

Association of Gestational Diabetes Mellitus With Adverse Pregnancy Outcomes and Its Interaction With Maternal Age in Chinese Urban Women

Xueyin Wang (✉ xueyin0925@163.com)

Peking University First Hospital <https://orcid.org/0000-0003-4461-324X>

Xiaosong Zhang

Peking University First Hospital

Min Zhou

Peking University First Hospital

Juan Juan

Peking University First Hospital

Xu Wang

Peking University First Hospital

Research

Keywords: gestational diabetes mellitus, pregnancy outcomes, maternal age, cesarean section, preterm birth, large-for-gestational age, macrosomia

Posted Date: December 31st, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-136722/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: The prevalence of gestational diabetes mellitus (GDM) has been dramatically increasing worldwide. The aims of this study were to examine associations of GDM with pregnancy outcomes in Chinese urban women, and to evaluate the interaction between GDM and other major risk factors for the risk of adverse pregnancy outcomes.

Methods: A retrospective analysis included 8,844 women who delivered live singletons at ≥ 28 weeks of gestation between June 2012 and March 2013 among Chinese urban women. Structured questionnaires were used to collect the information on demographic characteristics, lifestyle behavior, medical history and pregnancy outcomes. The diagnosis of GDM was made between 24 and 28 gestational weeks according to the International Association of Diabetes and Pregnancy Study Groups criteria. Logistic regression models were used to assess the association of GDM with pregnancy outcomes, and to examine the interaction between GDM and other major risk factors including maternal age, prepregnancy body mass index and gestational weight gain for the risk of pregnancy outcomes.

Results: 13.9% of women were diagnosed with GDM. We found that GDM was associated with higher risk of cesarean delivery (Odds Ratio [OR] = 1.69, 95% CI [confidence interval]: 1.48-1.92), preterm birth (OR=1.32, 95% CI: 1.07-1.64), macrosomia (OR=1.69, 95% CI: 1.34-2.13) and large-for-gestational age (LGA, OR=1.43, 95% CI: 1.18-1.73) after adjustment for potential confounders. We also observed the interaction between GDM and maternal age for the risk of cesarean delivery (P for interaction = 0.025), and the prevalence of cesarean delivery was higher in women with GDM than those unaffected of GDM regardless of maternal age (age <35 years: 58.5% vs. 44.3%; age ≥ 35 years: 67.7% vs. 64.3%). Women aged ≥ 35 years and above and having GDM had a 2.10-fold increased risk of cesarean delivery compared to those who was under 35 years old and did not having GDM (OR=2.10, 95% CI: 1.48-2.93).

Conclusions: GDM was associated with increased risk of cesarean delivery, preterm birth, macrosomia and LGA in Chinese urban women, and there was the interaction between GDM and maternal age for the risk of cesarean delivery.

Background

GDM is a medical condition of hyperglycemia or glucose intolerance with first diagnosis in the second or third trimester of pregnancy that is not clearly overt disease prior to gestation [1]. GDM has become a major health concern in pregnant women, and its prevalence has been dramatically increasing worldwide. According to the data from the International Diabetes Federation, GDM was estimated to affect 13.2% of live births in 2019 [2], while the prevalence of GDM ranges from 9.3–19.7% in different areas of China and the societal economic burden of GDM was \$ 5.59 billion in 2015 at the Chinese national level [3–6]. GDM has been associated with a number of short- and long-term perinatal outcomes not only for the mothers but also for their offspring. For the mothers, GDM is associated with adverse pregnancy complications and outcomes including pregnancy-induced hypertension (PIH), preeclampsia and

cesarean delivery, as well as the lifetime risk of type 2 diabetes and metabolic syndrome [7–9]. For their offspring, it may increase the risk of macrosomia, large-gestational-age (LGA), birth injury, neonatal hypoglycemia and diabetes, and subsequently diabetes and obesity later in life [8–9].

As major risk factors of GDM, maternal age, prepregnancy body mass index (BMI) and weight gain during pregnancy were also found to be associated with the risk of adverse maternal and infant outcomes [10]. The average age at childbearing has been rising steadily with the fertility rate nearly doubling among women aged above 35 years in recent decades, and women giving birth at advanced maternal age have higher risks of a range of pregnancy complications such as gestational hypertensive disorders, GDM, postpartum haemorrhage, cesarean delivery and preterm birth [11–12]. Apart from maternal age, prepregnancy overweight and obesity, affecting 6 ~ 24% of Chinese women of childbearing age, have an important influence on both GDM and other maternal and neonatal outcomes such as cesarean delivery, GDM, PIH, neonatal adiposity and low Apgar scores [10, 13–14]. Our previous research also reported the associations between prepregnancy overweight and obesity and higher risk of macrosomia and LGA [10]. Furthermore, excessive gestational weight gain (GWG) may contribute to increased risk of cesarean delivery, macrosomia, LGA, hypertensive diseases of pregnancy, and childhood obesity for the offspring, whereas low GWG has been associated with elevated rates of SGA, low birth weight and preterm birth [15–16]. Although several studies examined the association of the forementioned risk factors with adverse perinatal outcomes, little is known about the interactive effect between GDM and other risk factors on adverse pregnancy outcomes in urban Chinese women.

Therefore, the objective of the present study was to evaluate associations of GDM with adverse pregnancy outcomes in Chinese urban women and further to assess the associations stratified by maternal age, prepregnancy BMI and GWG categories, and we also examined the interaction between GDM and maternal age, prepregnancy BMI and GWG for the risk of adverse pregnancy outcomes, respectively.

Methods

Study design and participants

This multicenter, retrospective cohort study of postpartum women was conducted in 14 clinical centers located in urban areas of China from June 2012 to March 2013. Details of this study have been described elsewhere [10]. Briefly, we recruited postpartum women aged 18 years or above with a gestational age of 28–42 weeks and who gave live birth during 10th–19th of the last month of every quarter in order to control for seasonal variations. Among 9,152 participants with full medical records, 308 women with pregestational diabetes (n=38), multiple gestation (n=223), pre-conception history of severe heart disease or chronic renal disease (n=48) were excluded. Overall, the present analysis was restricted to 8,844 deliveries. This study was approved by the institutional review board of Peking University First Hospital, and all participants provided written informed consent.

Data collection

Information on demographic characteristics, lifestyle behavior, medical history of pregnancy, and pregnancy outcomes were collected by using a structured questionnaire after delivery. In-person interviews were conducted to collect information on demographic characteristics such as age, education, employment and annual household income, as well as lifestyle behavior including drinking and passive smoking during pregnancy, and clinical data such as medical history and pregnancy outcomes was extracted from the medical records.

Gestational age at delivery was determined from the date of last menstrual period to the date of delivery and expressed in the week after the last menstrual period. If the date was uncertain, ultrasonography was used to determine gestational age. Weight and height at the first antenatal visit prior to the 13th gestational week, and weight at the last antenatal visit within 2 weeks before delivery or the time of delivery were extracted from the medical records. Prepregnancy BMI was calculated as the weight in kilograms divided by the square of height measured in meters, and classified into three groups according to the Chinese standard [17]: underweight (BMI <18.5 kg/m²), normal weight (18.5 kg/m² ≤ BMI <24 kg/m²), overweight and obese (BMI ≥ 24 kg/m²). The GWG was calculated by subtracting the weight measured at the first antenatal visit from the final weight measured at the last antenatal visit or the time of delivery. All participants were divided into three groups according to GWG, defined by 25th and 75th percentile of GWG (12.0 and 19.0 kg): lower (GWG <12 kg), middle (12 kg ≤GWG <19 kg), higher (≥19 kg).

Diagnosis of GDM

According to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, the diagnosis of GDM should be made when any one 75-g oral glucose tolerance test value met or exceeded 5.1 mmol/L at 0 h, 10.0 mmol/L at 1 h, 8.5 mmol/L at 2 h when performed between 24 and 28 gestational weeks [18].

Definition of adverse pregnancy outcomes

The main outcomes of the study were cesarean delivery, preterm birth, low birth weight, small-for-gestational age (SGA), macrosomia and LGA. Preterm birth was defined as all birth before 37 completed weeks or before 259 completed days since the first day of a women's last menstrual period [19]. Low birth weight was defined as the neonatal birth weight <2500 g, and macrosomia as birth weight ≥ 4000 g, respectively. LGA and SGA were indicated by birth weight less than and greater than the 10th and 90th percentile, respectively, for the same gestational age by sex, according to the Chinese neonatal birth weight curve [20].

Statistical analysis

Demographics characteristics and pregnancy outcomes were expressed as numbers and frequency distributions for categorical variables, or median and interquartile range for continuous variables. To compare between groups, the chi-square test and Mann-Whitney U test were performed for categorical variables and skewed distributed continuous variables, respectively. Logistic regression models were conducted to estimate odds ratios (ORs) and their 95% confidence intervals (CIs) of pregnancy outcomes and GDM, and interaction between GDM and maternal age/prepregnancy BMI/GWG groups. Models were adjusted for maternal age (continuous), education (high school and below, college or graduate school), employment (unemployed, employed), annual household income (<10000 RMB, 10000-20000 RMB, <20000 RMB), drinking during pregnancy (yes, no), passive smoking during pregnancy (yes, no), prepregnancy BMI categories (underweight, normal weight, overweight/obese), parity (primiparous, multiparous), use of assisted reproductive technology (ART, yes, no), folic acid supplementation (yes, no), gestational age at delivery (continuous, except for the outcome of preterm birth) and GWG categories (lower, middle, higher). The non-GDM group was used as the reference group. Stratified analyses were performed according to maternal age groups (<35 years, ≥ 35 years), prepregnancy BMI categories (underweight, normal weight, overweight/obese) and GWG categories (lower, middle, higher). Analyses were carried out using SAS software version 9.2 (SAS Institute, Cary, NC). All *P* values are two-sided, and statistical significance was defined as $P < 0.05$.

Results

Participant characteristics

Among 8,844 postpartum women, 1,229 (13.9%) were diagnosed with GDM. The average age of study participants was 28.7 years. Distribution of GDM status by study centers is shown in **Supplementary Table 1**. Table 1 shows demographic characteristics of participants according to GDM status. Women with GDM had a higher likelihood of advanced maternal age (≥ 35 years), prepregnancy overweight and obesity, and use of ART than non-GDM counterparts (all $P < 0.05$). Compared to those unaffected of GDM, women with GDM were more likely to be exposed to passive smoking during pregnancy, and less likely to drink during pregnancy and to be in the middle group of GWG (all $P < 0.05$).

Table 1
Characteristics of participants by gestational diabetes mellitus

	All	GDM	Non-GDM	P value
Participants, n (%)	8844	1229 (13.9)	7615 (86.1)	-
Maternal age, year, median (IQR)	28 (26, 31)	29 (26, 32)	28 (26, 30)	< 0.001
Maternal age, n (%)				< 0.001
<35 years	8095 (91.5)	1074 (87.4)	7021 (92.2)	
≥ 35 years	749 (8.5)	155 (12.6)	594 (7.8)	
Education, n (%)				0.801
High school and below	3346 (37.8)	461 (37.5)	2885 (37.9)	
College or graduate school	5498 (62.2)	768 (62.5)	4730 (62.1)	
Employment, n (%)				0.304
Unemployed	6456 (73.0)	912 (74.2)	5544 (72.8)	
Employed	2388 (27.0)	317 (25.8)	2071 (27.2)	
Annual household income, RMB, n (%)				0.874
< 10000	7071 (80.0)	980 (79.7)	6091 (80.0)	
10001–20000	1288 (14.6)	184 (15.0)	1104 (14.5)	
> 20000	485 (5.4)	65 (5.3)	420 (5.5)	
Drinking during pregnancy, n (%)				0.014
No	8607 (97.3)	1209 (98.4)	7398 (97.2)	
Yes	237 (2.7)	20 (1.6)	217 (2.8)	
Passive smoking during pregnancy, n (%)				0.014
No	7059 (79.8)	949 (77.2)	6110 (80.2)	

Abbreviations: ART, assisted reproductive technology; BMI, body mass index; GDM, gestational diabetes mellitus. Values are median (interquartile range) or n (%).

	All	GDM	Non-GDM	P value
Yes	1785 (20.2)	280 (22.8)	1505 (19.8)	
prepregnancy BMI categories, n (%)				< 0.001
Underweight	7732 (87.4)	963 (78.4)	6769 (88.9)	
Normal weight	946 (10.7)	204 (16.6)	742 (9.7)	
Overweight/Obesity	166 (1.9)	62 (5.0)	104 (1.4)	
Parity, n (%)				0.136
primiparous	7237 (81.8)	987 (80.3)	6250 (82.1)	
Multiparous	1607 (18.2)	242 (19.7)	1365 (17.9)	
Use of ART, n (%)				0.020
No	8680 (98.2)	1196 (97.3)	7484 (98.3)	
Yes	164 (1.8)	33 (2.7)	131 (1.7)	
Folic acid supplementation, n (%)				0.237
No	4067 (46.0)	546 (44.4)	3521 (46.2)	
Yes	4777 (54.0)	683 (44.6)	4094 (53.8)	
Gestational age at delivery, week, median (IQR)	39 (38, 40)	39 (38, 39)	39 (38, 40)	< 0.001
Gestational weight gain, kg				< 0.001
Lower	1282 (14.5)	245 (19.9)	1037 (13.6)	
Middle	6367 (72.0)	833 (67.8)	5534 (72.7)	
Higher	1195 (13.5)	151 (12.3)	1044 (13.7)	
Abbreviations: ART, assisted reproductive technology; BMI, body mass index; GDM, gestational diabetes mellitus. Values are median (interquartile range) or n (%).				

Prevalence of pregnancy outcomes by GDM

Figure 1 and **Supplementary Table 2** illustrates the prevalence of adverse pregnancy outcomes by GDM status. Women with GDM had a higher likelihood of cesarean delivery (60.0% vs. 45.8%), macrosomia (9.4% vs. 6.1%) and LGA (14.0% vs. 9.7%) than those who did not having GDM (all $P < 0.001$). However, the prevalence of preterm birth, low birth weight and SGA was comparable between the two groups (all $P > 0.05$).

Associations of GDM with pregnancy outcomes

Table 2 shows associations of adverse pregnancy outcomes with GDM status. After adjustment for potential confounders, GDM was associated with higher risk for cesarean delivery (OR = 1.69, 95% CI: 1.48–1.92), preterm birth (OR = 1.32, 95% CI: 1.07–1.64), macrosomia (OR = 1.69, 95% CI: 1.34–2.13) and LGA (OR = 1.43, 95% CI: 1.18–1.73).

Table 2
ORs (95% CIs) for pregnancy outcomes by gestational diabetes mellitus

	Case/Non-case	Model 1		Model 2	
		OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Cesarean delivery	4227/4617	1.75 (1.54, 1.99)	< 0.001	1.69 (1.48, 1.92)	< 0.001
Preterm birth*	800/8044	1.37 (1.11, 1.70)	0.004	1.32 (1.07, 1.64)	0.011
Low birth weight	454/8390	1.17 (0.88, 1.56)	0.276	0.86 (0.59, 1.25)	0.422
SGA	548/8296	0.76 (0.57, 1.01)	0.062	0.75 (0.56, 1.01)	0.051
Macrosomia	579/8265	1.58 (1.26, 1.97)	< 0.001	1.69 (1.34, 2.13)	< 0.001
LGA	908/7936	1.50 (1.24, 1.81)	< 0.001	1.43 (1.18, 1.73)	< 0.001

Abbreviations: CI, confidence interval; OR, odds ratio; SGA, small-for-gestational age; LGA, large-for-gestational age.

Model 1 was adjusted for demographic characteristics including maternal age, education, employment, annual household income and study centers. Model 2 was further adjusted for drinking during pregnancy, passive smoking during pregnancy, prepregnancy body mass index categories, parity, use of assisted reproductive technology, folic acid supplementation, gestational age at delivery, gestational weight gain categories. Preterm birth was not adjusted for gestational age at delivery*.

The effect of the interaction between GDM and maternal age on pregnancy outcomes

There was a significantly statistical interaction between GDM and maternal age (< 35 years, \geq 35 years) for the risk of cesarean delivery after adjustment for potential confounders (P for interaction = 0.025, Table 3). The prevalence of cesarean delivery was higher in women with GDM than those who did not have GDM regardless of maternal age (age < 35 years: 58.5% vs. 44.3%; age \geq 35 years: 67.7% vs. 64.3%). Among women of age < 35 years, the OR of GDM for cesarean delivery was in 1.71 (95% CI: 1.49–1.97)

after adjustment for potential confounders, while GDM was not significantly associated with the risk of cesarean delivery among those aged 35 years and above. In addition, we further performed the combined analysis to evaluate the effect of GDM and maternal age on the risk of cesarean delivery (Fig. 2). Compared to those aged < 35 years and having not GDM, women with GDM and aged \geq 35 years had a 2.10-fold odds of cesarean delivery (OR = 2.10, 95% CI: 1.48–2.93).

Table 3

ORs (95% CIs) for pregnancy outcomes by gestational diabetes mellitus, stratified by maternal age

	Age < 35 years		Age ≥ 35 years		<i>P</i> for interaction
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	
Cesarean delivery					
Model 1	1.75 (1.53, 2.01)	< 0.001	1.27 (0.84, 1.91)	0.255	0.042
Model 2	1.71 (1.49, 1.97)	< 0.001	1.13 (0.74, 1.73)	0.559	0.025
Preterm birth*					
Model 1	1.49 (1.19, 1.88)	< 0.001	0.75 (0.40, 1.41)	0.376	0.158
Model 2	1.45 (1.15, 1.83)	0.002	0.73 (0.38, 1.40)	0.334	0.133
Low birth weight					
Model 1	1.25 (0.92, 1.69)	0.155	0.83 (0.37, 1.89)	0.665	0.539
Model 2	0.81 (0.54, 1.22)	0.319	2.28 (0.55, 9.43)	0.256	0.383
SGA					
Model 1	0.81 (0.60, 1.10)	0.176	0.63 (0.26, 1.51)	0.298	0.532
Model 2	0.80 (0.59, 1.08)	0.143	0.63 (0.25, 1.58)	0.322	0.463
Macrosomia					
Model 1	1.49 (1.18, 1.90)	0.001	1.58 (0.81, 3.08)	0.178	0.830
Model 2	1.65 (1.28, 2.11)	< 0.001	1.52 (0.73, 3.16)	0.265	0.954
LGA					
Model 1	1.43 (1.17, 1.75)	< 0.001	1.55 (0.89, 2.72)	0.121	0.963
Model 2	1.39 (1.13, 1.70)	< 0.001	1.35 (0.75, 2.44)	0.316	0.898
Abbreviations: CI, confidence interval; OR, odds ratio; SGA, small-for-gestational age; LGA, large-for-gestational age.					
Model 1 was adjusted for demographic characteristics including maternal age, education, employment, annual household income and study centers. Model 2 was further adjusted for drinking during pregnancy, passive smoking during pregnancy, prepregnancy body mass index categories, parity, use of assisted reproductive technology, folic acid supplementation, gestational age at delivery, gestational weight gain categories. Preterm birth was not adjusted for gestational age at delivery*.					

We also examined the relationships between GDM and pregnancy outcomes by prepregnancy BMI and GWG categories, respectively. Results were generally consistent pertaining to associations of GDM with

the risk of pregnancy outcomes across different prepregnancy BMI (**Supplementary Table 3**) and GWG groups (**Supplementary Table 4**).

Discussion

In this retrospective cohort study of Chinese urban women, 13.9% of women were diagnosed with GDM. We found that GDM was associated with higher risk of cesarean delivery, preterm birth, macrosomia and LGA after adjustment for potential confounders. We also observed the interaction between GDM and maternal age for the risk of cesarean delivery, and women with GDM had a stronger effect on the risk of cesarean delivery in those aged below 35 years than in those with 35 years and older.

The positive associations of GDM with increased risk of macrosomia and LGA have reported in different populations, which is in accordance with our study [21–23]. A retrospective cohort study enrolling more than 21,000 Thai women indicated that the rate of macrosomia was significantly higher in the GDM than in the control, and GDM was associated with a 48% increased risk of macrosomia [21]. In addition, the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study conducted in 15 centers in nine countries demonstrated the continuous positive associations between maternal glucose concentrations and birth weight even among those who had plasma glucose previously considered normal for pregnancy [24]. Previous randomized controlled trials also implied that glycemic control through dietary intervention, physical activity, and/or insulin therapy was able to reduce the risk of macrosomia and LGA [25–26]. Recently, a prospective cohort study based on a US population suggested that GDM was associated with a larger fetal size that started at gestational week 20 and became significant at gestational week 28, indicating that interventions to mitigate fetal overgrowth related to GDM should be initiated before the diagnosis of GDM [27]. The mechanisms and pathways for the relationship between maternal hyperglycemia and neonatal birth weight are not well described. It might be explained by that maternal hyperglycemia and insulin resistance might cause fetal hyperinsulinemia, and thus enhanced the utilization of nutrients and consequently leading to fetal overgrowth and adiposity [23, 28].

Another finding of our study is that GDM was associated with an increased risk of preterm birth. Prior research on the relationship between GDM and risk of preterm birth has been still controversial. Similar to our findings, a population-study focusing on more than 327,000 singleton pregnancies in Canada indicated that GDM was associated with increased risk of spontaneous preterm and labor-induced preterm in singleton pregnancies [29]. Moreover, a population-based study conducted in northeastern Germany reported that GDM resulted in higher percentage of late preterm infants with a gestational age of 32–36 weeks (11.1% vs. 7.0%) [30]. However, several retrospective studies found no increased risk for preterm delivery in women having GDM in comparison to non-GDM counterparts [31–32]. Therefore, further research is needed to explore the relationship and underlying mechanisms between GDM and the risk of preterm birth.

In addition, we also observed that GDM was associated with a 62% increased risk of cesarean delivery. Consistent with our findings, the data from the Massachusetts Pregnancy to Early Life Longitudinal Data

System has been shown that women with GDM during one of two sequential pregnancies had increased risk of cesarean delivery [33]. A large-scale observational national study in France found that the risk of cesarean delivery was increased in women with GDM compared with the non-diabetic population in deliveries after 28 weeks [34]. Another observational study conducted at 15 medical centers in Beijing demonstrated that GDM women had an elevated risk of cesarean delivery compared with normal blood glucose women [35]. The HAPO study revealed that the odds ratio for primary cesarean section increased across categories of maternal glycemia with an OR of 1.86 in the highest category of 1-hour plasma glucoses [24]. The association between GDM and the increased risk of cesarean delivery may be influenced by two aspects: on one hand, maternal hyperglycemia might contribute to fetal overgrowth and large neonatal birth weight, which could lead to the higher risk of cesarean delivery; on the other hand, women developing GDM may affect clinical decision making due to the higher rates of abnormalities in labor, birth trauma and fetal distress, which might increase the risk of cesarean delivery [36]. However, potential mechanisms need further exploration in future research.

One interesting finding of our study is that we found a significant interaction between GDM and maternal age in relation to the risk of cesarean delivery. Specifically, we observed that women aged of 35 years and above and having GDM had a 2.1-fold increased risk of cesarean delivery compared to those who was under 35 years old and did not having GDM. Moreover, the stratified analysis of our study indicated that GDM was much more important in women aged below 35 years than in those with 35 years and above among Chinese urban women. In contrast to our finding, a previous retrospective study focusing on 880 Portuguese women also found the interaction between GDM and maternal age for cesarean delivery by reporting that women older than 35 years presented a higher association between GDM and non-elective cesarean delivery than women younger than 35 years [36]. Differences in findings may be partly due to ethnicity disparities and focusing on different types of cesarean delivery. Overall, our finding emphasizes the important public health implications of glycemic control by lifestyle intervention among pregnancy women developing GDM, which is particularly crucial in Chinese urban women below 35 years old.

The main strengths of our study include a relatively large sample size, using the IADPSG criteria for GDM diagnosis that is reported to be more robust for diagnosis of GDM and its influence on adverse maternal and perinatal outcomes [37], further assessing the interaction of GDM and other major factors for adverse pregnancy outcomes, and adjusting for potential confounding factors comprehensively. However, our study has a few limitations. Firstly, we did not distinguish between emergency and elective cesarean deliveries, and did not differentiate spontaneous and indicated preterm birth. Secondly, our data included only Chinese Han population, and it is unclear whether the results can be extrapolated to women of other ethnic groups. Lastly, we did not collect blood specimens and specific plasma glucose levels such as fasting, 1-hour and 2-hour plasma glucose level, so we were unable to examine associations of pregnancy outcomes with certain glycemic parameters.

Conclusion

In summary, our study indicated that GDM was associated with higher risk of cesarean delivery, preterm birth, macrosomia and LGA. We also observed the interaction between GDM and maternal age for the risk of cesarean delivery. Our findings emphasize the important public health implications of glycemic control by implementing healthy lifestyle strategies among pregnancy women who suffered from GDM, which is particularly crucial in Chinese urban women below 35 years old.

Abbreviations

ART: assisted reproductive technology; BMI: body mass index; CI: confidence interval; GDM, gestational diabetes mellitus; GWG, gestational weight gain; HAPO, Hyperglycemia and Adverse Pregnancy Outcome; IADPSG, the International Association of Diabetes and Pregnancy Study Groups; LGA, large-for-gestational age; OR: odds ratio; PIH: pregnancy-induced hypertension; SGA, small-for-gestational age.

Declarations

Acknowledgements

We thank all participants and investigators, and all staff of medical record section in 14 hospitals.

Funding

This study was funded by the Scientific Research Seed Fund of Peking University First Hospital Project (2019SF37).

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Xueyin Wang designed this study, analyzed the data, and wrote the manuscript. X.Z. and M.Z. contributed to discussion, and edited the manuscript. J.J. and Xu Wang collected and analyzed the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the institutional review board of Peking University First Hospital. Informed consent was provided by all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019, 42:S13-S28.
2. Jin C, Lin L, Han N, Zhao Z, Liu Z, Luo S, Xu X, Liu J, Wang H: Effects of dynamic change in fetuin-A levels from the first to the second trimester on insulin resistance and gestational diabetes mellitus: a nested case-control study. *BMJ Open Diabetes Res Care* 2020, 8.
3. Xu T, Dainelli L, Yu K, Ma L, Silva Zolezzi I, Detzel P, Fang H: The short-term health and economic burden of gestational diabetes mellitus in China: a modelling study. *BMJ Open* 2017, 7:e018893.
4. Leng J, Shao P, Zhang C, Tian H, Zhang F, Zhang S, Dong L, Li L, Yu Z, Chan JC, et al: Prevalence of gestational diabetes mellitus and its risk factors in Chinese pregnant women: a prospective population-based study in Tianjin, China. *PLoS One* 2015, 10:e0121029.
5. Li G, Wei T, Ni W, Zhang A, Zhang J, Xing Y, Xing Q: Incidence and Risk Factors of Gestational Diabetes Mellitus: A Prospective Cohort Study in Qingdao, China. *Front Endocrinol (Lausanne)* 2020, 11:636.
6. Zhu WW, Yang HX, Wang C, Su RN, Feng H, Kapur A: High Prevalence of Gestational Diabetes Mellitus in Beijing: Effect of Maternal Birth Weight and Other Risk Factors. *Chin Med J (Engl)* 2017, 130:1019-1025.
7. Lee KW, Ching SM, Ramachandran V, Yee A, Hoo FK, Chia YC, Wan Sulaiman WA, Suppiah S, Mohamed MH, Veettil SK: Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2018, 18:494.
8. Saravanan P: Gestational diabetes: opportunities for improving maternal and child health. *Lancet Diabetes Endocrinol* 2020, 8:793-800.
9. Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD: Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. *Diabetologia* 2016, 59:1396-1399.
10. Wang X, Zhang X, Zhou M, Juan J: Association of prepregnancy body mass index, rate of gestational weight gain with pregnancy outcomes in Chinese urban women. *Nutr Metab (Lond)* 2019, 16:54.
11. Fitzpatrick KE, Tuffnell D, Kurinczuk JJ, Knight M: Pregnancy at very advanced maternal age: a UK population-based cohort study. *Bjog* 2017, 124:1097-1106.
12. Kato T, Yorifuji T, Yamakawa M, Inoue S, Doi H, Eboshida A, Kawachi I: Association of maternal age with child health: A Japanese longitudinal study. *PLoS One* 2017, 12:e0172544.
13. Stang J, Huffman LG: Position of the Academy of Nutrition and Dietetics: Obesity, Reproduction, and Pregnancy Outcomes. *J Acad Nutr Diet* 2016, 116:677-691.

14. Hung TH, Hsieh TT: Pregestational body mass index, gestational weight gain, and risks for adverse pregnancy outcomes among Taiwanese women: A retrospective cohort study. *Taiwan J Obstet Gynecol* 2016, 55:575-581.
15. Voerman E, Santos S, Inskip H, Amiano P, Barros H, Charles MA, Chatzi L, Chrousos GP, Corpeleijn E, Crozier S, et al: Association of Gestational Weight Gain With Adverse Maternal and Infant Outcomes. *JAMA* 2019, 321:1702-1715.
16. Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH, Li N, Hu G, Corrado F, Rode L, et al: Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis. *JAMA* 2017, 317:2207-2225.
17. Wang Y, Mi J, Shan XY, Wang QJ, Ge KY: Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. *Int J Obes (Lond)* 2007, 31:177-188.
18. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva A, Hod M, Kitzmiller JL, et al: International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010, 33:676-682.
19. Chen CM: Overview of obesity in Mainland China. *Obes Rev* 2008, 9 Suppl 1:14-21.
20. Li H, Zheng J, Wang H, Huang G, Huang Q, Feng N, Xiao J: Maternal cosmetics use during pregnancy and risks of adverse outcomes: a prospective cohort study. *Sci Rep* 2019, 9:8030.
21. Srichumchit S, Luewan S, Tongsong T: Outcomes of pregnancy with gestational diabetes mellitus. *Int J Gynaecol Obstet* 2015, 131:251-254.
22. Seghieri G, Di Cianni G, Seghieri M, Lacaria E, Corsi E, Lencioni C, Gualdani E, Voller F, Francesconi P: Risk and adverse outcomes of gestational diabetes in migrants: A population cohort study. *Diabetes Res Clin Pract* 2020, 163:108128.
23. Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE, Lowe LP, Trimble ER, Coustan DR, Hadden DR, et al: The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes. *Diabetes Care* 2012, 35:780-786.
24. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, et al: Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008, 358:1991-2002.
25. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, Wapner RJ, Varner MW, Rouse DJ, Thorp JM, Jr., et al: A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009, 361:1339-1348.
26. Yang X, Tian H, Zhang F, Zhang C, Li Y, Leng J, Wang L, Liu G, Dong L, Yu Z, et al: A randomised translational trial of lifestyle intervention using a 3-tier shared care approach on pregnancy outcomes in Chinese women with gestational diabetes mellitus but without diabetes. *J Transl Med* 2014, 12:290.
27. Li M, Hinkle SN, Grantz KL, Kim S, Grewal J, Grobman WA, Skupski DW, Newman RB, Chien EK, Sciscione A, et al: Glycaemic status during pregnancy and longitudinal measures of fetal growth in a

- multi-racial US population: a prospective cohort study. *Lancet Diabetes Endocrinol* 2020, 8:292-300.
28. Kc K, Shakya S, Zhang H: Gestational diabetes mellitus and macrosomia: a literature review. *Ann Nutr Metab* 2015, 66 Suppl 2:14-20.
 29. Lai FY, Johnson JA, Dover D, Kaul P: Outcomes of singleton and twin pregnancies complicated by pre-existing diabetes and gestational diabetes: A population-based study in Alberta, Canada, 2005-11. *J Diabetes* 2016, 8:45-55.
 30. Domanski G, Lange AE, Ittermann T, Allenberg H, Spoo RA, Zygmunt M, Heckmann M: Evaluation of neonatal and maternal morbidity in mothers with gestational diabetes: a population-based study. *BMC Pregnancy Childbirth* 2018, 18:367.
 31. Yogev Y, Langer O: Spontaneous preterm delivery and gestational diabetes: the impact of glycemic control. *Arch Gynecol Obstet* 2007, 276:361-365.
 32. Nordin NM, Wei JW, Naing NN, Symonds EM: Comparison of maternal-fetal outcomes in gestational diabetes and lesser degrees of glucose intolerance. *J Obstet Gynaecol Res* 2006, 32:107-114.
 33. Kim SY, Kotelchuck M, Wilson HG, Diop H, Shapiro-Mendoza CK, England LJ: Prevalence of Adverse Pregnancy Outcomes, by Maternal Diabetes Status at First and Second Deliveries, Massachusetts, 1998-2007. *Prev Chronic Dis* 2015, 12:E218.
 34. Billionnet C, Mitanchez D, Weill A, Nizard J, Alla F, Hartemann A, Jacqueminet S: Gestational diabetes and adverse perinatal outcomes from 716,152 births in France in 2012. *Diabetologia* 2017, 60:636-644.
 35. Song G, Wei YM, Zhu WW, Yang HX: Cesarean Section Rate in Singleton Primiparae and Related Factors in Beijing, China. *Chin Med J (Engl)* 2017, 130:2395-2401.
 36. Gorgal R, Gonçalves E, Barros M, Namora G, Magalhães A, Rodrigues T, Montenegro N: Gestational diabetes mellitus: a risk factor for non-elective cesarean section. *J Obstet Gynaecol Res* 2012, 38:154-159.
 37. Todi S, Sagili H, Kamalanathan SK: Comparison of criteria of International Association of Diabetes and Pregnancy Study Groups (IADPSG) with National Institute for Health and Care Excellence (NICE) for diagnosis of gestational diabetes mellitus. *Arch Gynecol Obstet* 2020, 302:47-52.

Figures

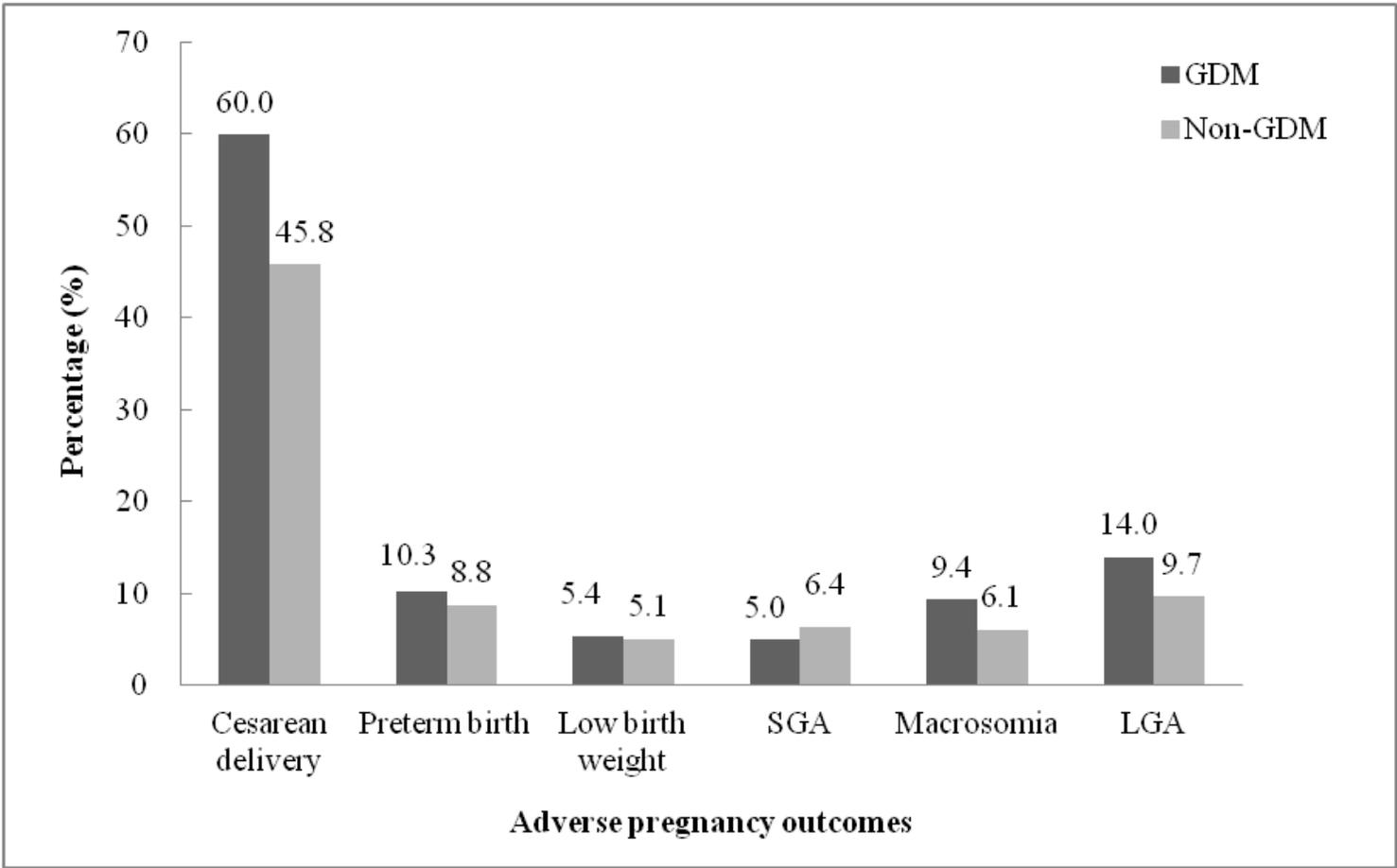


Figure 1

Percentage of adverse pregnancy outcomes by gestational diabetes mellitus. Abbreviations: GDM, gestational diabetes mellitus; SGA, small-for-gestational age; LGA, large-for-gestational age.

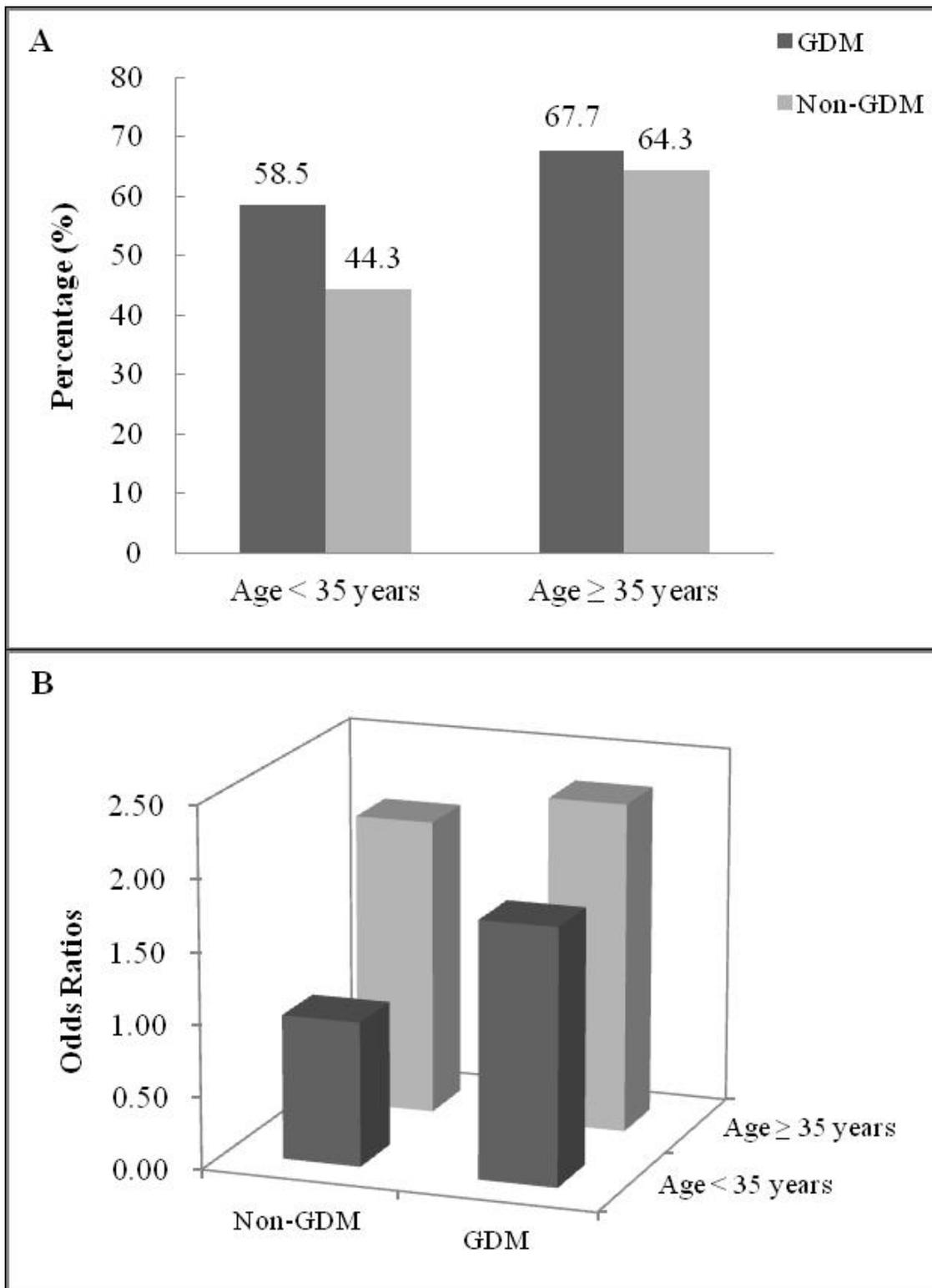


Figure 2

Associations of gestational diabetes mellitus and maternal age with the risk of cesarean delivery. Abbreviations: GDM, gestational diabetes mellitus. A. Percentage of gestational diabetes mellitus by maternal age groups. Values are n (%). B. Adjusted Odds ratios for cesarean delivery according to different gestational diabetes mellitus and maternal age groups. Values are odds ratios. Adjusted for maternal age, education, employment, annual household income, study centers, drinking during

pregnancy, passive smoking during pregnancy, prepregnancy body mass index categories, parity, use of assisted reproductive technology, folic acid supplementation, gestational age at delivery, gestational weight gain categories. Abbreviations: GDM, gestational diabetes mellitus.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalTables.docx](#)