnancy. *Clin. Obstet. Gynecol.* **50** (4), 938–948 (2007).
11. Metzger, B. E. et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care*. **33** (3), 676–682 (2010).
12. Diagnostic Criteria *And Classification of Hyperglycaemia First Detected in Pregnancy* (Geneva, 2013).
13. ACOG Practice Bulletin No. 201: pregestational diabetes mellitus. *Obstet. Gynecol.* **132** (6), e228–e248 (2018).
14. Wong, T., Ross, G. P., Jalaludin, B. B. & Flack, J. R. The clinical significance of overt diabetes in pregnancy. *Diabet. Med.* **30** (4), 468–474 (2013).
15. Oppermann, M. L., Campos, M. A., Hirakata, V. N. & Reichelt, A. J. Overt diabetes imposes a comparable burden on outcomes as pregestational diabetes: a cohort study. *Diabetol. Metab. Syndr.* **14** (1), 177 (2022).
16. Sugiyama, T. et al. Comparison of pregnancy outcomes between women with gestational diabetes and overt diabetes first diagnosed in pregnancy: a retrospective multi-institutional study in Japan. *Diabetes Res. Clin. Pract.* **103** (1), 20–25 (2014).
17. Mañé, L. et al. Impact of overt diabetes diagnosed in pregnancy in a multi-ethnic cohort in Spain. *Gynecol. Endocrinol.* **35** (4), 332–336 (2019).
18. Corrado, F. et al. Perinatal outcome in a Caucasian population with gestational diabetes and preexisting diabetes first diagnosed in pregnancy. *Diabetes Metab.* **42** (2), 122–125 (2016).
19. Schiller, T. et al. Prediabetes in pregnancy - follow-up, treatment, and outcomes compared to overt pregestational diabetes. *J. Matern Fetal Neonatal Med.* **36** (1), 2191153 (2023).
20. Regnault, N. et al. Maternal and neonatal outcomes according to the timing of diagnosis of hyperglycaemia in pregnancy: a nationwide cross-sectional study of 695,912 deliveries in France in 2018. *Diabetologia* **67** (3), 516–527 (2024).
21. Cosson, E. et al. Prognosis associated with Sub-Types of hyperglycaemia in pregnancy. *J. Clin. Med.* **10** (17), 3904 (2021).
22. Skajaa, G. Ø., Fuglsang, J., Kampmann, U. & Ovesen, P. G. Parity increases insulin requirements in pregnant women with type 1 diabetes. *J. Clin. Endocrinol. Metab.* **103** (6), 2302–2308 (2018).
23. Dori-Dayan, N. et al. Insulin requirements during pregnancy in women with type 1 diabetes treated with insulin pump. *Diabetes Metab. Res. Rev.* **40** (3), e3771 (2024).
24. 2. Diagnosis and classification of diabetes: standards of care in Diabetes-2024. *Diabetes Care*. **47** (Suppl 1), S20–S42 (2024).
25. Benhalima, K. et al. The 2019 Flemish consensus on screening for overt diabetes in early pregnancy and screening for gestational diabetes mellitus. *Acta Clin. Belg.* **75** (5), 340–347 (2020).
26. Gupta, Y. et al. Cardiometabolic profile of women with a history of overt diabetes compared to gestational diabetes and normoglycemia in index pregnancy: results from CHIP-F study. *J. Diabetes*. **16** (5), e13461 (2024).
27. Wei, Y., Yang, H., Zhu, W., Hod, M. & Hadar, E. Adverse pregnancy outcome among women with pre-gestational diabetes mellitus: a population-based multi-centric study in Beijing. *J. Matern Fetal Neonatal Med.* **30** (20), 2395–2397 (2017).
28. Wei, Y., Zhang, Q., Juan, J. & Yang, H. Is it suitable for DM diagnosis using an abnormal two-hour glucose value only after 24th gestational weeks in China. *J. Matern Fetal Neonatal Med.* **35** (6), 1075–1080 (2022).
29. Hadden, D. R. & McLaughlin, C. Normal and abnormal maternal metabolism during pregnancy. *Semin Fetal Neonatal Med.* **14** (2), 66–71 (2009).
30. Wei, Y. et al. Preconception diabetes mellitus and adverse pregnancy outcomes in over 6.4 million women: A population-based cohort study in China. *PLoS Med.* **16** (10), e1002926 (2019).
31. Simmons, D. Paradigm shifts in the management of diabetes in pregnancy: the importance of type 2 diabetes and early hyperglycemia in pregnancy: the 2020 Norbert Freinkel award lecture. *Diabetes Care*. **44** (5), 1075–1081 (2021).
32. Murphy, H. R. et al. Changes in the glycemic profiles of women with type 1 and type 2 diabetes during pregnancy. *Diabetes Care*. **30** (11), 2785–2791 (2007).
33. Obstetrics & Subgroup Society of obstetrics and gynecology CMA. Diagnosis and management for pregnancy with diabetes (article in Chinese). *Chin. J. Obstet. Gynecol.* **49** (8), 561–569 (2014).
34. National Health and Family Planning Commission. WS/T 428–2013. Criteria of Weight for Adults. Beijing. Standards Press of China.
35. National, H. C. Standard of recommendation for weight gain during pregnancy period (WS/T 801–2022).(article in Chinese). (2022).
36. Cui Jinhui, L. P. Ouyang liping Ll, Chen Xinjuan Fj. Analysis of perinatal outcomes and related risk factors of gestational mellitus in twin pregnancies (in Chinese). *Chin. J. Diabetes Mellitus*. **13** (9), 852–858 (2021).
37. Society of Obstetrics and Gynecology CMA. Diagnosis and treatment of hypertensive disorders of pregnancy (2020)(article in Chinese). *Chin. J. Obstet. Gynecol.* **55** (4), 227–238 (2020).
38. Capital Institute of Pediatrics HL. Growth standard curves of birth weight, length and head circumference of Chinese newborns of different gestation (article in Chinese). *Chin. J. Pediatr.* **58** (9), 738–746 (2020).
39. Dai, L. et al. Population-based birth weight reference percentiles for Chinese twins. *Ann. Med.* **49** (6), 470–478 (2017).
40. Shao, X. M. & Qiu, H. M. Y. *XS. Practice of Neonatology (Book in Chinese)(5th Edition)* (People's Medical Publishing House, 2019).

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Author contributions

X.S., J.J. and H.Y. contributed to the conception and design of the study. X.S., J.J., X.K., X.C., Z.W., L.K., H.C., S.C., F.G., P.Z., J.Y., X.X., L.Z., Y.W., and Y.M. collected, entered and validated the medical data. X.S. performed the statistical analysis. X.S and J.J. wrote the first draft of the manuscript. M.Y. and H.Y. revised the manuscript. H.Y. funded and supervised the study. All the authors have read and approved this manuscript for submission.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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