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Universal screening for hyperglycemia in early pregnancy and the risk of adverse pregnancy outcomes

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Abstract

Introduction This study aimed to evaluate the screening outcomes in women with hyperglycemia in early pregnancy (fasting plasma glucose [FPG] 5.1–6.9 mmol/L and/or HbA1c 39–46 mmol/mol before 20 weeks of gestation).

Methods This multicenter retrospective cohort study was conducted in China between 2016 and 2022. In our setting, all women without pregestational diabetes performed both FPG and HbA1c screening at the first prenatal visit. Logistic regression models adjusted for confounders were performed to assess the associations of hyperglycemia in early pregnancy with adverse pregnancy outcomes. Subgroup analyses were explored according to the subsequent diagnosis of gestational diabetes (GDM, with or without).

Results Of the 42,999 women in the analysis, 2515 (5.8%) women had hyperglycemia in early pregnancy. Compared with women with normal FPG and HbA1c levels, women with FPG 5.1–6.9 mmol/L and/or HbA1c 39–46 mmol/mol had a 3-fold increased risk of GDM (aOR 3.85; 95% CI 3.52–4.20), and 1-fold higher risk of hypertensive disorders of pregnancy (1.42; 1.20–1.67), shoulder dystocia (1.30; 1.11–1.52), preterm birth (1.30; 1.11–1.52), large-for-gestational-age (1.26; 1.12–1.43), and macrosomia (1.43; 1.19–1.73). Women with hyperglycemia in early pregnancy complicated by GDM were associated with a 50%, 84%, 48% and 24% increase in the odds of developing hypertensive disorders of pregnancy (1.50; 1.21–1.84), preterm premature rupture of membranes (1.84; 1.09–3.10), preterm birth (1.48; 1.22–1.81) and large-for-gestational-age (1.24; 1.05–1.45), respectively, compared with those without hyperglycemia.

Conclusions Pregnant women with hyperglycemia in early pregnancy have an increased risk of adverse pregnancy outcomes, and women with these conditions complicated by GDM are at higher risk than those without. Further research is needed to explore whether the incidence of GDM can be reduced by early intervention and therefore prevent the relevant adverse pregnancy outcomes.

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Keywords Gestational diabetes, Antenatal screening, HbA1c, Prediabetes, Outcome

Introduction

Gestational diabetes (GDM) is the most common complication of pregnancy. Among women diagnosed with GDM, 30-70% have hyperglycemia detectable in early pregnancy (before 20 weeks of gestation) [1]. Recently, the TOBOGM trial has demonstrated that early diagnosis and treatment is beneficial for pregnancy outcomes, particularly before 14 weeks of gestation [2]. In view of these reasons, screening for hyperglycemia in early pregnancy is suggested to be integrated into routine prenatal care as part of a life course approach to GDM screening and diagnosis [3].

However, the most appropriate test and threshold remain undefined. While the OGTT test is the gold standard diagnostic tool for GDM, its use in early pregnancy is limited by feasibility [4, 5]. Studies have also evaluated the use of HbA1c or FPG to screen for hyperglycemia in early pregnancy and the risk of adverse pregnancy outcomes, but results vary due to different settings, screening approaches, and diagnostic criteria. The Chinese guideline recommends universal fasting plasma glucose (FPG) screening for women without pregestational diabetes at the first prenatal visit, while it does not recommend hemoglobin A1c (HbA1c) for early routine screening due to insufficient evidence [6]. In practice, some high-resource settings perform both FPG and HbA1c screening at the first prenatal visit. Evidence is still lacking on the risk of adverse pregnancy outcomes associated with hyperglycemia in early pregnancy under such a combined screening strategy. Additionally, whether hyperglycemia in early pregnancy is independently associated with adverse pregnancy outcomes apart from standard GDM is still unclear [3].

This study aimed to assess the risk of adverse maternal and neonatal outcomes in women with hyperglycemia in early pregnancy using a combined universal screening strategy of FPG and HbA1c, and to determine whether these risks were independent of standard GDM.

Materials and methods

Study design

This was a population-based retrospective cohort study conducted across three tertiary hospitals in China between 1 January 2016 and 31 December 2022. Approval for the study was obtained from the Independent Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital, Sun Yat-sen University (Ref. No. 2022.458). All data were collected from the hospital electronic medical record.

In our setting, all women performed FPG and HbA1c tests at the time of their first antenatal blood as a screening test for undiagnosed diabetes. We included women who performed FPG and HbA1c tests before 20 weeks of gestations. Exclusion criteria were pregestational diabetes (including diabetes diagnosed before pregnancy and diagnosed during pregnancy by FPG ≥ 7.0 mmol/L (126 mg/dL) or HbA1c ≥ 48 mmol/mol (6.5%)) [6], multiple pregnancies, miscarriage (fetal loss < 24 weeks of gestation) or termination of pregnancy due to fetal abnormalities, or missing data on pregnancy outcomes.

Definition of hyperglycemia in early pregnancy

In this study, we defined women with FPG 5.1–6.9 mmol/L and/or HbA1c 39–46 mmol/mol (5.7-6.4%) before 20 weeks of gestation as hyperglycemia in early pregnancy. The reasons are shown below.

Screening for undiagnosed diabetes at the first prenatal visit utilizing FPG or HbA1c is recommended by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) [7] and the American Diabetes Association (ADA) [8]. Such strategy also identifies women with hyperglycemia but not meeting the criteria for diabetes [9].

FPG 5.1–6.9 mmol/L (92–124 mg/dL) in early pregnancy is associated with gestational diabetes mellitus (GDM) [10–12], hypertensive disorders of pregnancy (HDP) [13], large-for-gestational-age (LGA) [12–15], primary cesarean delivery and preterm birth [13, 16]. The IADPSG initially recommended that an FPG value of 5.1–6.9 mmol/l before 24 weeks of gestation be classified as GDM and later reversed this recommendation based on studies focused on the outcome of GDM [7]. Subsequent evidence has also indicated that FPG 5.1–6.9 mmol/L in early pregnancy lead to higher rates of perinatal adverse outcomes [13, 16, 17].

The IADPSG [7] and the ADA [8] state that HbA1c 41–46 mmol/mol (5.9-6.4%) in early pregnancy is associated with adverse perinatal outcomes, with most evidence coming from mixed-ethnic population cohorts. Ethnic differences may influence HbA1c threshold and its relationship with pregnancy outcomes [18]. There is limited research in the Asian population. A multiethnic cohort has presented that the South-Central Asian population with HbA1c 39–46 mmol/mol (5.7-6.4%) in the first trimester have a higher risk of preeclampsia, LGA and macrosomia [18]. Another large Chinese cohort has indicated that HbA1c 39–46 mmol/mol in the first trimester is an independent risk factor for GDM, while its association with other pregnancy outcomes is not reported [10]. The Chinese guideline also highlights that pregnant women with an HbA1c of 39–46 mmol/mol

during the first trimester are at high risk of developing GDM [6].

In our setting, women identified as hyperglycemia in early pregnancy received simple oral advice on diet or physical activity or continued routine prenatal care without any counseling based on physician's choice. They did not receive standard lifestyle interventions before 24–28 weeks of gestation. The initiation of lifestyle interventions was only for those who had a diagnosis of GDM afterwards.

Outcomes

GDM was defined by the IADPSG criteria as one or more of the following 75 g OGTT criteria were met or exceeded between 24 and 28 weeks of gestation: FPG 5.1 mmol/L, 1-hour plasma glucose 10.0 mmol/L or 2-hour plasma glucose 8.5 mmol/L [19]. HDP consisted of gestational hypertension and preeclampsia. Gestational hypertension was characterized by the new onset of hypertension (blood pressure ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic) at or after 20 weeks of gestation. Preeclampsia was defined as gestational hypertension accompanied by one or more of the following conditions at or after 20 weeks of gestation as recommended by the International Society for the Study of Hypertension in Pregnancy [20]: proteinuria, other maternal organ dysfunction, or uteroplacental dysfunction. Women with chronic hypertension were excluded from the analysis of HDP. Other maternal outcomes including preterm premature rupture of membranes (PPROM) [21], postpartum hemorrhage (blood loss of more than 500 mL after vaginal delivery or 1000 mL after a caesarean section within the first 24 h of delivery) [22], placental abruption and primary cesarean section were included in the analysis. Neonatal outcomes included in the analysis were preterm birth < 37 weeks of gestation, shoulder dystocia [23, 24], large-for-gestational-age (LGA, >90th birth percentile for the same gestational age and sex) [25], small-for-gestational-age (<10th birth percentile for the same gestational age and sex) [25], macrosomia (birthweight ≥ 4000 g), stillbirth or neonatal death (from birth up to 28 days after birth) [22].

Statistical analysis

Descriptive data were depicted in mean with standard deviation or median with interquartile range for continuous variables and numbers with proportions for categorical variables. Comparison between the groups was by Student's *t* test or Mann-Whitney U test for continuous variables and χ^2 test or continuity correction test for categorical variables. Univariate and multivariate logistic regression were performed to explore the association between hyperglycemia in early pregnancy and adverse pregnancy outcomes, selecting variables from maternal age, pre-pregnancy BMI, parity, conception by invitro fertilization, delivery year and gestational age at first antenatal blood test with a p value of 0.05. Strongly correlated (absolute correlation coefficient > 0.8) and multicollinear (variance inflation factor > 10) variables were identified and removed. Adjusted OR (aOR) with 95% confidence interval (CI) was calculated. We further classified hyperglycemia in early pregnancy by gestational age (<14 weeks, 14–19 weeks), subtypes (identified by HbA1c, FPG, both FPG and HbA1c), and subsequent diagnosis of GDM (with or without). The descriptive data were computed for each subgroup, and aOR were calculated in different subgroups compared to the reference group of those with normoglycemia (hyperglycemia in early pregnancy without GDM was designated as reference group when compared to those with GDM). Data analyses were performed by SPSS Statistics 26.0 (SPSS Inc., Chicago, IL, USA). In all analyses, a *P* value of less than 0.05 was considered statistically significant.

Results

During the study period, there were 78,870 pregnant women underwent FPG and HbA1c at their first prenatal visit. 35,871 women were excluded due to missing pregnancy outcome ($n = 1054$), diabetes mellitus ($n = 391$), screening at ≥ 20 weeks of gestation ($n = 32322$), miscarriage or termination of pregnancy ($n = 197$), and multiple pregnancies ($n = 1907$). The remaining 42,999 women consisted of 2515 women (5.8%) with hyperglycemia in early pregnancy and 40,484 (94.2%) unaffected pregnancies. The study population flowchart and proportions of hyperglycemia in early pregnancy in different subgroups of women are shown in Supplemental Fig. 1.

Demographic characteristics and pregnancy outcomes of the two groups are presented in Table 1. Women with hyperglycemia in pregnancy had higher maternal age, pre-pregnancy BMI, and higher rates of multiparity, chronic hypertension, GDM, HDP, postpartum hemorrhage, primary cesarean section, shoulder dystocia, preterm birth, SGA, LGA, macrosomia and stillbirth or neonatal death than unaffected pregnancies.

The distribution of different subtypes of hyperglycemia in early pregnancy were as follows: 45.1% (1134 cases) were identified before 14 weeks of gestation, and 54.9% (1381 cases) were identified between 14 and 19 weeks. Among all affected cases, 71.6% (1800 cases) were identified through HbA1c, 21.1% (532 cases) through FPG, and 7.3% (183 cases) through both FPG and HbA1c. Additionally, 49.0% (1233 cases) of the cases had a subsequent diagnosis of GDM, while 51.0% (1282 cases) did not. Comparisons of demographic characteristics and pregnancy outcomes of the subgroups are listed in Supplemental Tables 1–3.

Table 1 Characteristics and pregnancy outcomes in women with and without hyperglycemia in early pregnancy

	Unaffected *N* = 40,484	Hyperglycemia in early pregnancy *N* = 2515	*P* value
Maternal age, y	30.8 ± 4.4	32.7 ± 4.9	<0.001
Pre-pregnancy BMI, kg/m^2	20.8 ± 2.8	22.9 ± 3.7	<0.001
Parity			
0	22,234 (54.9)	1028 (40.9)	<0.001
1	15,757 (38.9)	1202 (47.8)	
≥ 2	2493 (6.2)	285 (11.3)	
Conception by in vitro fertilization	2251 (5.6)	147 (5.8)	0.546
Chronic hypertension	251 (0.6)	67 (2.7)	<0.001
Fasting plasma glucose, mmol/L	4.4 (4.2–4.6)	5.2 (5.1–5.3)	<0.001
HbA1c, mmol/mol	31 (29–33)	34 (31–39)	<0.001
HbA1c, %	5.0 (4.8–5.2)	5.3 (5.0-5.7)	<0.001
Pregnancy outcomes			
Gestational age at delivery	39.3 (38.6–40.0)	39.1 (38.3–40.0)	<0.001
Gestational diabetes	6545 (16.2)	1233 (49.0)	<0.001
Hypertensive disorders of pregnancy [a]	1604 (4.0)	195 (8.0)	<0.001
Preeclampsia	800 (2.0)	91 (3.7)	
Gestational hypertension	804 (2.0)	104 (4.3)	
Preterm premature rupture of membranes	972 (2.4)	70 (2.8)	0.226
Postpartum hemorrhage	839 (2.1)	67 (2.7)	0.045
Placental abruption	377 (0.9)	21 (0.8)	0.625
Primary cesarean section	8624 (21.3)	491 (19.5)	0.034
Shoulder dystocia [b]	187 (0.7)	23 (1.6)	0.001
Preterm birth	2312 (5.7)	206 (8.2)	<0.001
Fetal birthweight	3185 ± 448	3230 ± 519	<0.001
Small-for-gestational-age	3520 (8.7)	162 (6.4)	<0.001
Large-for-gestational-age	3583 (8.9)	372 (14.8)	<0.001
Macrosomia	1179 (2.9)	144 (5.7)	<0.001
Stillbirth or neonatal death	82 (0.2)	10 (0.4)	0.040

Note: Data are expressed as mean ± SD, median (interquartile range) or number (percentage), as appropriate

[a] Data were analyzed in 42,681 women without chronic hypertension, including 40,233 unaffected cases and 2448 cases with hyperglycemia in early pregnancy

[b] Data were analyzed in 26,951 women had vaginal deliveries, including 26,741 unaffected cases and 210 cases with hyperglycemia in early pregnancy

The ORs for pregnancy outcomes with hyperglycemia in early pregnancy are shown in Fig. 1. After adjusting for confounding variables, compared with women with normal FPG and HbA1c levels, women with hyperglycemia in early pregnancy had a 3-fold increased risk of GDM (aOR, 3.87; 95% CI, 3.55–4.20), and 1-fold higher risk of HDP (aOR, 1.42; 95% CI, 1.20–1.67), shoulder dystocia (aOR, 1.29; 95% CI, 1.11–1.52), preterm birth (aOR, 1.30; 95% CI, 1.11–1.52), LGA (aOR, 1.26; 95% CI, 1.12–1.43), and macrosomia (aOR, 1.43; 95% CI, 1.19–1.73). The elevated odds maintained across pregnant women screened at < 14 weeks of gestation and 14–19 weeks of gestation (Fig. 2A, B).

After adjusting for confounding factors, all subtypes of hyperglycemia in early pregnancy were associated with higher odds of GDM, HDP and preterm birth compared to unaffected pregnancies (Fig. 3A, B, C). Pregnant women with hyperglycemia in early pregnancy identified by both FPG and HbA1c had noticeable higher odds for GDM (aOR 13.45; 95% CI, 9.00-21.10) than those identified by FPG (aOR 3.82; 95% CI, 3.45–4.23) or HbA1c (aOR 4.84; 95% CI, 4.13–5.68). Notably, the association of hyperglycemia in early pregnancy with LGA (aOR 1.30; 95% CI, 1.13–1.49) and macrosomia (aOR 1.49; 95% CI, 1.20–1.84) were only observed among pregnant women identified by FPG, rather than those identified by HbA1c or both FPG and HbA1c (Fig. 3A). Furthermore, pregnant women identified by both FPG and HbA1c had a significantly increased risk of PPROM (aOR 2.48; 95% CI, 1.36–4.53), whereas those identified by FPG or A1c did not (Fig. 3C).

In our population, 49% (n = 1233) of women with hyperglycemia in early pregnancy were subsequently diagnosed with GDM at 24–28 weeks of gestation. Women with hyperglycemia in early pregnancy complicated with GDM had increased maternal age, pre-pregnancy BMI, and higher prevalence of multiparity, conception by in vitro fertilization, chronic hypertension, HDP, PPROM, shoulder dystocia, preterm birth and LGA compared to those without (Supplemental Table 3). After adjusting for confounding variables, a 50%, 84%, 48% and 24% increase in the odds of developing HDP (aOR 1.50; 95% CI, 1.21–1.84), PPROM (aOR 1.84; 95% CI, 1.09–3.10), preterm birth (aOR 1.48; 95% CI, 1.22–1.81) and LGA (aOR 1.24; 95% CI, 1.05–1.45) were exhibited in those with GDM, respectively, compared with those without hyperglycemia (Fig. 4).

Discussion

Principle findings

This large cohort study demonstrated the prevalence of hyperglycemia in early pregnancy screened by FPG and HbA1c and found that it was associated with adverse maternal and neonatal outcomes including GDM, HDP, shoulder dystocia, preterm birth, LGA and macrosomia. Subgroup analyses suggested that the elevated risk persisted in cases performed screening during the first and early second trimester, as well as in cases identified by FPG, HbA1c and both, respectively. Furthermore, hyperglycemia in early pregnancy complicated by GDM had higher rates of adverse pregnancy outcomes than those without GDM.

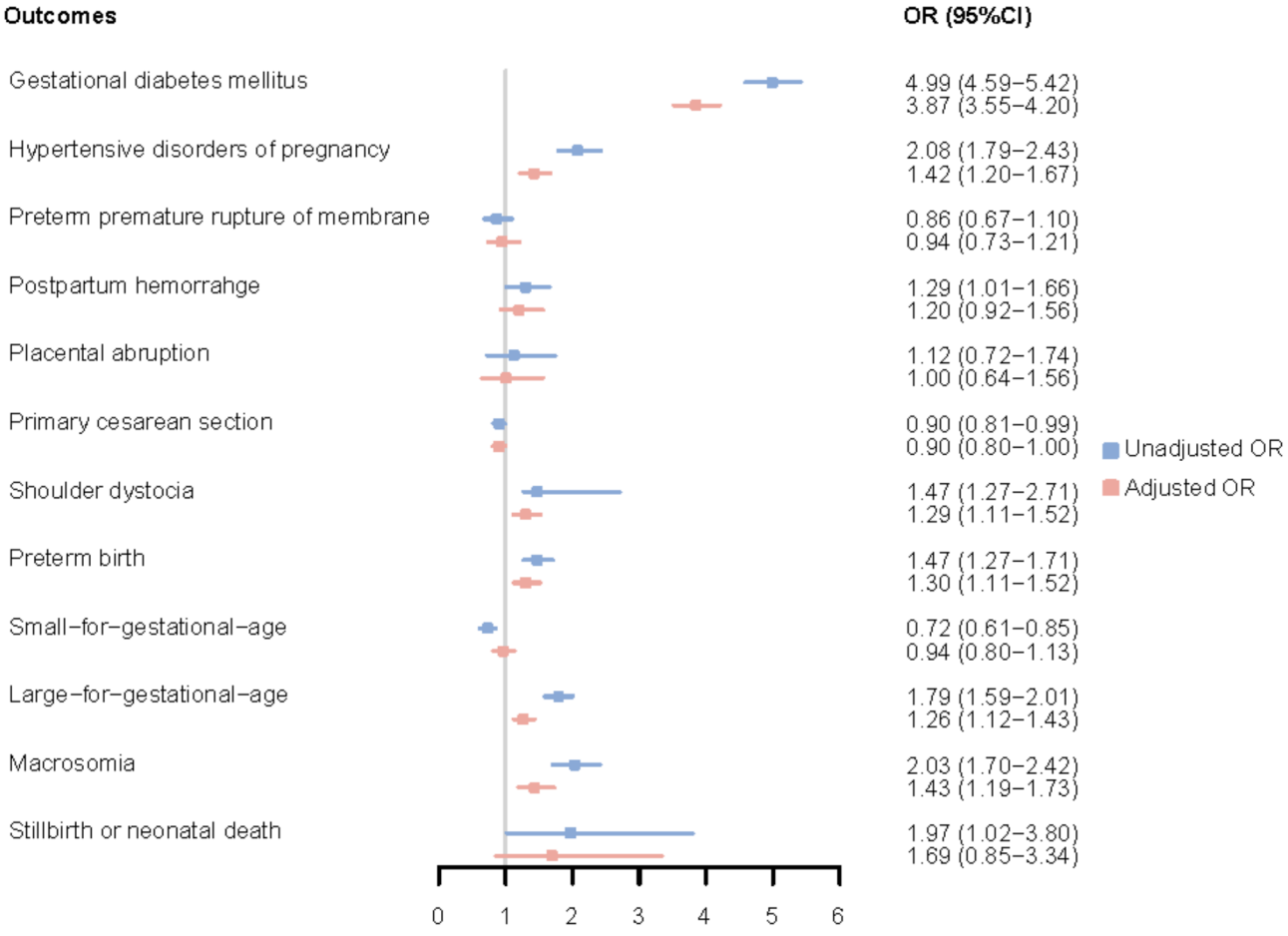

Fig. 1 The association between hyperglycemia in early pregnancy and pregnancy outcomes

Compared with previous studies

Our findings on the association between FPG 5.1–6.9 mmol/L in early pregnancy and adverse pregnancy outcomes are consistent with previous large cohort studies on GDM [11, 12, 15, 26], preterm birth [13, 16], LGA [12, 14, 15, 26] and macrosomia [12–15]. In addition, our study reported higher risk of HDP in women with FPG 5.1–6.9 mmol/L in early pregnancy, which was consistent with another cohort study conducted in Chinese population [13]. However, two studies found lack of relationship between FPG 5.1–6.9 mmol/L before 14 weeks of gestation and HDP [15, 16]. Our study demonstrated a higher risk of GDM, HDP and preterm birth in women with HbA1c 39–46 mmol/mol compared to those with HbA1c < 39 mmol/mol in early pregnancy. While previous studies in mixed ethnicities also suggested a higher risk of GDM in women with 39–46 mmol/mol in early pregnancy, they did not find significant associations with HDP or preterm birth [27, 28]. Another cohort study analyzed ethnic differences in the association between first-trimester HbA1c levels and obstetric complications and described that HbA1c was an independent predictor in Latin-American and South-Central Asian women, whereas no significant associations were found in Caucasian women [18]. The results in South-Central Asian population presented a higher risk of preeclampsia, LGA and macrosomia [18]. Interestingly, our results showed a nonsignificant association between women with HbA1c 39–46 mmol/mol in early pregnancy and LGA and macrosomia, which is consistent with previous findings comparing these women with those with HbA1c < 39 mmol/mol before 20 weeks of gestation [27–31]. The association remained nonsignificant in women screened at < 14 weeks or 14–19 weeks or at a higher cut-off of 41 mmol/mol in the present study (data not shown). The secondary analysis of the HAPO study speculated that the risks of preeclampsia and preterm birth were influenced by earlier glycemia in pregnancy, whereas anthropometric outcomes were more strongly associated with later glycemia in pregnancy [32]. Our results also suggested this hypothesis, as the HbA1c levels before 14 weeks and 14–19 weeks of gestation reflected the average blood sugar level at the time of conception and during the first trimester, respectively.

According to our results, women with hyperglycemia in early pregnancy complicated by GDM had an even

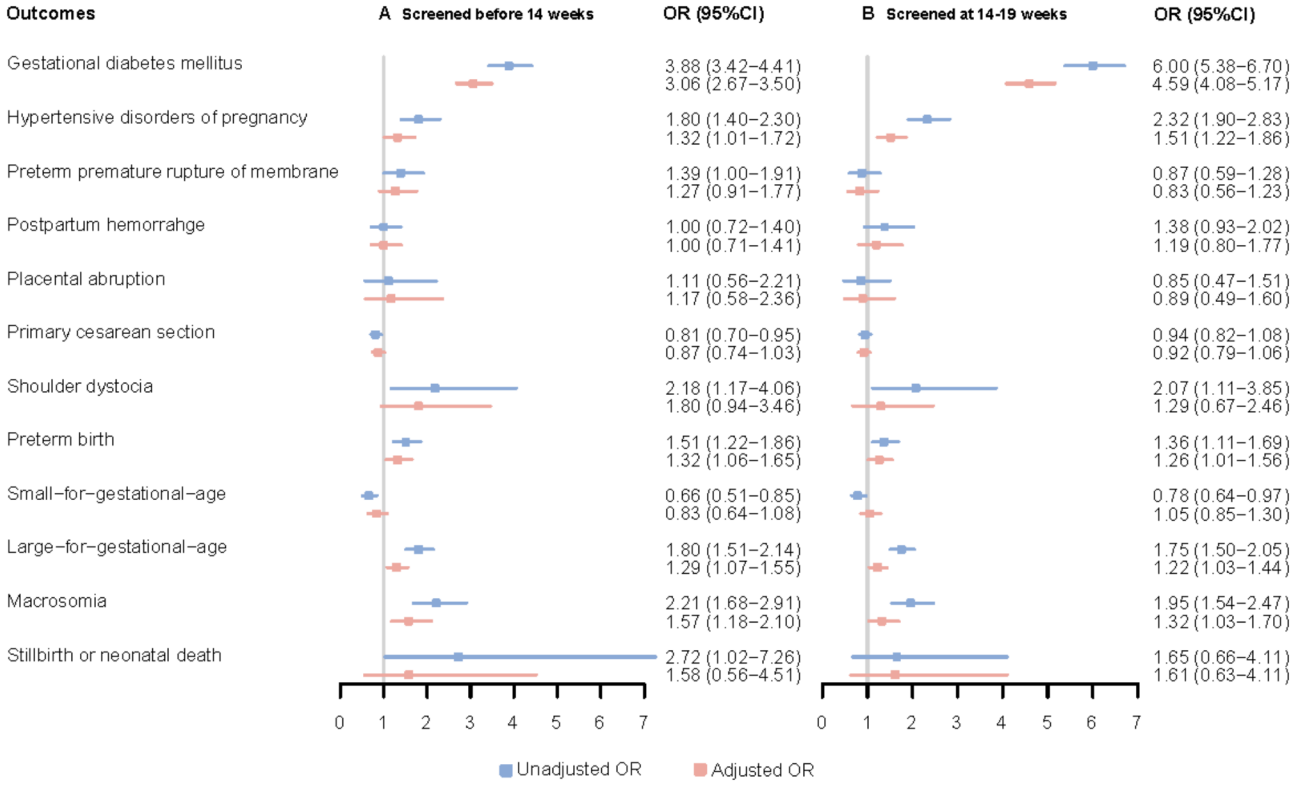

Fig. 2 The association between hyperglycemia in early pregnancy classified by gestational age and pregnancy outcomes. ORs are estimated in pregnant women screened before 14 weeks of gestation (**A**) and 14–19 weeks of gestation (**B**)

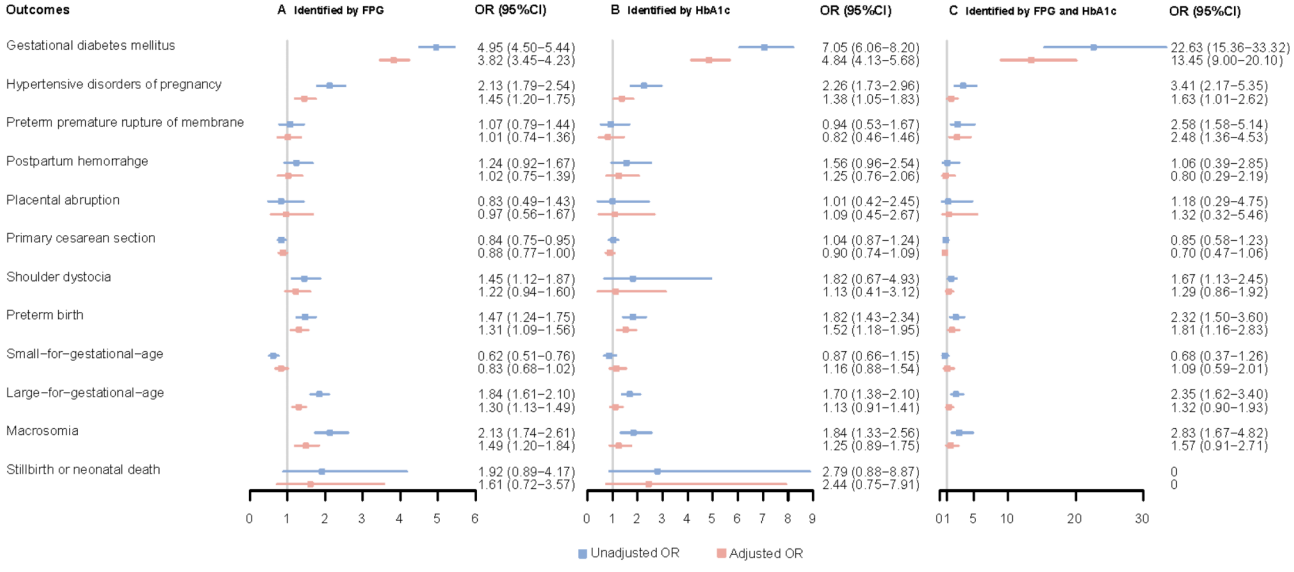

Fig. 3 The association between subtypes of hyperglycemia in early pregnancy and pregnancy outcomes. ORs are estimated in pregnant women identified by fasting plasma glucose (**A**), HbA1c (**B**) and both tests (**C**)

higher risk of HDP, PPROM, preterm birth and LGA than those without. Previous cohort studies have also demonstrated elevated risks of adverse outcomes in women with early hyperglycemia screened by FPG or HbA1c alone, regardless of GDM. A large cohort study found a higher risk of primary cesarean delivery, preterm birth, and neonatal distress after adjustments for confounding factors in pregnant women with first-trimester FPG 5.1–6.9 mmol/L without GDM compared to those with FPG < 5.1 mmol/L without GDM [16]. Similarly, an Asian

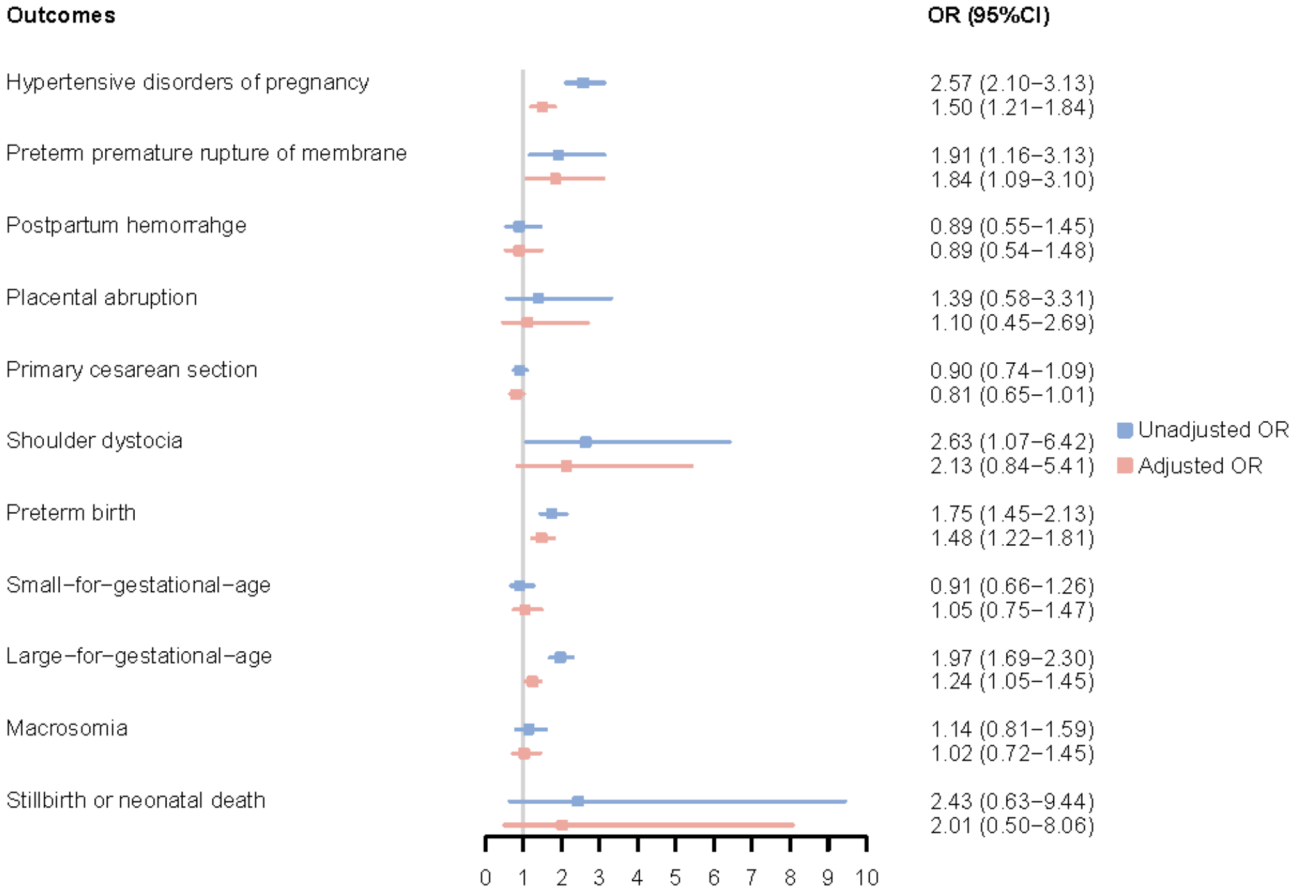

Fig. 4 The association between hyperglycemia in early pregnancy with or without subsequent diagnosis of gestational diabetes mellitus and pregnancy outcomes

Indian cohort study reported a significant association of first-trimester HbA1c 37–46 mmol/mol with preterm birth and primary caesarian delivery, even without GDM [31]. Other studies found a comparable risk of HDP, macrosomia and preterm birth in women with FPG 5.1–6.9 mmol/L or HbA1c 41–49 mmol/mol in early pregnancy compared with unaffected pregnant women with GDM [13, 33]. Together with our findings, the current evidence suggests that the additional burden of GDM in women with hyperglycemia in early pregnancy contributes to the increased risk of adverse maternal and neonatal outcomes [34].

Our study revealed that hyperglycemia in early pregnancy identified by both FPG and A1c was associated with a significantly higher proportion of GDM compared to FPG or A1c alone (83.1%, 44.8% and 51.7%, respectively). After adjusting for confounders, women with both elevated FPG and A1c had a 13.45-fold higher risk of GDM compared to unaffected women, emphasizing the need for ongoing follow-up and management in this high-risk group. Furthermore, our findings indicated that the risk of adverse pregnancy outcomes was comparable between pregnant women diagnosed before 14 weeks and those diagnosed at 14–19 weeks of gestation, respectively. This differs from a Chinese cohort study that observed increased risks of LGA and macrosomia in women with FPG 5.1–6.9 mmol/L diagnosed between 14 and 28 weeks of gestation but found no significant association before 14 weeks, and no significant association with preterm birth in either trimester [14]. Unlike previous studies that primarily assessed the risk of hyperglycemia in early pregnancy using a single index or a specific timeframe [4, 11–16, 18, 26–33, 35–39], our study uniquely stratified risks based on combined screening measures and screening age, thus highlighting potential windows for targeted interventions.

Clinical and research implications

According to our results, it is estimated that 830 thousand pregnant women in China suffer from hyperglycemia in early pregnancy every year. Pregnant women with hyperglycemia defined as FPG 5.1–6.9 mmol/L and/or HbA1c 39–46 mmol/mol, screened in either the first or early second trimester, warrant careful monitoring. It should be noted that hyperglycemia in early pregnancy not only indicates a higher risk of GDM but is also

independently associated with an increased incidence of adverse pregnancy outcomes, including HDP, preterm birth, LGA and macrosomia. In summary, there is an urgent need to explore the optimal early screening strategies and the effectiveness of early intervention.

The optimal cut-off values for FPG or HbA1c in early pregnancy for screening for adverse pregnancy outcomes are still unclear. The updated IADPSG consensus on FPG has stated that FPG ≥ 5.1 mmol/L was not justified for early detection of GDM [7]. The ADA has defined FPG 6.1–6.9 mmol/L before 15 weeks of gestation to identify individuals at higher risk of adverse pregnancy and neonatal outcomes since 2022 [40]. The Chinese guideline recommends that an FPG of 5.6–6.9 mmol/L be defined as impaired glucose metabolism based on the previous ADA recommendation in 2021 [6]. However, two subsequent large cohort studies in the Chinese population, together with our results, have suggested a higher risk of adverse pregnancy outcomes in women with FPG 5.1–6.9 mmol/L in early pregnancy compared with women with FPG < 5.1 mmol/L [13, 16]. There is a need to re-evaluate the threshold criteria for FPG screening in Chinese women at high risk for adverse pregnancy outcomes. Our results provide positive evidence regarding the impact of elevated HbA1c on pregnancy outcomes based on a universal screening strategy. The HbA1c test is more convenient and has greater preanalytical stability and reproducibility, but it may not be suitable for use alone because of decreased sensitivity compared with OGTT approaches [41]. Therefore, the optimized strategy for HbA1c screening in early pregnancy needs further investigation. Although the increased risk of adverse pregnancy outcomes was similar between those screened before 14 weeks and those screened between 14 and 19 weeks of pregnancy, the fact that half of women with hyperglycemia in early pregnancy were subsequently diagnosed with GDM suggests that screening be performed in the first trimester to allow sufficient time for management. However, whether intervention improves pregnancy outcomes needs further confirmation.

The worse pregnancy outcomes observed in women with hyperglycemia in early pregnancy complicated by GDM underline the potential benefit of early screening and glycemic control. The TOBOGM trial has demonstrated the benefits of early intervention in women diagnosed with early GDM screened by OGTT (IADPSG criteria). The TOBOGM cost-effectiveness analysis, which is the only health economic analysis for diagnosing and treating hyperglycemia in early pregnancy, showed that immediate treatment was associated with a 10% reduction in total healthcare costs [2]. FPG and/or HbA1c screening in early pregnancy remains a more pragmatic approach in China, however, this study was conducted in a high-resource setting that allowed universal screening with both FPG and HbA1c. Given the resource imbalance in different regions of China, the cost-effectiveness and feasibility challenges of implementing such strategies in low-resource settings should be considered. Comparing the incremental costs of screening with the benefits of treatment for the newly diagnosed population, adherence to treatment, and consideration of long-term maternal and offspring outcomes may influence cost-effectiveness [1]. To date, there have been no randomized controlled trials of these combined screening strategies in early pregnancy or in low-resource settings. Therefore, new evidence is needed to investigate whether early screening and lifestyle intervention can reduce the incidence of GDM and thus prevent the associated adverse pregnancy outcomes with this screening strategy [42, 43].

Strengths and limitations

The main strength of our study was the availability of both FPG and HbA1c results in a large number of populations, which allowed us to depict the epidemiologic results of the risk of adverse pregnancy outcomes in different trimesters and subtypes. Second, all pregnant women with elevated FPG and HbA1c but not meeting the criteria for diabetes still underwent OGTT at 24–28 weeks of gestation, which enabled the comparisons between those complicated by GDM and those without. Third, we were reporting results based on a multicenter cohort, all of which adopted universal screening strategy in women without preexisting diabetes at the time of their first prenatal visit, thus mitigates selection bias and improves the generalizability of our results in the Chinese population.

However, this study also had some limitations. The exclusion of women with missing data and those screened at ≥ 20 weeks of gestation may have caused selection bias. Additionally, important factors such as first-degree family history of diabetes mellitus and history of GDM or macrosomia were not available in this dataset, which could have influenced the association between hyperglycemia in early pregnancy and adverse pregnancy outcomes. We also could not assess the extent to which hyperglycemia in early pregnancy may reflect a higher genetic predisposition. Moreover, confounders like diet or physical activity that could affect glycemic control and pregnancy outcomes were not assessed in this study. Adherence to GDM treatment may vary between sites, which may influence the rates of adverse neonatal outcomes such as birthweight. The study was conducted in high-resource settings in the South region that enabled combined screening, which limits the generalizability to other regions, particularly those with fewer resources. The cost-effectiveness of this screening strategy has yet to be assessed and warrants further investigation.

Conclusion

Our findings showed that pregnant women with FPG 5.1–6.9 mmol/L and/or HbA1c 39–46 mmol/mol (5.7-6.4%) who were screened in either the first or early second trimester were independently associated with adverse pregnancy outcomes, and women with these conditions complicated by GDM were at higher risk than those without. Further research is needed to explore the optimal early screening strategy using FPG and HbA1c, as well as to investigate whether the incidence of GDM can be reduced by early intervention and therefore prevent the relevant adverse pregnancy outcomes.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07253-4.

Supplementary Material 1

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Author contributions

L.X.S and S.F.Z performed the statistical analysis, drafted the article and reviewed it critically for important intellectual content. J.Y.W, J.L, X.H.L and C.X.Z were involved in the conception of the study design, collected the study data, and reviewed the manuscript critically for important intellectual content. S.Q.C and L.P.X contributed to data collection, cleaning and interpretation and statistical analysis. Z.L.W and H.T.C designed the study, collected the study data, and revised the manuscript critically for important intellectual content. All authors provided final approval of the version to be published. Z.L.W and H.T.C are guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Data availability

Data are available on reasonable request by contacting the corresponding author.

Declarations

Ethics approval and consent to participate

This study was approved by the Independent Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital, Sun Yat-sen University (Ref. No. 2022.458). As this was a retrospective study, no additional adverse effects on patients were observed, and patient information and data were adequately protected. The Independent Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital, Sun Yat-sen University approved the waiver of informed consent for the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors declare that there is no conflict of interests.

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