

Characteristics of Glucose-Lipid Metabolism in Early Pregnancy Among Overweight and Obese Women and Their Predictive Value for Gestational Diabetes Mellitus

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Purpose: This study explores the link between women's pre-pregnancy overweight and obesity and glucose and lipid metabolism in their early pregnancy. It assesses how early pregnancy glucose and lipid levels predict gestational diabetes mellitus (GDM) risk, aiming to offer foundational weight management strategies for overweight and obese women to prevent GDM.

Patients and Methods: This study analyzed 2172 pregnant women from 2017 to 2021 at Waitan Street Community Health Service Center, Shanghai, monitoring early pregnancy (7–10 weeks) glucose and lipid levels (TG, TC, HDL-C, LDL-C, FBG, HbA1c) and 24-week OGTT values. Pre-pregnancy BMI categorized participants into overweight and obese, normal, and underweight groups. We compared early pregnancy glycemic and lipid metrics and GDM incidence across groups, examining the relationship between pre-pregnancy BMI and early pregnancy blood metrics. The overweight and obese cohort was further split into GDM and non-GDM groups, comparing early pregnancy glycolipid indicators and assessing their predictive value for GDM development.

Results: In the overweight and obese group, maternal FBG, HbA1c, TG, and LDL-C were higher, while HDL-C was lower than in normal and underweight groups ($P < 0.05$), with a higher GDM incidence ($P < 0.05$). Pre-pregnancy BMI positively correlated with FBG, HbA1c, TG, and LDL-C levels ($r = 0.556, 0.567, 0.686, 0.214$; $P < 0.05$) but not HDL-C. Each 1-unit BMI increase raised GDM risk by 0.204 times ($P < 0.05$). FBG, TG, and LDL-C had high predictive accuracy for GDM in overweight and obese women, with AUCs of 0.991, 0.994, and 0.935, respectively.

Conclusion: Pre-pregnancy overweight and obesity can cause early pregnancy glucose and lipid abnormalities, raising GDM risk. Early testing in such women is a strong predictor for GDM.

Keywords: pregnant women, overweight and obesity, pre-pregnancy body mass index, glucose and lipid metabolism, gestational diabetes mellitus

Introduction

Significant lifestyle changes have occurred with the continuous development of the economy and improvements in the quality of life. These changes have led to a steady increase in the incidence of overweight or obesity in women's pre-pregnancy Body Mass Index (BMI).¹ According to China's testing data, the prevalence of overweight and obesity among women of childbearing age (18 to 44 years old) in China can reach as high as 34.26%.² Moreover, pre-pregnancy overweight and obesity not only impact the individuals' health but also increase the likelihood of adverse pregnancy complications.³ Studies both domestically and internationally have consistently shown that pre-pregnancy overweight or obesity significantly increases the risk of developing gestational diabetes mellitus (GDM),^{4,5} and the incidence of GDM induced by pre-pregnancy overweight and obesity is higher in China.^{6,7} In the United States, the prevalence of GDM increased from 4.6% in 2006 to 8.2% in 2016. However, on a global scale, the prevalence of gestational diabetes varies from 3% to 25%, depending on different diagnostic criteria and population demographics.⁸ This increase is closely

related to the rise in overweight and obesity. As the prevalence of overweight and obesity continues to grow, the incidence of gestational diabetes is also on the rise.⁹ Overweight and obese mothers with GDM not only face significant short- and long-term health impacts but also influence the health of their offspring. GDM is associated with an increased risk of the mother developing type 2 diabetes and cardiovascular diseases in the future. For the fetus, GDM increases the dangers of macrosomia, birth injuries, and neonatal metabolic issues. The offspring are also at significantly higher risk of obesity and metabolic syndrome in childhood and adulthood.^{4,10} These factors contribute to a substantial economic burden, warranting greater attention and awareness.¹¹ Pathophysiologic studies also suggest that abdominal fat is negatively correlated with insulin sensitivity in adults and that the incidence of impaired glucose tolerance is higher in obese women, regardless of whether they are pregnant or not. After pregnancy, the placenta secretes large amounts of anti-insulin, which further increases the risk of diabetes mellitus.¹² Therefore, early detection and prevention of GDM are crucial, particularly for overweight and obese pregnant women. However, there are multiple challenges in the early diagnosis and management of GDM in this population. GDM often presents without apparent symptoms in the early stages, especially among obese women, where blood glucose fluctuations are more subtle, and the increased metabolic burden may cause mild metabolic abnormalities to be overlooked. Clinically, the most commonly used diagnostic method for GDM in recent years is the oral glucose tolerance test (OGTT) conducted between 24–28 weeks of gestation. However, this method only allows for the diagnosis of GDM after 24 weeks, which may affect the effectiveness of early treatment to some extent.¹³ Additionally, overweight and obese pregnant women often exhibit some degree of insulin resistance, and standard screening indicators such as fasting glucose and OGTT may not sensitively reflect decreased insulin sensitivity in the early stages, further complicating the diagnosis. These women face the dual challenges of weight management and glycemic control, requiring more personalized screening schedules and strategies. However, current clinical data and research supporting early diagnosis of GDM are insufficient. Therefore, how to diagnose early GDM in overweight and obese pregnant women is an important issue that needs to be addressed. This study aims to explore the relationship between pre-pregnancy overweight or obesity and early pregnancy glucose and lipid metabolism markers and their association with the development of GDM. The study hypothesizes that overweight or obese pregnant women are more likely to develop GDM due to early pregnancy glucose and lipid metabolism abnormalities. This could provide a scientific basis for early screening and intervention in this high-risk population, facilitating timely diagnosis and treatment of GDM.

Materials and Methods

Study Population

This retrospective analysis used clinical data from 2172 parturient women collected at our hospital from 2017 to 2021. The inclusion criteria were: (1) singleton natural conception; (2) visible primitive heart tube pulsation in early pregnancy ultrasound; (3) Absence of pre-pregnancy comorbidities influencing the study; (4) Maternal age ranged from 22 to 35 years; (5) Presence of complete clinical information; (6) establishment of medical records before 13 weeks of gestation; (7) Received education on early risk prevention methods for GDM. Exclusion criteria included: (1) Combination of severe insufficiency of vital organs such as heart, liver, and kidneys; (2) cognitive impairment precluding effective participation; (3) fetal abnormalities; (4) chronic hypertension or pre-pregnancy diabetes. (5) did not take diabetes-related medication before or during pregnancy; (6) neurological disorders; (7) autoimmune diseases; (8) malignant tumors; (9) acute or chronic infections; (10) a scarred uterus or fetal malformations; (11) underwent in vitro fertilization and embryo transfer; (12) reproductive tract malformations; (13) thyroid dysfunction. For the early risk prevention of gestational diabetes mellitus (GDM), it is recommended that pregnant women adopt a healthy dietary pattern, such as the Mediterranean diet or DASH diet. This includes increasing the intake of whole grains, vegetables, fruits, legumes, and nuts while reducing the consumption of red meat, fats, refined sugars, and sugary beverages. Pregnant women should also be encouraged to engage in moderate physical activity, such as walking or prenatal yoga, to help control weight, improve insulin sensitivity, and reduce the risk of GDM. The participant screening process and results flowchart are detailed in [Figure 1](#). All pregnant women should receive education and guidance at their initial

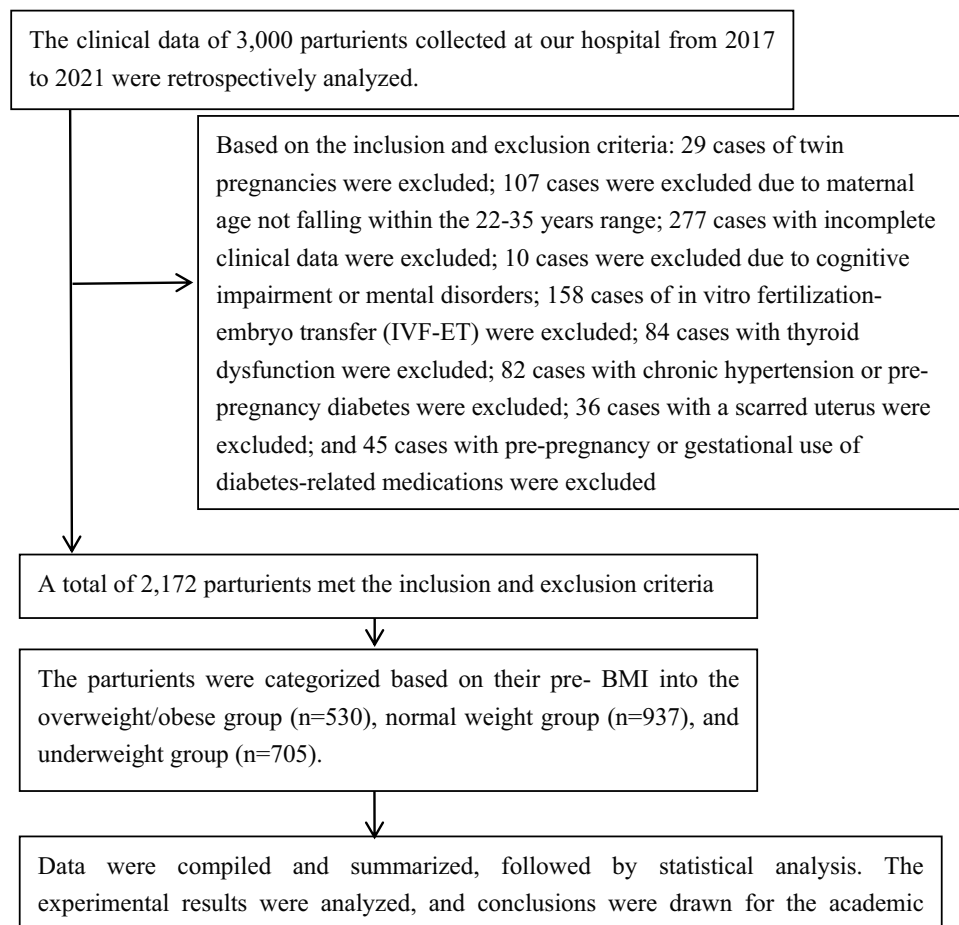


Figure 1 A flow diagram of the study participants.

prenatal visit. Pregnant women undergoing preventive pharmacological treatment were not included in the study group. All parturients provided informed consent for the study.

Data Source and Collection

The pre-pregnancy BMI was calculated by body weight/height (kg/m^2). These data were based on inquiries from the first prenatal visit. During early pregnancy (7–10 weeks), fasting blood was collected and centrifuged to obtain the supernatant (centrifugation speed 400 r/min, centrifugation radius 10 cm, centrifugation time 10 min). Fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) were measured using a glucose analyzer using the oxidase electrode method. At the same time, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were detected using an automatic biochemical analyzer. At 24 weeks of gestation, an oral glucose tolerance test (OGTT) was performed. Fasting for at least 8–12 hours was ensured before the test. A solution containing 75g of anhydrous glucose, with a total volume of 250–300 mL, was consumed within 5 minutes. Venous blood samples were measured 1 and 2 hours after oral glucose intake.

Diagnostic Criteria and Definition

Overweight and Obesity

Pre-pregnancy BMI was calculated using the formula $\text{BMI} = \text{weight}/\text{height}^2 (\text{kg/m}^2)$. According to the 2002 “Health Industry Standards of the People’s Republic of China: Criteria for Weight Determination in Adults”, pre-pregnancy BMI between 18.5 kg/m^2 and 24 kg/m^2 was considered normal weight, $\text{BMI} \geq 24 \text{ kg/m}^2$ was classified as overweight or obese, and $\text{BMI} < 18.5 \text{ kg/m}^2$ was classified as underweight. So, participants were divided into three subgroups based on pre-

pregnancy BMI: the normal weight subgroup (937 participants, the overweight and obese subgroup (530 participants, and the underweight subgroup (705 participants).

Gestational Diabetes Mellitus

All participants underwent OGTT at 24 weeks of gestation, following the standards in the 2014 Guidelines for the Diagnosis and Treatment of Gestational Diabetes.¹⁴ We could confirm a diagnosis if any of the following blood glucose levels were met or exceeded: fasting blood glucose (FBG) ≥ 5.1 mmol/L; blood glucose ≥ 10.0 mmol/L 1 hour after glucose ingestion; blood glucose ≥ 8.5 mmol/L 2 hours after glucose ingestion.

Statistical Analysis

Count data was described using frequencies (percentages). The Kruskal–Wallis rank-sum test was used for comparisons among multiple groups, and the χ^2 -test was used for comparisons between two groups in cross-tabulation. Quantitative data were expressed as mean \pm standard deviation ($\bar{x} \pm s$). One-way ANOVA was used for comparisons among multiple groups, while the independent samples *t*-test was used for comparisons between two groups. Paired *t*-tests were performed for within-group comparisons. The correlation between pre-pregnancy BMI and levels of blood glucose and lipids was analyzed using Spearman's rank correlation analysis. With GDM as the dependent variable and different pre-pregnancy BMI categories as the independent variables, logistic regression analysis was conducted to evaluate the effect of pre-pregnancy BMI on GDM. Furthermore, the predictive value of blood glucose and lipid levels on the risk of developing concomitant GDM in the overweight and obese group was examined by Receiver Operating Characteristic (ROC) curve analysis. The significance level (α) was set at 0.05. Two individuals entered all received data to minimize the influence of human factors and avoid bias in the experimental results. For quality control, the regression model included confounding factors as covariates.

Results

Clinical Characteristics of Participants

A total of 2172 parturient women were involved in this study. The BMI of the pre-pregnancy overweight and obese, normal weight, and underweight groups were 27.67 ± 2.09 , 22.21 ± 0.78 , and 17.52 ± 0.55 Kg/m², respectively. The differences were statistically significant ($t=10,931.422$, $P<0.001$). The body weights of the three groups were (73.28 ± 15.65), (58.98 ± 12.24), and (46.22 ± 7.00) kg, respectively, with statistically significant differences ($t=792.206$, $P<0.001$). The ages for the pre-pregnancy overweight and obese, normal weight, and underweight groups were 29.15 ± 3.03 , 28.82 ± 3.15 , and 29.05 ± 3.28 years old, respectively. The differences were not statistically significant ($t=2.133$, $P=0.119$). Comparisons of height, age distribution, educational level, and proportion of primiparas among the pre-pregnancy overweight and obese, normal weight and underweight groups showed no statistically significant differences (all $P>0.05$). As shown in Table 1

Comparison of Early Pregnancy Blood Glucose and Lipid Levels and the Incidence of GDM with Varying Pre-Pregnancy BMIs

The comparison of early pregnancy blood glucose and lipid levels and the incidence of GDM among pregnant women with varying pre-pregnancy BMIs are shown in Table 2. Maternal early pregnancy levels of FBG, HbA1c, TG, and LDL-C levels were higher in the overweight and obese group than in the normal weight and underweight groups ($P<0.05$), and HDL-C levels were lower than in the normal weight and underweight groups ($P<0.05$). Maternal FBG, HbA1c, and TG levels in early pregnancy were higher in the normal weight group than in the underweight group ($P<0.05$). In contrast, there was no statistically significant difference between the two groups when comparing the LDL-C and HDL-C levels in early pregnancy ($P>0.05$). The incidence of gestational diabetes mellitus was higher in the overweight and obese group of pregnant women compared to the normal weight and underweight groups ($P<0.05$). The incidence of maternal GDM was higher in the normal-weight group than the underweight group ($P<0.05$).

Table 1 Comparison of the Baseline Characteristics of the Parturients in the Different Pre-Pregnancy BMI Groups

Index	Classification	Overweight and Obesity Group (n=530)	Normal Weight Group (n=937)	Underweight Group (n=705)	χ^2/F value	P value
Pre-pregnancy height (m ²)		162.00±16.24	162.15±15.88	162.03±11.88	0.024	0.976
Pre-pregnancy weight (kg)		73.28±15.65	58.98±12.24	46.22±7.00	792.206	<0.001
Pre-pregnancy BMI (kg/m ²)		27.67±2.09	22.21±0.78	17.52±0.55	10,931.422	<0.001
Age (years)		29.13±3.07	28.83±3.15	29.05±3.28	1.817	0.163
Degree of education					3.028	0.082
Below junior high school		36 (6.79)	98 (10.46)	52 (7.38)		
High school and secondary school		78 (14.72)	98 (10.46)	80 (11.35)		
Junior college degree or above		416 (78.49)	741 (79.08)	573 (81.28)		
Primipara		107 (20.19)	191 (20.38)	150 (21.28)	0.203	0.652

Notes: Except for height, weight, BMI, and age are $\bar{x} \pm s$. Except for outside education level and primiparas are the number of cases, and inside the bracket are constituent ratios/%.

Abbreviation: BMI, body mass index.

Table 2 Comparison of Blood Glucose and Lipid Levels and the Incidence of GDM Among Pregnant Women with Different Preconception BMI

Index	Classification	Overweight and Obesity Group (n=530)	Normal Weight Group (n=937)	Underweight Group (n=705)	F/H value	P value
Blood glucose and lipid levels	FBG (mmol/L)	5.40±1.14 ^{ab}	4.18±0.79	4.04±0.47 ^a	504.923	<0.001
	HbA1c (%)	5.90±0.42 ^{ab}	5.51±0.31	5.25±0.35 ^a	515.153	<0.001
	TG (mmol/L)	1.69±0.32 ^{ab}	1.33±0.21	0.94±0.15 ^a	2321.211	<0.001
	HDL-C (mmol/L)	1.16±0.33 ^{ab}	1.30±0.36	1.34±0.39	27.014	<0.001
	LDL-C (mmol/L)	3.07±0.82 ^{ab}	2.90±0.72	2.85±0.57	247.614	<0.001
Pregnancy complications	GDM	109(20.57) ^{ab}	83(8.86)	9(1.28) ^a	134.298	<0.001

Notes: Except for blood glucose and lipid levels, they are $\bar{x} \pm s$, and outside the bracket of GDM is the number of cases, and inside the bracket are constituent ratios/%. Comparison to the preconception normal weight group, a: $P < 0.05$; Comparison to the preconception underweight group, b: $P < 0.05$.

Abbreviations: BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; GDM, gestational diabetes mellitus.

Correlation Between Pre-Pregnancy BMI and Early Pregnancy Blood Glucose and Lipid Levels

Spearman's rank correlation analysis (Table 3, Figures 2–5) revealed no significant correlation between pre-pregnancy BMI and HDL-C levels ($r=0.005$, $P > 0.05$). Conversely, there was a positive correlation between pre-pregnancy BMI and FBG, HbA1c, TG, and LDL-C levels ($P < 0.05$). Among them, pre-pregnancy BMI was strongly correlated with FBG, HbA1c, and TG levels ($r=0.556$, 0.567 , 0.686 , $P < 0.05$) but weakly correlated with LDL-C levels ($r=0.214$, $P < 0.05$).

Impact of Pre-Pregnancy BMI on Gestational Diabetes Mellitus

In binary logistic regression analysis (Table 4), we used gestational diabetes mellitus as the dependent variable and pre-pregnancy BMI as the independent variable. The risk of GDM was highly associated with pre-pregnancy BMI. The results indicated that for every 1-unit increase in pre-pregnancy BMI, the risk of developing GDM increased by 0.204 times ($P < 0.05$).

Comparison of Blood Glucose and Lipid Levels in the Overweight and Obese Group with GDM and the Non-GDM Group

As shown in Table 5, in overweight and obese parturients, the group with GDM exhibited higher levels of FBG, HbA1c, TG, and LDL-C compared to the group without GDM ($P < 0.05$). The comparison of HDL-C levels between the two groups showed no statistically significant difference ($P > 0.05$).

Table 3 Correlation Analysis of Pre-Pregnancy BMI and Blood Glucose and Lipid Levels

Spearman's Rank Correlation Coefficient Correlation		FBG	HbA1c	TG	HDL-C	LDL-C
Pre-pregnancy body mass index	Correlation coefficient	556**	567**	686**	0.005	214**
	Significance (two-tailed)	<0.001	<0.001	<0.001	0.862	<0.001

Notes: **indicates a statistically significant correlation at the 0.01 level (two-tailed).
Abbreviations: FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Predictive Value of FBG, HbA1c, TG, and LDL-C Levels in the Incidence of GDM in an Overweight and Obese Group

As shown in Table 6 and Figure 6, ROC curve analysis demonstrated that the AUCs of FBG, TG, and LDL-C levels for predicting GDM in the overweight and obese group were 0.991, 0.994, and 0.935, respectively. FBG, TG, and LDL-C indicated high accuracy. The optimal cutoff values determined by the ROC curves, corresponding to the maximum Youden index, were FBG: 5.595 mmol/L, TG: 2.000 mmol/L, and LDL-C: 3.465 mmol/L. This point's predictive sensitivity and specificity were high. 83.3%, 85.5%, 95% confidence interval 0.842–0.912 for FBG, 56.0%, 67.3%, 95% confidence interval 0.589–0.705 for HbA1c, 91.7% for TG, 100.0%, 95% confidence interval 0.990–0.998 for TG. TG's predictive sensitivity and specificity were 91.7%, 100.0%, 95% confidence interval 0.990–0.998, and the predictive sensitivity and specificity of LDL-C were 90.8%, 89.8%, and 95% confidence interval 0.910–0.961. It showed that the predictive value of the FBG, HbA1c, TG, and LDL-C levels for the maternal gestational diabetes mellitus complication in the overweight-obese group was good.

Discussion

In recent years, with the improvement of national living standards and changes in dietary structure, the number of overweight and obese people is increasing, posing a severe impact on both physical and mental health.¹⁵ Previous research has shown that pre-pregnancy overweight and obesity can trigger complications during pregnancy, severely impacting the physical and psychological health of both mother and child. Furthermore, it even leads to the risk of cardiovascular and cerebrovascular diseases in adulthood.^{16,17} Analysis of 20 international cohort studies indicates that

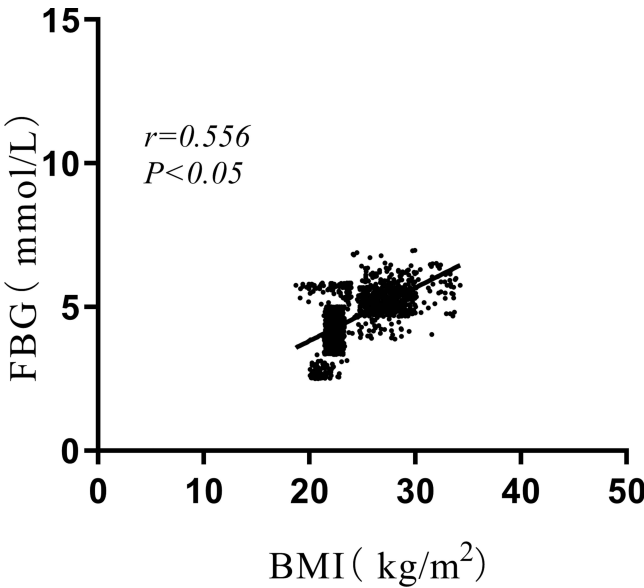


Figure 2 Scatter plot of correlation between pre-pregnancy BMI and FBG.
Abbreviations: BMI, body mass index; FBG, fasting blood glucose.

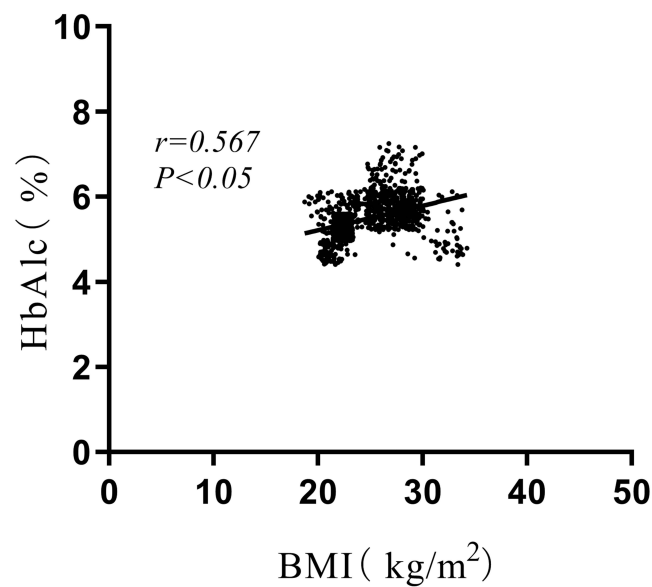


Figure 3 Scatter plot of correlation between pre-pregnancy BMI and HbA1c.
Abbreviations: BMI, body mass index; HbA1c, glycosylated hemoglobin.

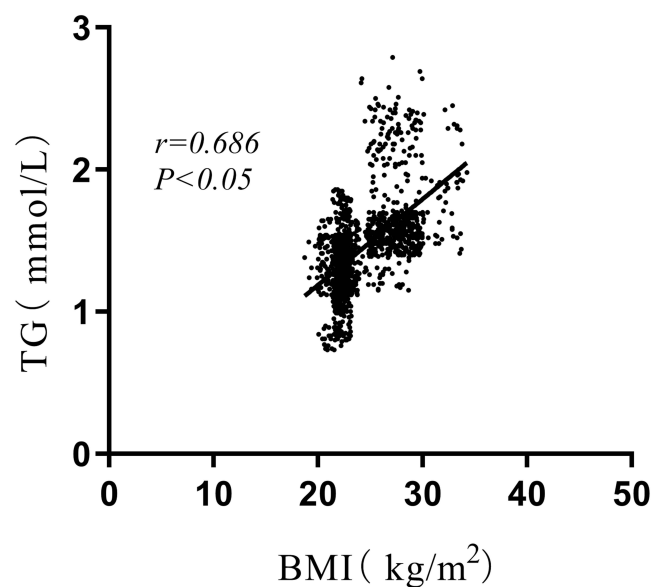


Figure 4 Scatter plot of correlation between pre-pregnancy BMI and TG.
Abbreviations: BMI, body mass index; TG, triglycerides.

compared to women with normal weight, the risk of GDM in overweight, obese, and severely obese women increases by 2-fold, 4-fold, and 8-fold, respectively. Additionally, this elevation in weight categories is associated with an increased risk of dystocia, postpartum hemorrhage, and stillbirth.¹⁸ Current research suggests that overweight or obese parturients with GDM have a significant association with various adverse pregnancy outcomes.^{19–21} If we can predict the occurrence of GDM before performing the OGTT test at 24 weeks, it would enable timely and effective prevention and treatment, ultimately improving pregnancy outcomes. This study analyzes the impact of pre-pregnancy overweight and obesity on early pregnancy glycolipid metabolism levels, the incidence of GDM, and the early predictive value of early pregnancy glycolipid metabolism levels in overweight and obese parturients for GDM. It provides a scientific and rational

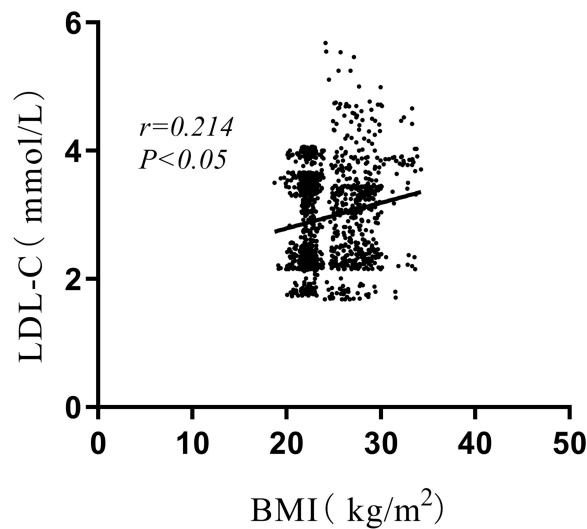


Figure 5 Scatter plot of correlation between pre-pregnancy BMI and LDL-C.
Abbreviations: BMI, body mass index; LDL-C, low-density lipoprotein cholesterol.

theoretical basis for developing weight management strategies for women of childbearing age, improving glycolipid metabolism during pregnancy, early prediction of GDM, and preventing pregnancy-related complications.

By comparing the glycemc and lipid metabolism indicators among parturients with varying pre-pregnancy BMIs, this study indicates that the differences between each group are statistically significant. Furthermore, it reveals that levels of FBG, TG, and LDL-C increase with the rise in pre-pregnancy BMI. This indicates that pre-pregnancy BMI is one of the significant factors affecting early pregnancy glycemc and lipid metabolism. Being overweight or obese before pregnancy can lead to abnormal glycemc and lipid metabolism during pregnancy, which is consistent with the findings of previous studies.^{22,23} The potential mechanisms underlying the observed associations may be as follows: First, individuals are more likely to develop insulin resistance as BMI increases. Insulin resistance is a crucial feature of type 2 diabetes and

Table 4 Correlation Analysis of Pre-Pregnancy BMI and GDM

Variable in an Equation	B value	95% CI	P value
GDM	1.204	1.161~1.248	<0.001

Abbreviation: GDM, gestational diabetes mellitus.

Table 5 Comparison of Blood Glucose and Lipid Levels Between the GDM Group and Non-GDM Group in the overweight and Obesity Group

Index	Gestational Diabetes Mellitus (n=109)	Non Gestational Diabetes Mellitus (n=421)	t value	P value
FBG (mmol/L)	5.88±0.42	5.18±0.49	27.691	<0.001
HbA1c (%)	5.93±0.48	5.72±0.47	7.669	<0.001
TG (mmol/L)	2.06±0.19	1.59±0.15	10.763	<0.001
HDL-C (mmol/L)	1.21±0.34	1.30±0.54	1.656	0.098
LDL-C (mmol/L)	4.44±0.68	2.91±0.66	9.244	<0.001

Notes: Except for blood glucose and lipid levels, are $\bar{x} \pm s$

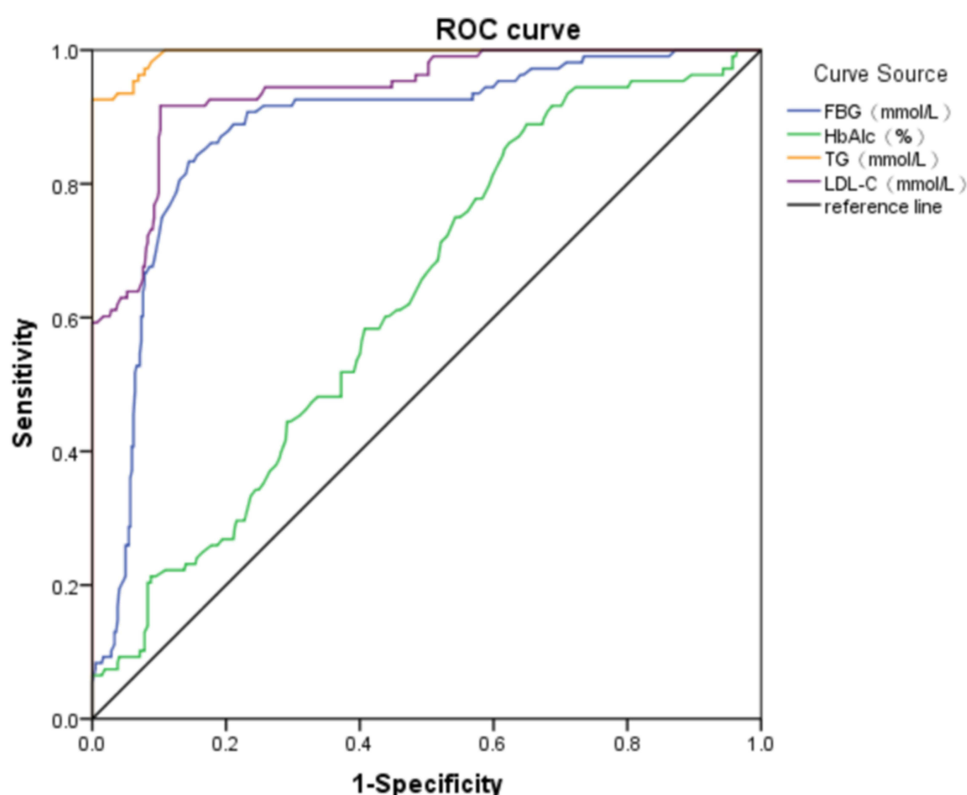
Abbreviations: FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 6 Analysis of the Predictive Value of FBG, HbA1c, TG, and LDL-C Levels in the Incidence of GDM in an Overweight and Obese Group

Test Items	AUC	Standard Error	Asymptotic Significance Level	95% Confidence Intervals		Optimal Critical value	Sensitivity	Specificity	Youden Index
				Lower Limit	Upper limit				
FBG	0.991	0.019	<0.001	0.842	0.916	5.595	85.5	68.8	0.833
HbA1c	0.641	0.028	<0.001	0.574	0.683	5.235	35.1	24.0	0.889
TG	0.994	0.002	<0.001	0.99	0.998	2.000	91.7	100.0	0.917
LDL-C	0.935	0.013	<0.001	0.91	0.961	3.465	90.8	89.8	0.806

Abbreviations: FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; GDM, gestational diabetes mellitus; ROC, receiver operating characteristic; AUC, area under curve.

metabolic syndrome, leading to elevated blood glucose levels and stimulating the liver to produce more glucose and lipids, which in turn increases levels of HbA1c (an indicator of long-term blood glucose control), TG, and LDL-C. Second, in overweight and obese women before pregnancy, changes in placental insulin, estrogen, progesterone, and thyroid hormones are more pronounced during gestation. Reduced thyroid hormone levels can exacerbate insulin resistance, affecting intestinal glucose absorption and resulting in abnormal glucose metabolism, as indicated by elevated HbA1c and FBG levels.²⁴ Simultaneously, a decrease in thyroid hormone levels can lead to a reduction in cholesterol content, resulting in decreased lipid utilization by the body, increased lipid levels, and abnormalities in lipid metabolism. This is manifested by pathologically elevated levels of TG and LDL-C, along with a reduction in HDL-C.²⁵ On the other, an increase in BMI is typically accompanied by fat accumulation, particularly abdominal fat. Abdominal fat is

**Figure 6** ROC curve of overweight and obesity group complicated with GDM by FBG, HbA1c, TG, and LDL-C levels.

Abbreviations: FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; GDM, gestational diabetes mellitus; ROC, receiver operating characteristic.

a metabolically active tissue that secretes various inflammatory cytokines and adipokines, interfering with insulin signaling, promoting fat synthesis and storage, and inhibiting fat breakdown. At the same time, abnormalities in lipid metabolism can lead to a continuous increase in body fat mass. This decreases the density of insulin receptors on the membranes of fat cells, leading to reduced insulin sensitivity and insulin resistance. It also further impacts glucose metabolism, exacerbating abnormalities in glucose metabolism. Insulin resistance affects the biological regulation of insulin, causing disturbances in the body's metabolism of fats and proteins. In turn, it exacerbates lipid metabolism abnormalities, creating a vicious cycle.^{12,26} The level of HDL-C is influenced by a combination of genetic and environmental factors, including diet, physical activity, smoking habits, alcohol consumption, and certain medications. Therefore, HDL-C levels may not change significantly, even with increased BMI. Thus, through the aforementioned multiple mechanisms, overweight and obese pregnant women are more prone to abnormalities in glycemic and lipid metabolism during pregnancy, and these abnormalities tend to occur earlier. Although this study only analyzed the correlation between early pregnancy lipid metabolism and pre-pregnancy BMI, research by Patricia Corrales and other scholars²⁶ has already proven that, in addition to early pregnancy, lipid metabolism during the mid and late stages of pregnancy also exhibits similar characteristics. Therefore, maintaining a reasonable BMI before pregnancy can reduce the levels of glycemic and lipid metabolism abnormalities throughout the pregnancy period, decrease the incidence of related metabolic diseases, and improve pregnancy outcomes for both mother and child.

The results of this study indicate that for every unit increase in pre-pregnancy BMI, the risk of developing GDM increases by 0.204 times ($P < 0.05$). This is consistent with previous research findings, indicating that pre-pregnancy overweight and obese pregnant women often exhibit metabolic syndrome, which is associated with a certain degree of endocrine and metabolic disorders within the body.^{27,28} Studies demonstrate that, on the one hand, pregnancy itself leads to significant alterations in the levels of estrogen and progesterone within the body, alongside a continuous increase in lipid levels. This results in decreased insulin sensitivity in peripheral tissues. Additionally, the development of the placenta releases inflammatory mediators that, to a certain extent, impair pancreatic function. On the other, if a woman is overweight or obese before pregnancy, the levels of adipose-derived cytokines (such as adiponectin and leptin) in the body are higher, increasing insulin sensitivity. Therefore, pregnant women who are overweight and obese can exert direct or indirect effects on insulin secretion and sensitivity through the aforementioned multiple pathways, making them more susceptible to gestational complications such as GDM and hypertension,²⁹ leading to adverse maternal and neonatal pregnancy outcomes. Therefore, maintaining a healthy body mass index before pregnancy holds significant clinical importance for reducing the incidence of gestational diabetes and improving adverse pregnancy outcomes.

In this study, by generating ROC curves, the results indicate that early pregnancy levels of FBG, TG, and LDL-C demonstrate considerable accuracy in predicting gestational diabetes among pregnant women in the overweight and obese group, with both sensitivity and specificity holding clinical value. This indicates that the development of GDM is significantly associated with abnormalities in glucose and lipid metabolism in early pregnancy.³⁰ Previous literature has demonstrated that GDM not only adversely affects maternal and neonatal outcomes^{31–33} but also impacts the mother's and offspring's quality of life in later life.^{10,34} The combination of GDM in overweight and obese women increases the incidence of the aforementioned adverse outcomes.³⁵ Therefore, early screening for GDM in women who are overweight or obese before pregnancy holds significant value. Currently, in clinical practice, the diagnosis of GDM is made by conducting an OGTT between 24 and 28 weeks of pregnancy. This timing is chosen because blood glucose levels in pregnant women peak most notably during this stage, enhancing the accuracy of GDM diagnosis.^{36,37} Simmons³⁸ et al demonstrated that early exposure to mild hyperglycemia may be more significant than previously thought, necessitating the early identification of high-risk pregnant women for timely intervention. If treatment for GDM is initiated only after the diagnosis via OGTT at 24–26 weeks, the therapeutic effect may be less pronounced.³⁹ Therefore, the early diagnosis and management of GDM in existing guidelines may require further review, particularly for overweight and obese pregnant women. However, the gestational week at which testing is conducted is relatively late, preventing timely prevention and intervention for high-risk populations. Addressing this limitation, the findings of WU Z Q et al support the perspective of this study, showing a specific correlation between FBG and TG levels measured in early pregnancy and OGTT glucose values at 24 to 32 weeks of gestation.^{40,41} This significantly advances the timeline for predicting GDM. Ueland T³⁰ et al also indicate that, from early pregnancy to delivery, pregnant women with GDM consistently

exhibit lower HDL-C levels and higher total cholesterol levels throughout the entire pregnancy period compared to normal pregnant women. Assessing GDM risk, elevated early LDL-C levels may indicate insulin resistance and lipid metabolism disorders. High LDL-C levels are associated with pregnancy complications such as gestational hypertension and GDM. Thus, as one of the early biochemical markers for GDM, they can provide additional information for risk prediction.⁴² Although HbA1c is commonly used in long-term diabetes management, its value in diagnosing GDM remains controversial; however, it can also serve as a tool for risk assessment in early pregnancy. A study suggested that higher HbA1c levels in early pregnancy are significantly associated with GDM, making it a potential tool for early GDM prediction.⁴³ This is consistent with the results of our study, indicating that overweight and obese pregnant women who develop GDM in the mid-trimester already exhibit abnormalities in glucose and lipid metabolism indicators detected in early pregnancy. Therefore, glucose and lipid metabolism tests in early pregnancy can serve as a supplement to the 24–32 weeks OGTT, potentially offering great value in the early prediction of GDM for women who are overweight or obese before pregnancy. This approach is beneficial for early identification of high-risk GDM populations,⁴⁴ conducive to clinical assessment and prevention, and holds significant practical value. This is consistent with the research conclusions of scholars such as Ying Zheng.⁴⁵ This study builds upon previous research by further exploring the impact of pre-pregnancy overweight and obesity on early blood glucose and lipid levels in women with GDM, as well as its predictive value for GDM. This has significant implications for the early identification of high-risk groups prone to gestational diabetes among overweight and obese pregnant women in clinical practice. Early screening and diagnosis enable physicians to implement timely interventions, such as dietary adjustments, increased physical activity, or pharmacological treatments, to prevent or delay the onset of gestational diabetes and reduce the risk of maternal and neonatal complications.

This study has the following limitations: it is a single-center retrospective study, and its data accuracy is not as high as that of large-scale, multicenter prospective randomized controlled trials. Additionally, the inclusion of pregnant women who are overweight or obese was based solely on first prenatal visit inquiries, which may lead to underestimation of weight data. Further investigation and validation through multicenter prospective studies are needed. In this study, biochemical indicators were measured simultaneously, which may not fully reflect the metabolic changes in pregnant women throughout the entire gestation period. Future research could consider multiple measurements to assess these indicators' trends and predictive value more accurately. Although individual indicators show good predictive value, a multi-factor combined model may improve prediction accuracy and practicality. Future studies could explore the interactions between these indicators and develop comprehensive predictive models. New biomarkers, such as inflammatory factors and hormone levels, could also be investigated beyond the conventional biochemical markers studied to enhance predictive sensitivity and specificity further.

Conclusion

In summary, pre-pregnancy overweight and obesity are likely to lead to abnormalities in glucose and lipid metabolism levels in early pregnancy, thereby increasing the incidence of gestational diabetes mellitus. By assessing glucose and lipid metabolism markers in early pregnancy, there is significant practical value in predicting and preventing the occurrence of gestational diabetes mellitus among pregnant women who are overweight or obese before pregnancy. Therefore, it is essential to leverage community-based platforms to collaborate with maternity hospitals to optimize pre-pregnancy BMI for women of childbearing age, conduct early pregnancy assessments, and manage glucose and lipid metabolism. Timely management and intervention guidance on nutritional status should be provided for pregnant women with higher BMI and abnormalities in glucose and lipid metabolism during early pregnancy.

Ethics Approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. The medical ethics committee of the Shanghai Huangpu District Waitan Street Community Health Service Center (No.2016001) granted ethical approval.

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Disclosure

All authors declare no conflicts of interest in this work.

References

1. Solmi F, Morris S. Overweight and obese pre-pregnancy BMI is associated with higher hospital costs of childbirth in England. *BMC Pregnancy Childb.* 2018;18(1):253. doi:10.1186/s12884-018-1893-z
2. Pasquali R, Casanueva F, Haluzik M, et al. European society of endocrinology clinical practice guideline: endocrine work-up in obesity. *Eur J Endocrinol.* 2020;182(1):G1–G32. doi:10.1530/EJE-19-0893
3. Cui D, Yang W, Shao P, et al. Interactions between pre-pregnancy overweight and passive smoking for macrosomia and large for gestational age in Chinese pregnant women. *Obes Facts.* 2021;14(5):520–530. doi:10.1159/000517846
4. Kej F, Liu S, Ge RL, et al. Associations of maternal pre-pregnancy BMI and gestational weight gain with the risks of adverse pregnancy outcomes in Chinese women with gestational diabetes mellitus. *BMC Pregnancy Childb.* 2023;23(1):414. doi:10.1186/s12884-023-05657-8
5. Machado C, Monteiro S, Oliveira MJ. Impact of overweight and obesity on pregnancy outcomes in women with gestational diabetes - results from a retrospective multicenter study. *Arch Endocrinol Metab.* 2020;64(1):45–51. doi:10.20945/2359-3997000000178
6. Yong HY, Mohd Shariff Z, Mohd Yusof BN, et al. Independent and combined effects of age, body mass index, and gestational weight gain on the risk of gestational diabetes mellitus. *Sci Rep.* 2020;10(1):8486. doi:10.1038/s41598-020-65251-2
7. Miao M, Dai M, Zhang Y, et al. Influence of maternal overweight, obesity and gestational weight gain on the perinatal outcomes in women with gestational diabetes mellitus. *Sci Rep.* 2017;7(1):305. doi:10.1038/s41598-017-00441-z
8. Zhou T, Du S, Sun D, et al. Prevalence and trends in gestational diabetes mellitus among women in the United States, 2006–2017: a population-based study. *Front Endocrinol.* 2022;13:868094. doi:10.3389/fendo.2022.868094
9. Najafi F, Hasani J, Izadi N, et al. Risk of gestational diabetes mellitus by pre-pregnancy body mass index: a systematic review and meta-analysis. *Diabetes Metab Syndr.* 2021;15(4):102181. doi:10.1016/j.dsx.2021.06.018
10. Moon JH, Jang HC. Gestational diabetes mellitus: diagnostic approaches and maternal-offspring complications. *Diabetes Metab J.* 2022;46(1):3–14. doi:10.4093/dmj.2021.0335
11. Modzelewski R, Stefanowicz-rutkowska MM, Matuszewski W, et al. Gestational diabetes mellitus-recent literature review. *J Clin Med.* 2022;12(1):11. doi:10.3390/jcm12010011
12. Trivett C, Lees ZJ, Freeman DJ. Adipose tissue function in a healthy pregnancy, gestational diabetes mellitus and pre-eclampsia. *Eur J Clin Nutr.* 2021;75(12):1745–1756. doi:10.1038/s41430-021-00948-9
13. Chen L. Metabolomic markers in early pregnancy for gestational diabetes mellitus. *Diabetes.* 2022;71(8):1620–1622. doi:10.2337/dbi22-0015
14. Zhang M, Zhou Y, Zhong J, et al. Current guidelines on the management of gestational diabetes mellitus: a content analysis and appraisal. *BMC Pregnancy Childb.* 2019;19(1):200. doi:10.1186/s12884-019-2343-2
15. Sun Y, Shen Z, Zhan Y, et al. Effects of pre-pregnancy body mass index and gestational weight gain on maternal and infant complications. *BMC Pregnancy Childb.* 2020;20(1):390. doi:10.1186/s12884-020-03071-y
16. Pettersen-dahl A, Murzakanova G, Sandvik L, et al. Maternal body mass index as a predictor for delivery method. *Acta Obstet Gynecol Scand.* 2018;97(2):212–218. doi:10.1111/aogs.13265
17. Wang N, Ding Y, Wu J. Effects of pre-pregnancy body mass index and gestational weight gain on neonatal birth weight in women with gestational diabetes mellitus. *Early Hum Dev.* 2018;124:17–21. doi:10.1016/j.earlhumdev.2018.07.008
18. Chu SY, Callaghan WM, Kim SY, et al. Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care.* 2007;30(8):2070–2076. doi:10.2337/dc06-2559a
19. Xu H, Ma Y, Zhang L, et al. Impact of pre-pregnancy body mass index, weight gain, and blood lipid level during pregnancy on pregnancy outcome in patients with gestational diabetes mellitus. *Zhejiang Da Xue Xue Bao Yi Xue Ban.* 2021;50(3):320–328. doi:10.3724/zdxbyxb-2021-0185
20. Aji AS, Lipoeto NI, Yusrawati Y, et al. Association between pre-pregnancy body mass index and gestational weight gain on pregnancy outcomes: a cohort study in Indonesian pregnant women. *BMC Pregnancy Childb.* 2022;22(1):492. doi:10.1186/s12884-022-04815-8
21. Alfaghli EM. Maternal obesity influences birth weight more than gestational diabetes author. *BMC Pregnancy Childb.* 2021;21(1):111. doi:10.1186/s12884-021-03571-5
22. Girchenko P, Lahti-pulkkinen M, HäMäläNen E, et al. Associations of polymetabolic risk of high maternal pre-pregnancy body mass index with pregnancy complications, birth outcomes, and early childhood neurodevelopment: findings from two pregnancy cohorts. *BMC Pregnancy Childb.* 2024;24(1):78. doi:10.1186/s12884-024-06274-9
23. Sormunen-harju H, Huvinen E, Girchenko PV, et al. Metabolomic profiles of nonobese and obese women with gestational diabetes. *J Clin Endocrinol Metab.* 2023;108(11):2862–2870. doi:10.1210/clinem/dgad288
24. Wang Y, Lu S, Xu X, et al. The interactive effects of pre-pregnancy body mass index, thyroid function, and blood lipid levels on the risk of gestational diabetes mellitus: a crossover analysis. *BMC Pregnancy Childb.* 2022;22(1):580. doi:10.1186/s12884-022-04908-4
25. Zhang S, Wu Y, Pan W, et al. Free-triiodothyronine to free-thyroxine ratio mediated the effect of pre-pregnancy body mass index or maternal weight gain during early pregnancy on gestational diabetes mellitus. *Endocr Pract.* 2022;28(4):398–404. doi:10.1016/j.eprac.2021.12.016
26. Corrales P, Vidal-puig A, Medina-gómez G. Obesity and pregnancy, the perfect metabolic storm. *Eur J Clin Nutr.* 2021;75(12):1723–1734. doi:10.1038/s41430-021-00914-5
27. Grieger JA, Bianco-miotto T, Grzeskowiak LE, et al. Metabolic syndrome in pregnancy and risk for adverse pregnancy outcomes: a prospective cohort of nulliparous women. *PLoS Med.* 2018;15(12):e1002710. doi:10.1371/journal.pmed.1002710

28. Chen L, Ma J, Su G, et al. The dynamic nexus: exploring the interplay of BMI before, during, and after pregnancy with Metabolic Syndrome (MetS) risk in Chinese lactating women. *BMC Public Health*. 2023;23(1):2423. doi:10.1186/s12889-023-17344-6
29. Carpenter MW. Gestational diabetes, pregnancy hypertension, and late vascular disease. *Diabetes Care*. 2007;30(Suppl 2):S246–250. doi:10.2337/dc07-s224
30. Ueland T, Roland MCP, Michelsen- AE, et al. Elevated cholesteryl ester transfer protein activity early in pregnancy predicts prediabetes 5 years later. *J Clin Endocrinol Metab*. 2020;105.
31. Ye W, Luo C, Huang J, et al. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2022;377:e067946. doi:10.1136/bmj-2021-067946
32. Aguilera J, Sanchez Sierra A, Abdel Azim S, et al. Maternal cardiac function in gestational diabetes mellitus at 35–36 weeks gestation and 6 months postpartum. *Ultrasound Obstet Gynecol*. 2020;56(2):247–254. doi:10.1002/uog.22118
33. Sonaglioni A, Barlocchi E, Adda G, et al. The impact of short-term hyperglycemia and obesity on biventricular and biatrial myocardial function assessed by speckle tracking echocardiography in a population of women with gestational diabetes mellitus. *Nutr, Metab Cardiovasc Dis*. 2022;32(2):456–468. doi:10.1016/j.numecd.2021.10.011
34. Xiang AH. Diabetes in pregnancy for mothers and offspring: reflection on 30 years of clinical and translational research: the 2022 Norbert Freinkel award lecture. *Diabetes Care*. 2023;46(3):482–489. doi:10.2337/dci22-0055
35. Zhu Y, Zheng Q, Pan Y, et al. Association between pre-pregnancy body mass index or gestational weight gain and adverse pregnancy outcomes among Chinese women with gestational diabetes mellitus: a systematic review and meta-analysis. *BMJ Open*. 2024;14(2):e075226. doi:10.1136/bmjopen-2023-075226
36. Wendland EM, Torloni MR, Falavigna M, et al. Gestational diabetes and pregnancy outcomes—a systematic review of the World Health Organization (WHO) and the international association of diabetes in pregnancy study groups (IADPSG) diagnostic criteria. *BMC Pregnancy Childb*. 2012;12(1):23. doi:10.1186/1471-2393-12-23
37. Francis EC, Powe CE, Lowe WL, et al. Refining the diagnosis of gestational diabetes mellitus: a systematic review and meta-analysis. *Commun Med*. 2023;3(1):185. doi:10.1038/s43856-023-00393-8
38. Simmons D, Immanuel J, Hague WM, et al. Effect of treatment for early gestational diabetes mellitus on neonatal respiratory distress: a secondary analysis of the TOBOGM study. *Bjog*. 2024. doi:10.1111/1471-0528.17938
39. Yildiz Atar H, Baatz JE, Ryan RM. Molecular mechanisms of maternal diabetes effects on fetal and neonatal surfactant. *Children*. 2021;8(4):281. doi:10.3390/children8040281
40. Valadan M, Bahramnezhad Z, Golshahi F, et al. The role of first-trimester HbA1c in the early detection of gestational diabetes. *BMC Pregnancy Childb*. 2022;22(1):71. doi:10.1186/s12884-021-04330-2
41. Lu L, Koulman A, Petry CJ, et al. An unbiased lipidomics approach identifies early second trimester lipids predictive of maternal glycemic traits and gestational diabetes mellitus. *Diabetes Care*. 2016;39(12):2232–2239. doi:10.2337/dc16-0863
42. Xu X, Luo S, Lin J, et al. Association between maternal lipid profiles and lipid ratios in early to middle pregnancy as well as their dynamic changes and gestational diabetes mellitus. *BMC Pregnancy Childb*. 2024;24(1):510. doi:10.1186/s12884-024-06692-9
43. Peng X, Liu M, Gang J, et al. Use of oral glucose tolerance testing and HbA1c at 6–14 gestational weeks to predict gestational diabetes mellitus in high-risk women. *Arch Gynecol Obstet*. 2023;307(5):1451–1457. doi:10.1007/s00404-022-06637-7
44. Yen IW, Lee CN, Lin MW, et al. Overweight and obesity are associated with clustering of metabolic risk factors in early pregnancy and the risk of GDM. *PLoS One*. 2019;14(12):e0225978. doi:10.1371/journal.pone.0225978
45. Zheng Y, Hou W, Xiao J, et al. Application value of predictive model based on maternal coagulation function and glycolipid metabolism indicators in early diagnosis of gestational diabetes mellitus. *Front Public Health*. 2022;10:850191. doi:10.3389/fpubh.2022.850191

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