Relationship between Oral Glucose Tolerance Test Characteristics and Adverse Pregnancy Outcomes among Women with Gestational Diabetes Mellitus

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Abstract

Background: Hyperglycemia is associated with adverse pregnancy outcomes. However, the relationships between them remain ambiguous. This study aimed to analyze the effect of different oral glucose tolerance test (OGTT) results on adverse perinatal outcomes.
Methods: This retrospective cohort study included data from 15 hospitals in Beijing from June 20, 2013 to November 30, 2013. Women with gestational diabetes mellitus (GDM) were categorized according to the number and distribution of abnormal OGTT values, and the characteristics of adverse pregnancy outcomes were evaluated. Chi-square test and logistic regression analysis were used to determine the associations.
Results: In total, 14,741 pregnant women were included in the study population, 2927 (19.86%) of whom had GDM. As the number of hyperglycemic values in the OGTT increased, the risk of cesarean delivery, preterm births, large-for-gestational age (LGA), macrosomia, and neonatal complications significantly increased. Fasting hyperglycemia had clear associations with macrosomia (odds ratios [*OR*s]:1.84, 95% confidence intervals [*CI*s]: 1.39–2.42, $P < 0.001$), LGA (*OR*: 1.70, 95% *CI*: 1.29–2.25, $P < 0.001$), and cesarean delivery (*OR*: 1.33, 95% *CI*: 1.15–1.55, $P < 0.001$). The associations were stronger as fasting glucose increased. GDM diagnosed by hyperglycemia at OGTT-2 h was more likely to lead to preterm birth (*OR*: 1.50, 95% *CI*: 1.11–2.03, $P < 0.01$).
Conclusions: Various characteristics of OGTTs are associated with different adverse outcomes. A careful reconsideration of GDM with hierarchical and individualized management according to OGTT characteristics is needed.

Key words: Cesarean Delivery; Gestational Diabetes Mellitus; Glucose Tolerance Test; Large-for-gestational Age; Macrosomia; Pregnancy Outcomes; Preterm Births

Introduction

For many years, gestational diabetes mellitus (GDM) has been defined as "any degree of glucose intolerance first recognized during pregnancy".[1] Recently, this definition has been redefined by the American Diabetes Association (ADA) as "hyperglycemia diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes".[2] According to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria, the incidence of GDM in China is approximately 17.5%, which is consistent with the epidemic increase in diabetes worldwide.[3]

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Hyperglycemia in pregnancy is independently associated with adverse outcomes for the mother, fetus, and neonate, both in the short- and long-term.[4] The Hyperglycemia and Adverse Pregnancy Outcome study demonstrated that the

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risk of adverse pregnancy outcomes continuously increased as a function of maternal glycemia at 24–28 weeks of gestation, even with glucose values previously considered normal.[5]

However, the precise relationships between different oral glucose tolerance test (OGTT) characteristics and adverse pregnancy outcomes among GDM patients remain ambiguous. It is unclear whether one, two, or three abnormal glucose values on the OGTT represent a higher risk profile for complications. In addition, it is unclear whether fasting or postload glucose values are more closely related to adverse perinatal outcomes and whether they represent different or specific risks.[4,6,7]

Understanding these relationships can facilitate the development of appropriate management strategies for GDM patients with different models of OGTT. Therefore, the aim of the current analysis was to estimate how different OGTT characteristics influenced pregnancy outcomes and to determine which OGTT parameter was best correlated with specific adverse pregnancy outcomes.

Methods

Ethical approval

The study was approved by the Ethics Committee of Peking University First Hospital (No. 2013[578]). All participants provided written informed consent, and the Ethics Committee approved the consent procedure.

Study population

We conducted a retrospective cohort analysis of data from the "Systemic Random Sampling Survey on the Prevalence of Gestational Diabetes Mellitus in Beijing (GDM prevalence survey [GPS])". In this survey, 15 Beijing hospitals were chosen using systemic cluster sampling, and random seed and sampling intervals were determined and sorted by the number of deliveries in 2012. Pregnant women who delivered from June 20, 2013 to November 30, 2013 were screened. The eligibility criteria include all women delivering from June 20, 2013 to November 30, 2013 who were carrying a singleton fetus and had performed a 75 g OGTT between 24 and 28 weeks of gestation. The exclusion criteria were women who had delivered before 28 weeks of gestation and those with either known prepregnancy diabetes mellitus or overt diabetes diagnosed during pregnancy.

Definitions

The participating pregnant women were tested for fasting plasma glucose (FPG) during their first prenatal visit using venous blood samples collected after at least 8 h of fasting. Women with FPG ≥7.0 mmol/L were considered to have overt diabetes and were excluded from the study. After 24 weeks of gestation, women received a 75 g OGTT. Women were considered to have GDM if any one of the following OGTT values was met or exceeded: fasting ≥5.10 mmol/L; 1 h ≥10.0 mmol/L; or 2 h ≥8.5 mmol/L. Glucose values above 7.0 mmol/L or 11.1 mmol/L at fasting and 2 h postglucose load, respectively, were considered to indicate overt diabetes.[8] Small for gestational age (SGA) was defined as a birth weight under the 10th percentile, while large for gestational age (LGA) was defined as a birth weight above the 90th percentile based on gender and gestational age.[9] Macrosomia was defined as a birth weight of more than 4000 g.[10] Preterm birth was defined as a delivery at gestational age <37 weeks and ≥28 weeks. Neonatal hypoglycemia was defined as glucose values <35 mg/dl by heel stick within 2 h of birth and before the first nonbreastfeeding. Neonatal hyperbilirubinemia was defined as values >95th percentile.[11] Hyperinsulinemia was defined as C-peptide levels from cord blood >95th percentile (>1.77 ng/ml).[12] Stillbirth was defined as an absence of signs of life at or after birth, and neonatal death was defined as death of a live born neonate during the first 7 days after birth.[13]

Data analysis

Patients diagnosed with GDM were divided into three groups: Group I, Group II, and Group III, which were divided according to the number of pathological values on the OGTT and consisted of women with one, two, and three pathological glucose values, respectively. The control group comprised pregnant women with normal OGTT results. Further, subgrouping was performed according to OGTT values: patients in Subgroups I_F, I_1, and I_2 were diagnosed with GDM according to a single abnormal value for fasting hyperglycemia, 1 h, and 2 h hyperglycemia, respectively [Table 1].

Comparisons were made between groups and subgroups regarding the following adverse pregnancy outcomes: cesarean delivery rate, macrosomia, LGA, SGA, and preterm birth. In addition, neonatal complications were studied and included any of the following: hypoglycemia, hyperbilirubinemia, hyperinsulinemia, admission to the Neonatal Intensive Care Unit, stillbirth, and neonatal death.

Statistical analysis

Statistical analysis was conducted with SPSS version 20.0 (IBM, Chicago, IL, USA) software. Categorical variables such as cesarean section, macrosomia, LGA, preterm birth, and neonatal complications were reported as percentages. Pearson's Chi-square or Fisher's exact test was also

Table 1: Grouping strategies for GDM patients based on 75 g oral glucose tolerance test

Groups	Non-GDM	GDM						
		Group I			Group II			Group III
		I_F	I_1	I_2	II_{F+1}	II_{F+2}	II_{1+2}	
Fasting glucose	–	↑	–	–	↑	↑	–	↑
1-h glucose	–	–	↑	–	↑	–	↑	↑
2-h glucose	–	–	–	↑	–	↑	↑	↑

Group I: GDM patients with one abnormal value on the OGTT; Group II: GDM diagnosed by two abnormal values; Group III: GDM patients with three abnormal values on the OGTT. ↑: Elevated glucose values that meet or exceed the GDM diagnostic criteria; (F): Fasting ≥5.10 mmol/L; (1): 1 h ≥10.0 mmol/L; (2): 2 h ≥8.5 mmol/L; –: Normal glucose value. GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test.

performed. Logistic regression was used in the multivariable analysis to identify the associations between fasting, 1 h, and 2 h hyperglycemia and adverse outcomes. Data were adjusted for gestational age at delivery, maternal age and maternal body mass index at enrollment, and odds ratios (*OR*s) with 95% confidence intervals (*CI*s) were computed relative to a control group of women without GDM. A $P < 0.05$ was considered statistically significant.

Results

In total, 15,194 pregnant women were included in the initial sample cohort. After excluding 253 women with a multiple pregnancy and 200 women with pregestational or overt diabetes, 14,741 pregnant women were eligible for analysis. The study group consisted of 2927 (19.86%) women with GDM and a control group of 11,814 (80.14%) pregnant women with a normal OGTT.

Adverse pregnancy outcomes among gestational diabetes mellitus patients

Table 2 illustrates the relationship of maternal GDM with adverse pregnancy outcomes. Compared to non-GDM women, GDM patients had a higher risk of cesarean delivery, macrosomia, LGA infants, preterm birth, and neonatal complication, but a lower risk of SGA infants.

GDM patients were also divided into three groups: Group I, Group II, and Group III which consisted of patients with one, two, and three abnormal glucose values, respectively [Table 3]. More cesarean deliveries, preterm births, and neonatal complications were observed in Group II than those in Group I ($P < 0.001$). The prevalence of cesarean delivery, macrosomia, LGA, preterm birth, and neonatal complications was higher in Group III than those in Group II ($P < 0.001$) [Table 3]. The *OR*s, relative to the non-GDM group, were presented in Supplementary Table 1. As the number of abnormal glucose parameters increased, the associations with adverse pregnancy outcomes became stronger, with the strongest association in Group III.

Relationship between fasting glucose and adverse outcomes

GDM patients in each group were further subclassified, and the rates of adverse outcomes by OGTT subgroup were shown in Table 4. In Subgroup I_F, in which a single abnormal fasting OGTT value served as the GDM diagnostic criteria, significantly more macrosomia and LGA were detected than in Subgroups I_1 and I_2, in which 1 h or 2 h glucose values were abnormal, respectively. In Group II, which had two abnormal OGTT values, Subgroups II_{F+1} and II_{F+2}, which had abnormal fasting glucose and one of the postload values over the threshold, demonstrated significantly higher rates of macrosomia and LGA than in GDM patients with both postload glucose values but a normal fasting glucose (Subgroup II_{1+2}). Similar trends were observed for operative delivery [Table 4].

The *OR*s are shown in Table 5 and Supplementary Table 1. Fasting hyperglycemia had the strongest association with macrosomia (*OR*: 1.84, 95% *CI*: 1.39–2.42, $P < 0.001$), LGA (*OR*: 1.70, 95% *CI*: 1.29–2.25, $P < 0.001$), and cesarean delivery (*OR*: 1.33, 95% *CI*: 1.15–1.55, $P < 0.001$).

Relationship between 2 h oral glucose tolerance test and adverse outcomes

GDM mothers with abnormal 2 h OGTT were more likely to have preterm birth [Table 4]. For GDM patients with

Table 2: Prevalence of adverse pregnancy outcomes in patients with and without GDM

Parameters	Non-GDM (n = 11,814)	GDM (n = 2927)	*OR*	95% *CI*	χ^2	*P*
Cesarean section	4790 (40.55)	1435 (49.03)	1.41	1.3–1.53	68.99	<0.001
Macrosomia	861 (7.29)	283 (9.67)	1.36	1.18–1.57	18.57	<0.001
LGA	694 (5.87)	273 (9.33)	1.65	1.42–1.91	45.62	<0.001
Preterm birth	588 (4.98)	184 (6.29)	1.28	1.08–1.52	8.10	0.004
Neonatal complication	1314 (11.12)	386 (13.19)	1.21	1.07–1.37	9.74	0.002
SGA	611 (5.17)	115 (3.93)	0.75	0.61–0.92	7.74	0.005

Data were presented as *n* (%). GDM: Gestational diabetes mellitus; LGA: Large for gestational age; SGA: Small for gestational age; *CI*: Confidence interval; *OR*: Odds ratio.

Table 3: Adverse pregnancy outcomes in different GDM groups

Adverse pregnancy outcomes	Non-GDM (n = 11,814)	GDM		
		Group I (n = 2182)	Group II (n = 544)	Group III (n = 201)
Cesarean delivery	4790 (40.6)	1041 (47.8)*	282 (51.9)*,†	112 (56.0)*,‡
Macrosomia	861 (7.3)	210 (9.6)*	49 (9.0)	24 (12.0)*,‡
LGA	694 (5.9)	202 (9.3)*	47 (8.6)*	24 (12.0)*,‡
Preterm birth	588 (5.0)	124 (5.7)	39 (7.2)*,†	21 (10.5)*,‡
Neonatal complication	1314 (11.2)	283 (13.1)*	75 (13.9)†	28 (14.2)‡
SGA	611 (5.2)	90 (4.1)*	16 (2.9)*	9 (4.5)

Data are presented as *n* (%). *P<0.05 versus non-GDM Group; †P<0.001 versus Group I; ‡P<0.01 versus Group II. Group I: GDM patients with one abnormal value on the OGTT; Group II: GDM diagnosed by two abnormal values; Group III: GDM patients with three abnormal values on the OGTT. GDM: Gestational diabetes mellitus; LGA: Large for gestational age; SGA: Small for gestational age; OGTT: Oral glucose tolerance test.

Table 4: Adverse pregnancy outcomes in different OGTT subgroups

Groups	Non-GDM (n = 11,814)	GDM						
		Group I			Group II			Group III (n = 201)
		I_F (n = 1370)	I_1 (n = 385)	I_2 (n = 427)	II_{F+1} (n = 161)	II_{F+2} (n = 95)	II_{1+2} (n = 288)	
Cesarean delivery	4790 (40.6)	683 (50.0)*	172 (44.7)†	186 (43.6)†	94 (58.4)*,§	55 (57.9)*,§	133 (46.3)	112 (56.0)*
Macrosomia	861 (7.3)	149 (10.9)*	32 (8.3)†	29 (6.8)†	21 (13.0)*,§	16 (16.8)*,§	12 (4.2)*	24 (12.0)*
LGA	694 (5.9)	143 (10.5)*	34 (8.8)*	25 (5.8)†	16 (9.9)*,§	16 (16.8)*,§	5 (5.2)*	167 (12.0)*
Preterm birth	588 (5.0)	74 (5.4)	20 (5.2)	30 (7.0)	10 (6.2)	8 (8.4)	21 (7.3)	21 (10.5)
Neonatal complication	1314 (11.2)	177 (13.0)*	46 (12.0)	60 (14.2)	20 (12.6)	15 (15.8)	40 (14.0)	28 (14.2)
SGA	611 (5.2)	50 (3.7)*	15 (3.9)	25 (5.8)†,‡	4 (2.5)	3 (3.2)‖	9 (3.1)‖	9 (4.5)

Data are presented as n (%). *P<0.05 versus non-GDM Group; †P<0.001 versus Group IF; ‡P<0.001 versus Group I1; §P<0.001, versus Group II_{1+2}; ‖P<0.001 versus Group II_{F+1}. Group I: GDM patients with one abnormal value on the OGTT; Subgroups I_F, I_1, and I_2 were diagnosed as GDM according to a single abnormal value for fasting hyperglycemia, 1-h and 2-h hyperglycemia, respectively; Group II: GDM diagnosed by two abnormal values; Group III: GDM patients with three abnormal values on the OGTT. GDM: Gestational diabetes mellitus; LGA: Large for gestational age; SGA: Small for gestational age; OGTT: Oral glucose tolerance test.

Table 5: *OR*s of adverse pregnancy outcomes for hyperglycemia (n = 14,741)

Outcomes	*OR*	95% *CI*	*P*
Cesarean section			
Fasting glucose	1.33	1.15–1.55	<0.001
OGTT 1 h	1.02	0.88–1.19	0.755
OGTT 2 h	0.95	0.81–1.10	0.475
Macrosomia			
Fasting glucose	1.84	1.39–2.42	<0.001
OGTT 1 h	0.83	0.63–1.07	0.152
OGTT 2 h	0.74	0.56–0.97	0.028
LGA			
Fasting glucose	1.70	1.29–2.25	<0.001
OGTT 1 h	0.88	0.67–1.14	0.323
OGTT 2 h	0.77	0.58–1.01	0.057
Preterm birth			
Fasting glucose	0.96	0.71–1.31	0.794
OGTT 1 h	1.19	0.88–1.62	0.265
OGTT 2 h	1.50	1.11–2.03	0.009
Neonatal complication			
Fasting glucose	0.99	0.80–1.24	0.944
OGTT 1 h	0.16	0.77–1.21	0.789
OGTT 2 h	1.14	0.91–1.42	0.251
SGA			
Fasting glucose	0.81	0.55–1.18	0.267
OGTT 1 h	0.86	0.58–1.29	0.471
OGTT 2 h	1.28	0.87–1.87	0.210

Lga: large for gestational age; sga: small for gestational age; *CI*: Confidence interval; *OR*s: Odds ratios; OGTT: Oral glucose tolerance test.

one abnormal glucose result, Subgroup I_2, which included patients with abnormal 2 h OGTT, we found higher rates of preterm labor than in Subgroups I_F and I_1, which included GDM with normal 2 h OGTT. A similar distribution was observed in Group II, which had 8.4% premature infants in Subgroup II_{F+2}; 7.3% in Subgroup II_{1+2}; and 6.2% in Subgroup II_{F+1}. That is, 2 h hyperglycemia seemed to be associated with more preterm labor in GDM mothers. The *OR* for the association was 1.50 (95% *CI*: 1.39–2.42, P = 0.009) [Table 5].

GDM patients diagnosed according to a 2 h glucose ≥8.50 mmol/L in the OGTT had less macrosomia, LGA, and cesarean delivery, whether in Group I or Group II [Table 4]. Moreover, it is worth noting that although GDM diagnosis did not increase the rate of SGA infants according to our data, some differences were observed in the SGA distribution of different OGTT models. After comparing the prevalence of SGA, Subgroup I_2 which included GDM patients with elevated 2 h OGTT as the diagnostic criteria had the highest rate of SGA (5.8%). Patients with abnormal 2 h OGTT exhibited a nonsignificant trend for having more SGA infants than patients with normal 2 h OGTT. In Subgroups II_{F+2} and II_{1+2}, in which abnormal 2 h OGTT was one of the diagnostic thresholds, there were more SGA infants than in Subgroup II_{F+1}, which had normal 2 h OGTT, with rates of 3.1% and 3.2% compared to 2.5%, respectively (P = 0.002) [Table 4]. Based on this finding, it seemed that there might have been an association between 2 h OGTT glucose and fetal growth restriction in GDM patients, with an *OR* of 1.28 (95% *CI*: 0.87–1.88, P = 0.210) for SGA and 0.74 (95% *CI*: 0.56–0.97, P = 0.028) for macrosomia [Table 5].

Association between fasting hyperglycemia and adverse pregnancy outcomes

Fasting hyperglycemia was associated with perinatal outcomes, including macrosomia, LGA, and cesarean delivery. The fasting glucoses on the OGTT were further stratified into 0.5-unit increments [Table 6]. Among pregnant women, the group with a fasting glucose level of 4.60 to 6.59 mmol/L was associated with macrosomia, LGA, and cesarean delivery (P < 0.001) when compared against the group with fasting glucose <4.1 mmol/L. As fasting glucose increased, the risk of adverse pregnancy outcomes was higher. The *OR*s of macrosomia (up to 5.36 folds), LGA (up to 5.74 folds), and cesarean delivery (up to 2.94 folds) were higher in subgroups with higher fasting glucose levels. However, the subgroup with values in the 6.60 to 6.99 mmol/L range did not show statistical significance for macrosomia, LGA, or cesarean delivery.

Table 6: *OR*s of pregnancy outcomes according to different ranges of fasting glucose in the 75 g OGTT

Outcomes	*n* (%)	*OR*	95% *CI*	*P*
Macrosomia				
<4.10	1749 (12.67)	1.00		<0.001
4.10–4.59	5586 (40.45)	1.17	0.93–1.48	0.185
4.60–5.09	4909 (35.55)	1.77	1.49–2.58	<0.001
5.10–5.59	1286 (9.31)	1.96	1.49–2.58	<0.001
5.60–6.09	208 (1.51)	3.28	2.15–5.03	<0.001
6.10–6.59	51 (0.37)	5.36	2.72–10.57	<0.001
6.6–6.99	19 (0.14)	0.97	0.13–7.32	0.974
LGA				
<4.10	1749 (12.67)	1.00		<0.001
4.10–4.59	5586 (40.45)	1.40	1.06–1.85	0.019
4.60–5.09	4909 (35.55)	2.35	1.79–3.08	<0.001
5.10–5.59	1286 (9.31)	2.78	2.03–3.80	<0.001
5.60–6.09	208 (1.51)	4.69	2.97–7.40	<0.001
6.10–6.59	51 (0.37)	5.74	2.68–12.29	<0.001
6.6–6.99	19 (0.14)	1.49	0.20–11.31	0.702
Cesarean delivery				
<4.10	1749 (12.67)	1.00		<0.001
4.10–4.59	5586 (40.45)	1.03	0.93–1.16	0.552
4.60–5.09	4909 (35.55)	1.28	1.15–1.43	<0.001
5.10–5.59	1286 (9.31)	1.76	1.52–2.04	<0.001
5.60–6.09	208 (1.51)	2.23	1.67–2.99	<0.001
6.10–6.59	51 (0.37)	2.94	1.64–5.27	<0.001
6.6–6.99	19 (0.14)	1.17	0.47–2.92	0.741

LGA: Large for gestational age; *CI*: Confidence interval; *OR*s: Odds ratios; OGTT: Oral glucose tolerance test.

Discussion

In 2011, based on the IADPSG guidelines, the ADA recommended for the first time that all pregnant women not known to have prior diabetes undergo a 75-g OGTT at 24–28 weeks of gestation.[14] The National Health and Family Planning Commission of China adopted testing and diagnostic criteria based on the IADPSG guidelines. Through these guidelines, single abnormal blood glucose levels can be diagnosed, which means more pregnant women are included as having GDM. Moreover, these GDM patients have different hyperglycemia characteristics, which may lead to different pregnant outcomes.

First, GDM results in further adverse maternal, fetal, and neonatal outcomes, including cesarean deliveries, macrosomia, LGA, preterm birth, and neonatal complications. Moreover, in addition to the plasma glucose levels in OGTT, the number of abnormal OGTT parameters also identified different degrees of maternal hyperglycemia and maternal/fetal risk. We found consistent trends between the number of abnormal glucose parameters and frequencies of adverse outcomes, such as cesarean delivery, premature delivery, and neonatal complications. Increasing numbers of abnormal parameters in the OGTT were associated with higher odds of the incidence of adverse perianal outcomes. This association may warrant a tailored management strategy for GDM. Compared with one hyperglycemic value, patients with two or more elevated glucose values may have a more severe disruption in glucose metabolic balance and insulin sensitivity. This finding should be taken into account during pregnancy follow-up and management of hyperglycemia with stricter glucose control, including regulation of diet and exercise and administration of insulin, to attain satisfactory glycemic control.

Not all abnormal glucose OGTT values resulted in the same adverse outcomes or in the same risk of a specific adverse outcome. The metabolic physiology of pregnancy is characterized by fasting hypoglycemia due to insulin-independent glucose uptake by the placenta, postprandial hyperglycemia, and carbohydrate intolerance as a result of diabetogenic placental hormones. In addition, insulin resistance increases exponentially during the second trimester and levels off toward the end of the third trimester. For GDM patients, fasting hyperglycemia may mean that glucose metabolic abnormalities are more prone to causing adverse perinatal outcomes. However, the associations between fasting hyperglycemia and adverse perinatal outcomes seem more obvious in regard to fetal growth, as GDM is characterized by increased risk of macrosomia, without a risk threshold.[5] Previous studies have suggested that fasting glucose levels are associated with neonatal adiposity including body fat percentage and increased skinfold thickness in neonates born to women with both diet- and insulin-treated gestational diabetes.[15] Higher fasting glucose levels have been associated with macrosomia and LGA.[16] Consistent with those reports, our data also showed positive associations of fasting hyperglycemia with macrosomia and LGA. Moreover, the association was stronger with increases in fasting glucose, although the highest risk was not observed in the 6.60–6.99 mmol/L group, likely due to the limited samples available for the analysis. Moreover, it was worth noting that these results were in contrast to those reported in studies by de Veciana *et al*.[17] and Combs *et al*.,[7] who described a consistent association between postprandial glucose values and birth weight, frequency of LGA, and macrosomia.

Macrosomia and LGA indicated a greater likelihood of operative delivery. Our data presented a similar distribution between cesarean delivery and macrosomia and LGA. More GDM patients diagnosed by fasting OGTT ≥5.1 mmol/L received a cesarean section. However, it should be considered that the diagnosis of GDM itself shifts obstetric practice toward operative delivery because of its association with macrosomia. Meanwhile, some confounders, such as previous GDM, previous macrosomia, and social psychological factors, may also influence clinical decisions regarding the mode of delivery. In addition to this increase in operative delivery, macrosomic infants are at risk for a variety of perinatal complications, including higher rates of shoulder dystocia and birth trauma. Moreover, longitudinal population studies have documented that macrosomia and LGA confer high risks for infants' long-term health. Fetal overgrowth and increased neonatal fat mass have

been linked to the development of obesity and metabolic syndrome in childhood and adolescence.[18,19] Given the close relationship of fasting glucose with macrosomia and LGA, the normalization of fasting glucose in GDM has immediate benefits and could potentially improve long-term health outcomes for mothers and neonates.

Offspring of diabetic mothers may be macrosomic, SGA, or of normal birth weight, depending on the severity of the mother's diabetes, presence or absence of complications, and the degree of diabetic control.[20] In poorly controlled diabetes without severe complications, newborn infants will often be overweight and macrosomic.[21] Improved glycemic control would normalize fetal growth, while severe diabetes or overly strict control may often result in SGA offspring.[22] Our study demonstrated no association between GDM and SGA. This lack of association might be because our population included GDM patients who had received interventions such as diet, exercise, and insulin treatment after diagnosis, and these interventions might have resulted in good control without deterioration to severe uncontrolled diabetes. However, it is worth noting that GDM patients with abnormal 2 h OGTT values had a trend toward more SGA infants than GDM women with normal 2 h OGTT. A clear difference was observed in GDM patients with one abnormal glucose parameter; when combined with elevated 0 h or 1 h glucose, the effect of 2 h hyperglycemia on SGA seemed to be attenuated. As SGA is a risk factor for a variety of diseases including hypertension, cardiovascular disease, and diabetes, these results suggest that more attention is needed for SGA prevention in GDM mothers, especially if they show an abnormal 2 h OGTT value.[21,23]

Preterm delivery was also associated with GDM.[24] Furthermore, it appeared to be more closely related to elevated postload glucose than abnormal fasting values, with the highest risks of preterm delivery observed among women with normal fasting and two elevated postload glucose values.[16] Our data demonstrate a trend toward more preterm infants in mothers with hyperglycemia in the 2 h OGTT. Further research efforts should determine the precise influence of 2 h OGTT values on premature birth.

There were several limitations to this study. First, it was worth noting that the patients investigated in this study accepted some form of intervention, including diet, exercise, and insulin treatment. It was reasonable to speculate that, if not treated, GDM mothers and their offspring would have had worse adverse outcomes and that the links between different parameters of OGTT and adverse perinatal outcomes would thus be more severe. In addition, participants' nutritional status could affect fetal growth and other perinatal outcomes, but we did not have data on these variables.

In conclusion, our study indicated the following: first, as the number of hyperglycemic values in the OGTT increased, there was a significant increase in cesarean delivery, preterm birth, LGA infants, macrosomia, and neonatal complications. In addition, fasting hyperglycemia was associated with more macrosomia, LGA, and cesarean delivery, and the association was stronger for higher glucose values. Finally, hyperglycemia according to the 2 h OGTT was associated with a greater possibility of preterm birth and SGA.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: *OR*s of adverse pregnancy outcomes in different GDM groups

Groups	Cesarean delivery	Macrosomia	LGA	Preterm birth	Neonatal complication	SGA
Group I	1.34 (1.22–1.47)	1.36 (1.16–1.59)	1.64 (1.39–1.93)	1.15 (0.94–1.41)	1.19 (1.04–1.37)	0.79 (0.63–0.99)
I_F (n = 1370)	1.23 (1.09–1.38)	1.46 (1.21–1.77)	1.61 (1.32–1.95)	1.09 (0.85–1.40)	1.19 (1.00–1.40)	0.76 (0.56–1.02)
I_1 (n = 385)	0.93 (0.78–1.19)	1.16 (0.79–1.70)	1.38 (0.95–1.99)	1.05 (0.66–1.65)	1.08 (0.79–1.48)	0.80 (0.48–1.36)
I_2 (n = 427)	0.90 (0.74–1.10)	1.02 (0.69–1.51)	0.97 (0.64–1.47)	1.44 (0.98–2.11)	1.31 (0.99–1.73)	1.21 (0.80–1.84)
Group II	1.58 (1.33–1.88)	1.26 (0.93–1.70)	1.52 (1.11–2.06)	1.48 (1.05–2.06)	1.28 (0.99–1.64)	0.56 (0.34–0.92)
II_{F+1} (n = 161)	1.43 (1.03–1.98)	1.74 (1.08–2.83)	1.38 (0.81–2.34)	1.27 (0.66–2.41)	1.14 (0.71–1.83)	0.55 (0.20–1.49)
II_{F+2} (n = 95)	1.26 (0.83–1.92)	2.73 (1.55–4.81)	2.68 (1.55–4.66)	1.76 (0.85–3.64)	1.48 (0.85–2.58)	0.72 (0.23–2.28)
II_{1+2} (n = 288)	0.92 (0.72–1.18)	0.60 (0.33–1.07)	0.83 (0.49–1.40)	1.50 (0.96–2.36)	1.29 (0.92–1.81)	0.65 (0.33–1.28)
Group III (n = 200)	1.86 (1.41–2.47)	1.74 (1.13–2.67)	2.19 (1.42–3.37)	2.24 (1.42–3.55)	1.31 (0.88–1.96)	0.86 (0.44–1.70)

Data are presented as *OR* (95% *CI*). Group I: GDM patients with one abnormal value at the OGTT; Group II: GDM diagnosed by two abnormal values; Group III: GDM patients with three abnormal values at the OGTT. *CI*: Confidence interval; *OR*s: Odds ratios; GDM: Gestational diabetes mellitus; LGA: Large for gestational age; SGA: Small for gestational age; OGTT: Oral glucose tolerance test.