

RESEARCH

Open Access



# Association between maternal plasma glucose levels during pregnancy and risk of preterm birth: a retrospective study

Na Wang<sup>1\*†</sup>, Bingqi Han<sup>2†</sup>, Sumiao Hong<sup>1</sup>, Xinrui Shi<sup>2</sup>, Guankai Lin<sup>3</sup>, Xiaoyang Xu<sup>1</sup>, You Zhou<sup>1</sup>, Xiaoting Wen<sup>1</sup>, Baochang Sun<sup>3</sup>, Hexing Wang<sup>2</sup>, Min Huang<sup>1</sup>, Quqing Wang<sup>2</sup>, Jiwei Wang<sup>2\*</sup>, Yue Chen<sup>4</sup> and Qingwu Jiang<sup>2</sup>

## Abstract

**Background** Preterm birth is a leading cause of health problems and death in infants. This study aims to investigate the association between maternal plasma glucose levels during pregnancy and risk of preterm birth.

**Methods** This population-based retrospective study of 6,842 pregnant women used data from a tertiary hospital in China from January 2016 to December 2022. Plasma glucose levels were measured at fasting, 1 h, and 2 h after a 75-g OGTT between 24 and 28 weeks of gestation. The primary outcome of interest was preterm birth. Analysis was performed using restricted cubic splines and logistic regression models.

**Results** The proportion of gestational diabetes mellitus (GDM) and preterm birth in this study were 7.92% and 5.86%, respectively. The levels of fasting plasma glucose (aOR: 1.26; 95% CI: 1.08, 1.47;  $P=0.003$ ;  $P$  for nonlinear = 0.264), 1-hour plasma glucose (aOR: 1.10; 95% CI: 1.03, 1.17;  $P=0.003$ ;  $P$  for nonlinear = 0.535), and 2-hour plasma glucose (aOR: 1.10; 95% CI: 1.02, 1.19;  $P=0.012$ ;  $P$  for nonlinear = 0.368) showed statistically significant linear associations with an increased risk of preterm birth.

**Conclusion** Elevated plasma glucose levels during pregnancy statistically significantly increase the risk of preterm birth. Given that hyperglycemia during pregnancy can be prevented and managed, it is crucial to enhance health education and glucose monitoring for pregnant women. Timely interventions should be implemented to control plasma glucose levels, thereby reducing the incidence of preterm birth.

**Keywords** Plasma glucose level, Gestational diabetes mellitus, Preterm birth, Retrospective study

<sup>†</sup>Na Wang and Bingqi Han are joint first authors for this article and contributed equally to this work.

\*Correspondence:

Na Wang  
Wangna760320@163.com  
Jiwei Wang  
jiweiwang@fudan.edu.cn

<sup>1</sup>Department of the obstetrics, The People's Hospital of Pingyang, Wenzhou, Zhejiang 325400, China

<sup>2</sup>Key Lab of Health Technology Assessment of Ministry of Health, School of Public Health, Fudan University, 130 Dong-An Road, Shanghai 200032, China

<sup>3</sup>Wenzhou Center for Disease Control and Prevention, 490 Shifu Road, Wenzhou, Zhejiang 325000, China

<sup>4</sup>School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, 600 Peter Morand Crescent, Ottawa, ON, Canada



## Introduction

Preterm birth, defined as delivery before 37 weeks of gestation, is the leading cause of perinatal morbidity and mortality and is linked to a range of short- and long-term comorbidities in the neonate [1–3]. However, from 1990 to 2015, the proportion of preterm births in China showed an upward trend to 7.04% [4]. This rise imposes significant financial and psychological burdens on families and substantial costs on the healthcare system [5, 6].

As the most prevalent metabolic disorder during pregnancy, gestational diabetes mellitus (GDM) is a significant risk factor for preterm birth and other pregnancy complications [7, 8]. A recent review indicates that the global standardized prevalence of GDM is 14.0% [9]. In China, demographic shifts following the implementation of the “two-child” and “three-child” policies have contributed to an increase in maternal age at childbirth, which is an important factor underlying the rising prevalence of GDM in recent decades [10]. Glucose is the primary energy substrate for fetal growth and is mainly transported from the mother to the fetus through the placenta [11, 12]. However, in the context of maternal hyperglycemia such as in GDM, excess glucose can induce structural and functional alterations in the placenta. Studies have shown that placental developmental abnormalities are consistently observed in GDM pregnancies, most notably an increased incidence of villous immaturity, heightened angiogenesis, and increased placental weight [13, 14]. These pathological changes can impair placental efficiency and nutrient transport, and are mechanistically linked to an elevated risk of preterm birth. Therefore, maternal glucose homeostasis is considered an important determinant of normal fetal metabolism and growth [15]. Despite the existence of clinical guidelines for GDM screening, several studies have reported that elevated maternal glucose levels during pregnancy, both fasting and postprandial, are associated with an increased risk of adverse birth outcomes such as preterm birth, even when maternal glucose levels have not yet reached the diagnostic threshold for GDM [16, 17]. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study confirmed a linear relationship between maternal glucose concentrations and preterm birth [18]. However, this large study did not include pregnant women from mainland China, and thus the evidence of such associations within the Chinese population remains insufficient. Furthermore, there is some recent evidence suggesting the existence of a possible nonlinear relationship between maternal plasma glucose and preterm birth [17, 19]. Specifically, Dr. Shaw reported that elevated glucose measures were associated with an increased risk of preterm delivery, and subsequent meta-analyses have further confirmed that glucose exposure is linked to a wide range of adverse perinatal outcomes, including preterm birth.

Therefore, this retrospective study was conducted among 6842 pregnant women from a tertiary hospital in China to explore the relationship between maternal fasting, 1-hour, and 2-hour plasma glucose levels and the risk of preterm birth during pregnancy, without being limited to diagnostic thresholds. We included women both with and without GDM, as the main novelty of this study lies in evaluating risks across the full spectrum of maternal glucose levels, rather than restricting analyses to those with diagnosed cases. We hypothesized that elevated maternal glucose levels during pregnancy would be continuously associated with increased risk of preterm birth, regardless of glucose levels were measured in different states, including fasting, 1-hour, and 2-hour glucose.

## Materials and methods

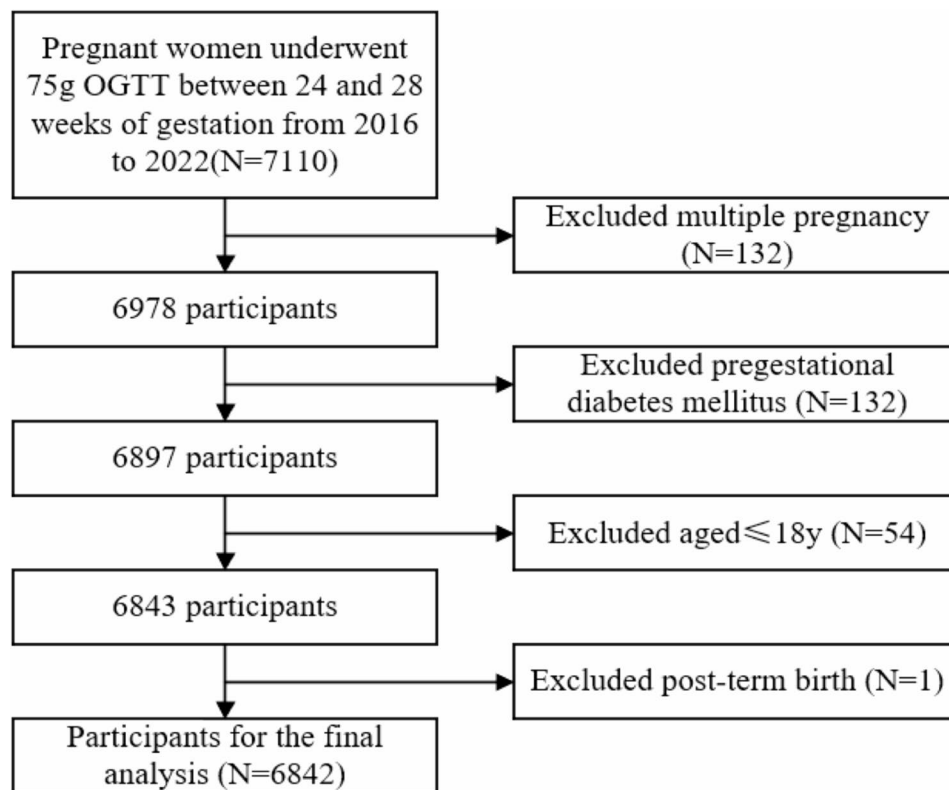
### Study population and data collection

This retrospective cohort study utilized data from pregnant women who delivered at the People’s Hospital of Pingyang, Wenzhou City, Zhejiang Province, China between January 2016 and December 2022. The hospital is the sole tertiary hospital in Pingyang county and serves as the primary provider of pregnancy registration, examination and delivery services for expectant mothers. Data used in this study were extracted from the hospital information system (HIS) by trained researchers.

In this study, 7,110 women underwent a standard 75-g oral glucose tolerance test (OGTT) between 24 and 28 gestational weeks. The analysis was confined to women with singleton live births. Exclusion criteria included those with multiple pregnancies, pregestational diabetes mellitus, age below 18 years, and post-term births. In line with routine prenatal care practice in China, all women undergo first-trimester screening for pregestational diabetes using fasting plasma glucose and/or HbA1c, ensuring reliable exclusion of women with pre-existing diabetes. Ultimately, a total of 6,842 pregnant women were included in this study (Fig. 1). This retrospective study used existing data and all the information on the personal identification was removed. Ethical approval was obtained from the Medical Research Ethics Committee of the School of Public Health, Fudan University (The international registry no. IRB00002408 & FWA00002399).

### Definitions of variables

Plasma glucose levels were measured in the fasting, 1 h, and 2 h after a 75-g OGTT between 24 and 28 weeks of gestation. The OGTT was performed in the morning after an overnight fast of at least 8 h. All participants were instructed to maintain their usual diet and avoid smoking, excessive physical activity, and additional calorie intake during the fasting period. Blood samples were collected in fluoride tubes and centrifuged promptly; plasma



**Fig. 1** Flowchart of study participants

glucose levels were determined using enzymatic methods (Beckman Diagnostics, Fullerton, CA). GDM was diagnosed if one or more of the following criteria were met: fasting plasma glucose  $\geq 5.1$  mmol/L, 1-hour postprandial plasma glucose level  $\geq 10.0$  mmol/L, or 2-hour postprandial plasma glucose level  $\geq 8.5$  mmol/L.

The primary outcome of interest was preterm birth, defined as birth before 37 weeks of gestation. Gestational age was calculated based on the last menstrual period and was confirmed with ultrasound measurements. In this study, preterm birth included both spontaneous and iatrogenic preterm births.

Information on maternal age, parity (previous live births), in vitro fertilization, and neonatal sex was recorded by the physicians at the first pregnancy registration visit. Mothers of advanced maternal age were classified according to whether they were over 35 years old.

#### Statistical analysis

Continuous variables were summarized as mean (standard deviation, SD) or median (interquartile range, IQR), and categorical variables were presented as numbers (percentages, %). Student's t-test was used to test the difference in maternal plasma glucose levels between the term birth and preterm birth groups. To investigate the association between maternal glucose levels and preterm birth, logistic regression analyses were conducted.

For associations of glucose levels with preterm birth, GDM status and each glucose measurement was considered as a continuous variable in logistic regression analysis. Maternal age was entered into the models as a binary variable, with women aged  $\geq 35$  years classified as advanced maternal age. To assess potential multicollinearity among the covariates, variance inflation factor (VIF) values were calculated, and logistic regression models were then used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for preterm birth. Two models were constructed for these regression analyses: model 1 was a univariate model, and model 2 adjusted for age, parity, in vitro fertilization, and neonatal sex. To assess the potential nonlinear relationships among fasting, 1-hour, and 2-hour plasma glucose levels as continuous variables with preterm birth risk, restricted cubic spline regression analysis with 3 knots was performed. All statistical analyses were performed in R 4.3.2 (<http://www.R-project.org>). A P value  $< 0.05$  was considered statistically significant.

## Results

### Characteristics of study participants

A total of 6,842 women were included in this retrospective study; 7.92% were diagnosed with GDM, and 5.86% experienced preterm births (Fig. 1; Table 1). The mean age of the pregnant women at delivery was  $30.50 \pm 4.61$

**Table 1** Characteristics of study participants according to preterm birth status

Characteristics	Entire Sample	Full-term birth	Preterm birth	P
Participants, n (%)	6842	6441 (94.14%)	401 (5.86%)	
Maternal age, mean (SD), y	30.50 (4.61)	30.47 (4.61)	30.98 (4.57)	
Maternal age group, n (%)				0.29
< 35	5612 (82.02%)	5291 (94.28%)	321 (5.72%)	
≥ 35	1230 (17.98%)	1150 (93.50%)	80 (6.50%)	
Parity group, n (%)				0.72
None	2786 (40.72%)	2628 (94.33%)	158 (5.67%)	
1	3745 (54.74%)	3523 (94.07%)	222 (5.93%)	
2 or more	311 (4.55%)	290 (93.25%)	21 (6.75%)	
In vitro fertilization, n (%)				0.59
No	6697 (97.88%)	6303 (94.12%)	394 (5.88%)	
Yes	145 (2.12%)	138 (95.17%)	7 (4.83%)	
Neonatal sex				0.02
Male	3683 (53.83%)	3445 (93.54%)	238 (6.46%)	
Female	3159 (46.17%)	2996 (94.84%)	163 (5.16%)	
GDM, n (%)				<0.001
No	5516 (80.65%)	5220 (94.63%)	296 (5.36%)	
Yes	1326 (19.38%)	1221 (92.08%)	105 (7.92%)	
Fasting plasma glucose, median (IQR), mmol/L	4.44 (4.20, 4.72)	4.44 (4.20, 4.71)	4.48 (4.22, 4.83)	0.03
1-h plasma glucose, median (IQR), mmol/L	7.65 (6.51, 8.80)	7.64 (6.51, 8.78)	7.86 (6.62, 9.18)	0.01
2-h plasma glucose, median (IQR), mmol/L	6.59 (5.80, 7.52)	6.58 (5.78, 7.51)	6.73 (6.06, 7.81)	0.001

GDM gestational diabetes mellitus, SD Standard deviation, IQR Interquartile range

years, with 17.98% classified as having advanced maternal age. Among the pregnant women, 40.72% were primiparous, and 2.12% conceived through in vitro fertilization. Median (IQR) levels of fasting, 1-hour, and 2-hour plasma glucose were 4.44 (4.20, 4.72) mmol/L, 7.65 (6.51, 8.80) mmol/L, and 6.59 (5.80, 7.52) mmol/L, respectively.

#### Association between maternal glucose concentrations and preterm birth

Figure 2 shows the mean levels of maternal plasma glucose in the full-term and preterm birth groups.

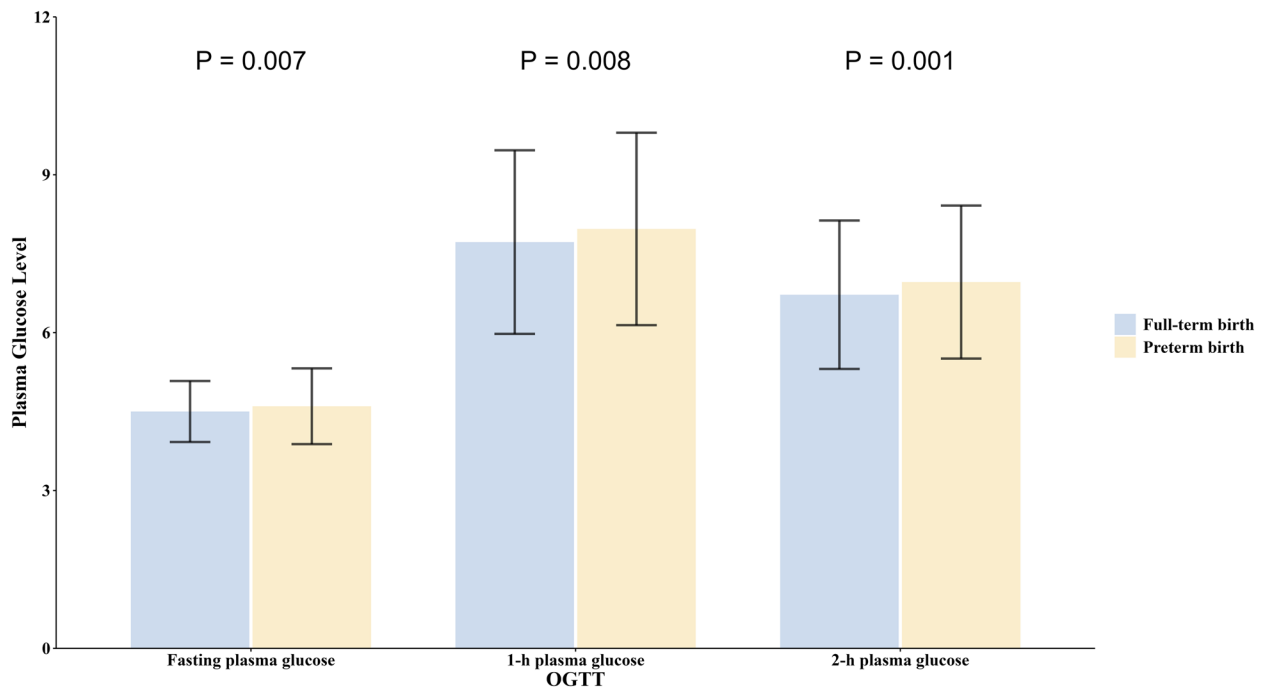
Levels of fasting plasma glucose ( $P=0.007$ ), 1-h plasma glucose ( $P=0.008$ ), and 2-h plasma glucose ( $P=0.001$ ) were higher in women with preterm birth compared to those with term birth. All covariates had  $VIF < 5$ , indicating no significant multicollinearity.

Unadjusted and adjusted odds ratios for the association of maternal glucose concentrations as continuous and categorical variables with preterm birth are presented in Table 2. Compared to women without GDM, the odds of preterm birth was significantly higher in women with GDM (aOR: 1.42; 95% CI: 1.10, 1.84;  $P=0.007$ ). Analyses of glucose levels as continuous variables revealed significant associations with an increased risk of preterm birth: fasting plasma glucose (aOR: 1.26; 95% CI: 1.08, 1.47;  $P=0.003$ ), 1-hour plasma glucose (aOR: 1.10; 95% CI: 1.03, 1.17;  $P=0.003$ ), and 2-hour plasma glucose (aOR: 1.10; 95% CI: 1.02, 1.19;  $P=0.012$ ).

Sensitivity analyses were conducted to assess the robustness of the associations between maternal plasma glucose levels and preterm birth (Table 3). When participants with GDM were excluded, the associations between fasting, 1-h, and 2-h plasma glucose and preterm birth were attenuated and no longer statistically significant. Stratified analyses by maternal age showed that among women aged  $\geq 35$  years, only 1-h plasma glucose remained marginally associated with preterm birth (aOR:1.14, 95% CI: 1.01, 1.30;  $P=0.04$ ). In contrast, among women aged  $< 35$  years, fasting, 1-h, and 2-h plasma glucose levels were all significantly associated with increased risk of preterm birth. To formally test whether age or parity modified the effect of glucose on preterm birth, we conducted interaction analyses. As shown in Table 4, none of the interaction terms between glucose measures and maternal age or parity were statistically significant ( $P$  for interaction  $> 0.10$ ), suggesting that the effects of maternal glycemia on preterm birth risk were consistent across age and parity groups.

We further performed subgroup analyses by gestational age at delivery to evaluate whether the associations between maternal glucose levels and preterm birth varied across early ( $< 34$  weeks) and late (34–36 weeks) preterm birth (Table 5). For early preterm birth, higher fasting plasma glucose was significantly associated with increased risk (aOR:1.38; 95% CI:1.03,1.85), whereas the associations for 1-hour and 2-hour plasma glucose did not reach statistical significance. For late preterm birth, fasting (aOR:1.22; 95% CI:1.05,1.43), 1-hour plasma glucose (aOR:1.07; 95% CI:1.01,1.14), and 2-hour plasma glucose (aOR:1.11;95% CI:1.03,1.19) were all positively associated with preterm birth risk.

The restricted cubic spline regression analysis of Fig. 3 revealed significant linear associations between maternal fasting plasma glucose ( $P$  for overall=0.002;  $P$  for nonlinear=0.264; Fig. 3A), 1-hour plasma glucose ( $P$



**Fig. 2** Levels of maternal plasma glucose according to preterm birth status. The bar charts show the mean values, and the error bars represent standard deviation ( $\pm$ SD). *P* value was calculated using *t* test

**Table 2** Association between maternal glucose levels and preterm birth

	Difference in risk (RD% [95% CI])	Model 1 <sup>a</sup>		Model 2 <sup>b</sup>	
		OR (95% CI)	<i>P</i>	aOR (95% CI)	<i>P</i>
GDM	2.46 (1.67,3.25)	1.45 (1.12, 1.87)	0.004	1.42 (1.10, 1.84)	0.007
Fasting plasma glucose		1.27 (1.09, 1.48)	0.002	1.26 (1.08, 1.47)	0.003
1-h plasma glucose		1.10 (1.04, 1.17)	0.002	1.10 (1.03, 1.17)	0.003
2-h plasma glucose		1.11 (1.03, 1.19)	0.006	1.10 (1.02, 1.19)	0.012

RD Difference in risk, GDM Gestational diabetes mellitus, OR Odds ratio, aOR Adjusted odds ratio, CI, Confidence interval

<sup>a</sup> Univariate model

<sup>b</sup> Adjusted for age, parity, in vitro fertilization, and neonatal sex

for overall = 0.023; *P* for nonlinear = 0.535; Fig. 3B), and 2-hour plasma glucose (*P* for overall = 0.006; *P* for nonlinear = 0.368; Fig. 3C) levels and the risk of preterm birth. The nonlinear components were not statistically

significant (all *P*-nonlinear > 0.05), indicating that the associations followed a linear dose–response pattern.

## Discussion

This retrospective study demonstrated a linear and positive association between elevated gestational plasma glucose levels and the risk of preterm birth. Among women with GDM, the odds of preterm birth were 1.42 times higher than those of non-diabetic mothers. These results underscore the importance of better controlling maternal plasma glucose levels during pregnancy to reduce the risk of preterm birth due to hyper-glycaemia, thereby alleviating the medical burden on both the healthcare system and individuals.

Women with GDM were more likely to experience preterm birth, consistent with findings from studies conducted in various regions [20–22]. A study conducted in China similarly found that GDM is a significant risk factor for preterm birth and stillbirth [23]. Another study demonstrated that GDM independently increases the risk of spontaneous preterm birth [20]. Furthermore,

**Table 3** Sensitivity analyses of the association between maternal plasma glucose levels and risk of preterm birth

	Excluding participants with GDM		Excluding participants aged < 35 years		Excluding participants aged $\geq$ 35 years	
	aOR (95% CI)	<i>P</i>	aOR (95% CI)	<i>P</i>	aOR (95% CI)	<i>P</i>
Fasting plasma glucose	0.99 (0.70, 1.39)	0.94	1.10 (0.76, 1.58)	0.61	1.29 (1.11, 1.49)	<0.001
1-h plasma glucose	1.08 (0.99, 1.18)	0.10	1.14 (1.01, 1.30)	0.04	1.06 (1.00, 1.13)	0.05
2-h plasma glucose	1.11 (0.99, 1.25)	0.08	1.12 (0.97, 1.31)	0.13	1.11 (1.03, 1.20)	0.01

**Table 4** Interaction effects between maternal age, parity, and OGTT glucose levels on risk of preterm birth

Model	Main Glucose Effect (aOR, 95% CI)	Maternal Age (aOR, 95% CI)	Parity (aOR, 95% CI)	Interaction Term (aOR, 95% CI)	P for interaction
Fasting plasma glucose × Age	1.08 (0.75–1.55)	0.40 (0.06–2.42)	1.02 (0.84–1.23)	1.19 (0.81–1.76)	0.38
1-h plasma glucose × Age	1.13 (1.00–1.29,0.029)	1.53 (0.45–5.14)	1.02 (0.84–1.23)	0.94 (0.82–1.08)	0.39
2-h plasma glucose × Age	1.12 (0.97–1.30)	0.97 (0.28–3.34)	1.01 (0.84–1.23)	0.99 (0.84–1.17)	0.93
Fasting plasma glucose × Parity	1.25 (1.09–1.44)**	0.59 (0.32–1.06)	0.69 (0.40–1.18)	1.55 (0.87–2.77)	0.13
1-h plasma glucose × Parity	1.08 (1.02–1.14)*	0.61 (0.34–1.10)	0.70 (0.41–1.20)	1.53 (0.86–2.71)	0.15
2-h plasma glucose × Parity	1.11 (1.04–1.19)**	0.62 (0.34–1.11)	0.70 (0.41–1.19)	1.54 (0.87–2.73)	0.14

Values are adjusted for IVF treatment and neonatal sex

\*P < 0.05

\*\*P < 0.01

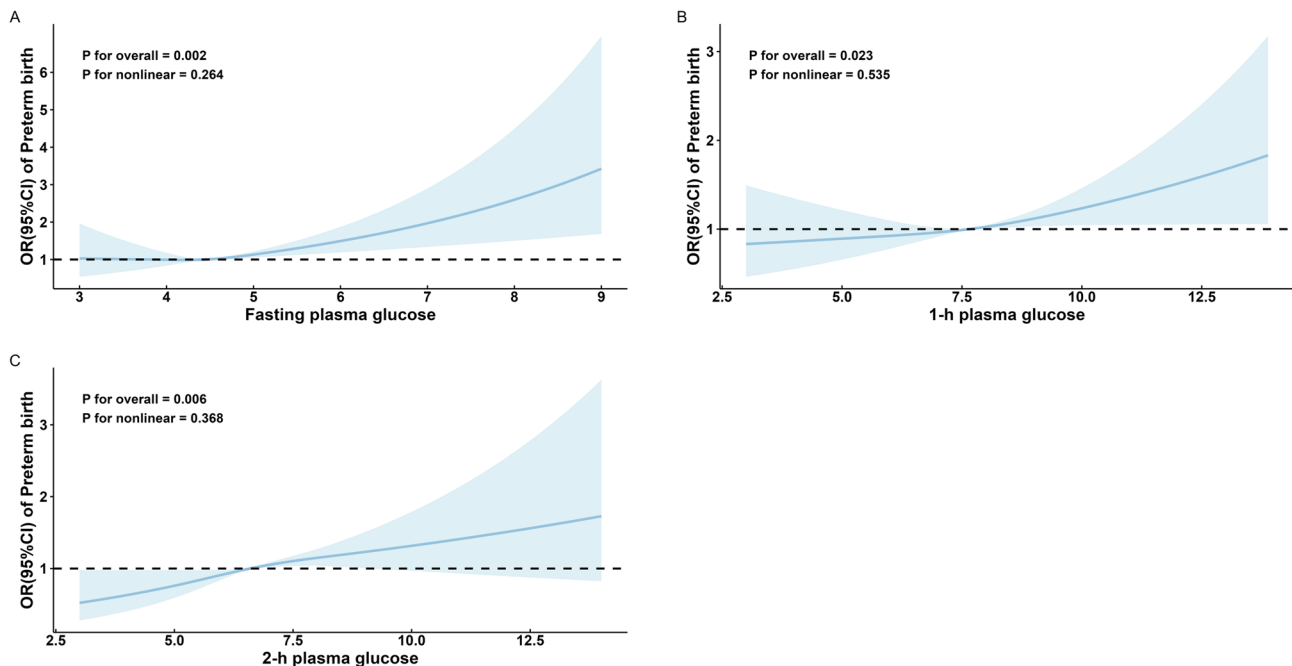
**Table 5** Association of fasting, 1-hour, and 2-hour plasma glucose levels with early and late preterm birth: multinomial logistic regression analysis

Factor	Early preterm			Late preterm		
	Fasting plasma glucose	1-h plasma glucose	2-h plasma glucose	Fasting plasma glucose	1-h plasma glucose	2-h plasma glucose
	Exp β [95% C.I.]	Exp β [95% C.I.]	Exp β [95% C.I.]	Exp β [95% C.I.]	Exp β [95% C.I.]	Exp β [95% C.I.]
(Intercept)	0 [0, 0.01]***	0 [0, 0.01]***	0 [0, 0.01]***	0.02 [0.01, 0.04]***	0.03 [0.02, 0.05]***	0.02 [0.01, 0.05]***
plasma glucose	1.38 [1.03, 1.85]*	1.11 [0.97, 1.28]	1.15 [0.98, 1.34]	1.22 [1.05, 1.43]**	1.07 [1.01, 1.14]*	1.11 [1.03, 1.19]**
Maternal age group	0.56 [0.32, 0.99]*	0.58 [0.33, 1.02]	0.59 [0.33, 1.04]	0.99 [0.73, 1.34]	1.01 [0.75, 1.37]	1.03 [0.76, 1.4]
Parity group	1.55 [0.97, 2.47]	1.56 [0.98, 2.49]	1.56 [0.97, 2.48]	0.94 [0.77, 1.15]	0.94 [0.77, 1.16]	0.94 [0.77, 1.15]
In vitro fertilization	0.75 [0.1, 5.57]	0.78 [0.11, 5.78]	0.75 [0.1, 5.58]	0.78 [0.34, 1.8]	0.79 [0.34, 1.8]	0.77 [0.34, 1.77]
Neonatal sex	1.54 [0.91, 2.6]	1.54 [0.91, 2.61]	1.55 [0.92, 2.62]	1.22 [0.98, 1.52]	1.22 [0.98, 1.52]	1.22 [0.98, 1.53]

\*P < 0.05

\*\*P < 0.01

\*\*\*P < 0.001



**Fig. 3** Adjusted\* odds ratios and 95 % confidence intervals for preterm birth in association with maternal glucose concentrations in restricted cubic spline regression. **A** Fasting plasma glucose; **B** 1-hour plasma glucose; **C** 2-hour plasma glucose

\* Adjusted for age, parity, in vitro fertilization, and neonatal sex. Solid line indicates odds ratio; shaded area indicates 95% confidence interval

some studies indicated that women diagnosed with GDM in early pregnancy, even those receiving treatment, still face increased risks of preterm birth and other adverse outcomes [24, 25]. The metabolism of pregnant women with gestational diabetes is altered, and high levels of plasma glucose may induce endothelial dysfunction, oxidative stress, and impaired vasodilation, leading to the occurrence of preterm birth [26, 27]. Studies have also shown that placental developmental abnormalities persist in pregnant women with GDM, such as an increased incidence of villous immaturity, enhanced angiogenesis, and increased placental weight [13, 14]. These alterations can impair placental function and nutrient transport, potentially leading to uteroplacental insufficiency and increasing the risk of preterm birth. However, the exact biological mechanisms linking GDM to preterm birth are not yet fully understood and require further investigation.

Few studies have explored the relationship between gestational glucose levels as continuous variables and the risk of preterm birth among Chinese pregnant women. To objectively assess the form of these associations, we employed restricted cubic spline (RCS) regression, which does not presuppose linearity and allows for flexible modeling of potential nonlinear trends. Our findings showed that fasting, 1-hour, and 2-hour plasma glucose levels are independent predictors of preterm birth, with significant linear associations observed even after adjusting for potential confounders. This linear relationship aligns with findings from the HAPO study [18]. Specifically, in our study, fasting, 1-hour, and 2-hour glucose levels during pregnancy was associated with adjusted odds ratios (aORs) of 1.26, 1.10, and 1.10 for preterm birth, respectively. These results indicate statistically significant increases in the odds of preterm birth with higher maternal glucose levels. However, sensitivity analysis found that when women diagnosed with GDM were excluded from the cohort, the associations between all OGTT glucose measures and preterm birth were no longer significant. This indicates that the observed population-level linear relationship is primarily driven by the metabolic dysregulation present in women with GDM. The current diagnostic thresholds effectively identify a population at substantially increased risk for preterm birth due to hyperglycemia. Compared with 1-hour and 2-hour plasma glucose, fasting plasma glucose demonstrated a superior predictive effect on the risk of preterm birth. Consistent with our findings, existing studies have also reported that fasting plasma glucose exhibits a stronger correlation with adverse outcomes compared to post-load glucose concentrations [16, 19]. A recent retrospective cohort study suggested a potential nonlinear association between gestational glucose levels and preterm birth [17]. These inconsistent risk relationships

might be attributed to differences in study populations and statistical methods. Future studies involving larger and more diverse populations are essential to derive consistent and replicable conclusions, which will be critical for understanding the risks associated with gestational glucose levels and for establishing accurate diagnostic criteria for GDM.

Subgroup analyses indicated that elevated fasting plasma glucose may be particularly important for predicting early preterm delivery, whereas all three glucose measures are associated with late preterm birth. These results suggest that fasting glucose monitoring could be particularly informative for identifying women at risk of very early delivery, enabling individualized monitoring and targeted interventions particularly for women who do not meet traditional GDM thresholds. Further studies are needed to validate these subgroup-specific associations and explore their underlying biological mechanisms.

Sensitivity analyses indicated that the significant associations between maternal glucose and preterm birth observed among younger women, but not among those aged  $\geq 35$  years, may reflect the relatively larger sample size in the younger group or the stronger influence of competing risk factors in advanced maternal age pregnancies. For example, women of advanced age have a higher prevalence of chronic hypertension and uterine factors, which already confer a higher baseline risk of preterm birth, potentially masking the effect of hyperglycemia. Further interaction analyses showed no significant effect modification by maternal age or parity, suggesting that the impact of elevated glucose on preterm birth risk is relatively consistent across different age groups and parity categories. This indicates that elevated glucose is a risk factor for preterm birth regardless of maternal age or reproductive history, underscoring the need for continuous glucose monitoring throughout pregnancy.

There are several limitations of our study. First, our study population was drawn from women who underwent OGTT between 24 and 28 weeks; women who did not receive OGTT were not included, which may limit the representativeness of the sample and could bias findings toward women considered at higher risk. Second, preterm birth was analyzed as a whole, and the existing data could not distinguish between spontaneous and iatrogenic PTB, which differ in etiology and may have distinct relationships with maternal glycemia. This may have introduced residual heterogeneity into our results. Third, since the data for this study were obtained from the HIS, data on pre-pregnancy BMI, family income, previous preterm birth history, smoking, maternal comorbidities, pregnant women's diet, nutritional status, and lifestyle were not available. Additionally, neonatal data on major congenital anomalies were lacking, preventing us

from excluding affected fetuses. The evaluators were also not blinded to the OGTT measurements when assessing the primary outcomes. These limitations related to incomplete HIS data may introduce potential biases and confounding effects. However, the primary outcome—preterm birth—is based on objective laboratory criteria, which partially mitigates the impact of this bias. Finally, the study was conducted in a single tertiary hospital, which may limit the generalizability of the findings. Future studies with multicenter data and the ability to stratify PTB into spontaneous and iatrogenic categories are warranted to better elucidate these associations.

## Conclusions

In summary, elevated plasma glucose levels during pregnancy statistically significantly increase the risk of preterm birth. Fasting, 1-hour, and 2-hour gestational plasma glucose all exhibited significant linear associations with preterm birth. Given that hyperglycemia during pregnancy can be prevented and managed, it is crucial to enhance health education and glucose monitoring for pregnant women. Timely interventions should be implemented to control plasma glucose levels, thereby reducing the incidence of preterm birth.

## Acknowledgements

We are grateful to the staff of the People's Hospital of Pingyang for their assistance in data collection.

## Authors' contributions

B.Q.H. & N.W. were responsible for the acquisition, analysis and interpretation of data, and the drafting of the manuscript. S.M.H. & G.K.L. & Q.Q.W. & Y.Z. contributed to the acquisition and interpretation of data, and critically reviewed the manuscript for important intellectual content. X.Y.X. & X.R.S. & X.T.W. & B.C.S. participated in data interpretation and revised the manuscript. H.X.W. & Q.W.J. & M.H. & Y.C. provided advice regarding study design and reviewed and revised the manuscript. N.W. & J.W.W. was the project coordinator and contributed to the design of the study, and the review and revision of the manuscript. All authors read and approved the final manuscript.

## Funding

No funding was received for conducting this study.

## Data availability

The datasets analyzed during the current study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Medical Research Ethics Committee of the School of Public Health, Fudan University (The international registry no. IRB00002408 & FWA00002399). Written informed consent was not required for this retrospective study because all patient identifying information was removed from the study data, requirement of consent was waived by the Medical Research Ethics Committee of the School of Public Health, Fudan University.

### Consent for publication

Not applicable.

## Competing interests

The authors declare no competing interests.

Received: 27 June 2025 / Accepted: 30 September 2025

Published online: 19 November 2025

## References

- Lin X-h, Wu D-d, Li C, Xu Y-j, Gao L, Lass G, et al. Maternal high triglyceride levels during early pregnancy and risk of preterm delivery: A retrospective cohort study. *J Clin Endocrinol Metabolism*. 2019;104(4):1249–58.
- Wood NS, Marlow N, Costeloe K, Gibson AT, Wilkinson AR, Grp EPS. Neurologic and developmental disability after extremely preterm birth. *N Engl J Med*. 2000;343(6):378–84.
- Han Z, Mulla S, Beyene J, Liao G, McDonald SD, Knowledge Synth G. Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. *Int J Epidemiol*. 2011;40(1):65–101.
- Jing S, Chen C, Gan Y, Vogel J, Zhang J. Incidence and trend of preterm birth in China, 1990–2016: a systematic review and meta-analysis. *Bmj Open*. 2020;10(12):e039303.
- Berard A, Le Tiec M, De Vera MA. Study of the costs and morbidities of late-preterm birth. *Archives Disease Childhood-Fetal Neonatal Ed*. 2012;97(5):F329–34.
- Waitzman NJ, Jalali A, Grosse SD. Preterm birth lifetime costs in the United States in 2016: an update. *Semin Perinatol*. 2021. <https://doi.org/10.1016/j.semperi.2021.151390>.
- Erjavec K, Poljicanin T, Matijevic R. Impact of the implementation of new WHO diagnostic criteria for gestational diabetes mellitus on prevalence and perinatal outcomes: A Population-Based study. *J Pregnancy*. 2016;2016:2670912.
- Colberg SR, Castorino K, Jovanovic L. Prescribing physical activity to prevent and manage gestational diabetes. *World J Diabetes*. 2013;4(6):256–62.
- Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF diabetes atlas: estimation of global and regional gestational diabetes mellitus prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's criteria. *Diabetes Res Clin Pract*. 2022. <https://doi.org/10.1016/j.diabres.2021.09050>.
- Juan J, Yang H. Prevalence, Prevention, and lifestyle intervention of gestational diabetes mellitus in China. *Int J Environ Res Public Health*. 2020;17:24.
- Scholl TO, Sowers M, Chen XH, Lenders C. Maternal glucose concentration influences fetal growth, gestation, and pregnancy complications. *Am J Epidemiol*. 2001;154(6):514–20.
- Devaskar SU, Chu A. Intrauterine growth restriction: hungry for an answer. *Physiology*. 2016;31(2):131–46.
- Molitierno R, Imparato A, Iavazzo N, Salzillo C, Marzullo A, Laganà AS, et al. Microscopic changes and gross morphology of placenta in women affected by gestational diabetes mellitus in dietary treatment: a systematic review. *Open Med*. 2025. <https://doi.org/10.1515/med-2025-1142>.
- Huynh J, Dawson D, Roberts D, Bentley-Lewis R. A systematic review of placental pathology in maternal diabetes mellitus. *Placenta*. 2015;36(2):101–14.
- Armistead B, Johnson E, VanderKamp R, Kula-Eversole E, Kadam L, Drevlo S, et al. Placental regulation of energy homeostasis during human pregnancy. *Endocrinology*. 2020. <https://doi.org/10.1210/endo/bqaa076>.
- Zhao D, Liu D, Shi W, Shan L, Yue W, Qu P, et al. Association between maternal blood glucose levels during pregnancy and birth outcomes: a birth cohort study. *Int J Environ Res Public Health*. 2023. <https://doi.org/10.3390/ijerph20032102>.
- Liang R, Panelli DM, Stevenson DK, Rehkopf DH, Shaw GM. Associations between pregnancy glucose measurements and risk of preterm birth: a retrospective cohort study of commercially insured women in the United States from 2003 to 2021. *Ann Epidemiol*. 2023. <https://doi.org/10.1016/j.annepidem.2023.03.002>.
- Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008;358(19):1991–2002.
- Farrar D, Simmonds M, Bryant M, Sheldon TA, Tuffnell D, Golder S et al. Hyperglycaemia and risk of adverse perinatal outcomes: systematic review and meta-analysis. *Bmj-British Med J*. 2016;354:i4694.
- Boriboonhirunsarn D, Tanpong S. Rate of spontaneous preterm delivery between pregnant women with and without gestational diabetes. *Cureus J Med Sci*. 2023;15(2):e34565.

21. Fadl HE, Ostlund IKM, Magnuson AFK, Hanson USB. Maternal and neonatal outcomes and time trends of gestational diabetes mellitus in Sweden from 1991 to 2003. *Diabet Med*. 2010;27(4):436–41.
22. Sudasinghe BH, Wijeyaratne CN, Ginige PS. Long and short-term outcomes of gestational diabetes mellitus (GDM) among South Asian women - A community-based study. *Diabetes Res Clin Pract*. 2018;145:93–101.
23. Feng R, Liu L, Zhang Y-Y, Yuan Z-S, Gao L, Zuo C-T. Unsatisfactory glucose management and adverse pregnancy outcomes of gestational diabetes mellitus in the real world of clinical practice: A retrospective study. *Chin Med J*. 2018;131(9):1079–85.
24. Bashir M, Baagar K, Naem E, Elkhatib F, Alshaybani N, Konje JC, et al. Pregnancy outcomes of early detected gestational diabetes: a retrospective comparison cohort study, Qatar. *BMJ Open*. 2019. <https://doi.org/10.1136/bmjopen-2018-023612>.
25. Sweeting AN, Ross GP, Hyett J, Molyneaux L, Constantino M, Harding AJ, et al. Gestational diabetes mellitus in early pregnancy: evidence for poor pregnancy outcomes despite treatment. *Diabetes Care*. 2016;39(1):75–81.
26. Li G, Xing Y, Wang G, Wu Q, Ni W, Jiao N, et al. Does recurrent gestational diabetes mellitus increase the risk of preterm birth? A population-based cohort study. *Diabetes Res Clin Pract*. 2023. <https://doi.org/10.1016/j.diabres.2023.110628>.
27. Forbes S, Godsland IF, Taylor-Robinson SD, Bell JD, Thomas EL, Patel N, et al. A history of previous gestational diabetes mellitus is associated with adverse changes in insulin secretion and VLDL metabolism independently of increased intrahepatocellular lipid. *Diabetologia*. 2013;56(9):2021–33.

### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.