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No role of the third-trimester inflammatory factors in the association of gestational diabetes mellitus with postpartum cardiometabolic indicators

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Abstract

Background The influence of gestational diabetes mellitus (GDM) on postpartum cardiometabolic indicators is primarily restricted to glucose and lipid metabolism, however the indicators for liver and kidney function have been rarely explored, and the role of the third-trimester inflammatory factors in these associations has never been investigated.

Methods Based on the Ma'anshan birth cohort (MABC), women with or without GDM history were selected and invited to participate in a 6-year postpartum follow-up. The fasting blood samples were collected to measure 16 comprehensive metabolic indicators during a 6-year postpartum follow-up: fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), triglycerides (TG), total cholesterol (TC), uric acid (UA), blood urea nitrogen (BUN), serum creatinine (SCR), etc. Seven inflammatory factors, including TNF- α , IFN- γ , IL-1 β , IL-6, IL-10, IL-12p70, and IL-17 A, were measured with serum samples collected during the third trimester of pregnancy. Linear regression models were used to analyze the associations between GDM and 6-year postpartum metabolic indicators, GDM and third-trimester inflammatory factors, and the third-trimester inflammatory factors and 6-year postpartum metabolic indicators. Mediating and moderating effect analyses were further performed to explore if the third-trimester inflammatory factors mediate or modify the association between GDM and postpartum cardiometabolic indicators.

Results From July 2021 to August 2022, 307 participants have been followed up, with 99 women with a prior GDM history. Compared with those without GDM, individuals with a prior history of GDM had significantly elevated levels of FPG ($\beta = 0.40$, 95% CI: 0.18 to 0.62, $P_{FDR} < 0.001$), HbA1c ($\beta = 0.22$, 95% CI: 0.09 to 0.34, $P_{FDR} = 0.009$), TyG ($\beta = 0.22$, 95% CI: 0.07 to 0.37, $P_{FDR} = 0.024$) at 6 years postpartum, and the association between GDM and SCR ($\beta = 2.43$, 95% CI: 0.02 to 4.85, $P_{FDR} = 0.144$) reached nominal significance level. GDM history was associated with a decreased level of

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third-trimester IL-17 A ($\beta = -0.58$, 95% CI: -0.99 to -0.18, $P_{FDR} = 0.035$). No significant association between third-trimester inflammatory factors and 6-year postpartum metabolic indicators was observed. And no mediating or moderating effect of third-trimester inflammatory factors was observed in those associations.

Conclusion A prior history of GDM was significantly associated with elevated FPG, HbA1c, and TyG in women at 6 years postpartum, whereas third-trimester inflammatory factors had no role in mediating or moderating these associations.

Keywords Gestational diabetes mellitus, Cardiometabolic indicators, Inflammatory factors, Cohort study

Background

Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance first diagnosed during pregnancy without a history of pre-existing diabetes [1], with a prevalence varying from 6.1 to 15.2% worldwide [2]. The adverse effects of GDM are not limited to short-term impacts such as macrosomia, premature delivery, and pre-eclampsia [3] but also increased lifetime risk of cardiovascular disease (CVD) [4, 5] in both mothers and their offspring. Of note, CVD is a leading cause of mortality and morbidity in women worldwide [6] and is also the case in China [7]. Therefore, for primary prevention of CVD, it is essential to establish the associations of prior GDM history with cardiovascular risk indicators and clarify the potential biological mechanisms.

It is well-established that metabolic indicators such as fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) are significantly associated with an increased risk of CVD in the general population [8–11]. Composite metabolic indicators like triglyceride-glucose index (TyG) and siMS (simple method for quantifying metabolic syndrome) index have also been used to predict the development of CVD [12, 13]. In recent years, many studies have reported associations between GDM and postpartum metabolic indicators, but the main focus of current studies has been on impaired glucose metabolism and dyslipidemia [14–16]. However, few studies have evaluated metabolic indicators of the liver and kidney, such as albumin (ALB), serum uric acid (UA), and blood urea nitrogen (BUN), which were significantly associated with the risk of CVD in the general population [17–19]. A meta-analysis on the CVD risk caused by GDM history showed that women with GDM had a 2-fold increased risk of developing CVD, irrespective of progression to T2DM [20]. Thus, for women with a prior GDM history, only an impaired glucose tolerance test postpartum might not be enough. Therefore, to gain a more comprehensive understanding of the mechanisms of developing CVD risk in GDM, it is essential to explore the relationship between GDM and cardiometabolic indicators using a comprehensive set of metabolic indicators.

The mechanisms underlying the doubled risk of CVD in women with previous GDM are unclear. Inflammatory factors play an important role in the development of both GDM and CVD. The occurrence of GDM may cause the persistence of chronic inflammation during pregnancy leading to changes in the number and type of immune cells and the release of pro-inflammatory factors [21]. Several clinical studies and animal experiments have shown that inflammatory factors influence the development of CVD by altering various signaling pathways that could promote the proliferation and migration of vascular smooth muscle cells (VSMC) and induce vascular endothelial dysfunction [22–25]. However, to our knowledge, no previous study has investigated the role of maternal inflammatory factors in linking GDM history with postpartum cardiovascular health indicators.

Therefore, based on the Ma'anshan birth cohort study (MABC), 99 women with GDM history and 208 women without were successfully followed at 6 years postpartum, with data from a comprehensive set of metabolic indicators and the third-trimester inflammatory factors, our study aims first to clarify the associations between GDM history and postpartum cardiometabolic indicators and second to examine the role of maternal inflammatory factors in them.

Methods

Study population

To investigate the long-term impact of GDM on women's health postpartum and the modifiable factors, we randomly selected a 1:2 ratio of 120 participants with prior GDM history and 240 women without it from the Ma'anshan birth cohort (MABC). MABC was a population-based prospective cohort established in Ma'anshan Maternal and Child Health Care Center, which aims to investigate the effects of maternal environmental exposures on health outcomes of children's development. The details of MABC's inclusion and exclusion criteria can be found elsewhere [26]. From May 2013 to September 2014, 3474 pregnant women were recruited at their first visit, and their information and fasting blood samples were collected during the first, second, and third trimesters of pregnancy. The blood samples were centrifuged and stored in the -80°C refrigerator for future detection.

Of them, women with accurate GDM diagnostic information were eligible for further follow-up. The study obtained ethics approval from the ethics committee of Anhui Medical University (20131195, 20210732). Written informed consent was obtained from all participating women.

Simple size

Comparing women without GDM, the between-group effect size (Cohen's d) of CVD postpartum proportion was assumed to be at least 0.38, which was demonstrated in a previous study [20]. Based on a dropout rate of 20% and an allocation rate of 1: 2 (GDM group versus non-GDM group), which was decided by the incidence of GDM in the original cohort and financial resources, the sample size of 103 women in the GDM group and 205 women in the non-GDM group was calculated using PASS version 21.0.3 (NCSS, LLC. Kaysville, Utah, USA), with an α of 5% and a statistical power ($1-\beta$) of 80%. Besides, considering the likelihood of GDM during follow-up in participants who were pre-determined to be in the non-GDM group, the final sample size of 120 women in the GDM and 240 women in the non-GDM group was proposed. And we selected 360 participants from women with or without prior GDM history in the cohort using a computerized random number method.

Measuring tools

Sociodemographic information

Information on demographic characteristics (age, ethnics, education, income, etc.) and lifestyle was collected through self-administered questionnaires at 6-year postpartum follow-up. Information during pregnancy was retrieved from the baseline database.

Lifestyle information

The lifestyle assessments of sleeping, physical activity, and dietary were performed during 6-year postpartum follow-up:

A modified Chinese version of the Pittsburgh Sleep Quality Index (PSQI) scale, a validated and widely used tool to measure sleep quality, was used to evaluate sleep quality [27]. It includes a total of 14 self-rated items, of which each has a range of 0–3 points [28]. The total PSQI score could be classified into 3 categories: excellent, average, and poor.

The International Physical Activity Questionnaire (IPAQ), with good reliability and validity [29], was used to assess the physical activity of the participants over the past 7 days, and the results were classified as low, moderate, and high physical activity levels.

The Food Frequency Questionnaire (FFQ) investigated the frequency (daily, weekly, monthly, and yearly), quantity, and grams of food intake, which was used to evaluate

the dietary habits and dietary nutrition of participants in the past year as red meat intake was strongly associated with the risk of CVD [30].

Anthropometric parameters

The height and weight of individuals were recorded to the nearest 0.1 kg and 0.1 cm, using a human body composition analyzer (GAIA KIKO, JAWON, Seoul, South Korea). Waist circumference (WC) at the level of the umbilicus was measured by a trained professional using non-stretchable sprung tape with the participants in the resting-standing position. Blood pressure was measured by one trained researcher using a mercury sphygmomanometer, and the average of the two readings was taken as the individual's blood pressure value.

Diagnosis of GDM

During the 24~28 week of pregnancy, women were given 75 g of glucose to consume orally for the OGTT at the center. The OGTT was conducted in the morning after a minimum of 8 h of fasting overnight. GDM was diagnosed if the plasma glucose levels met or exceeded either of the following values: 5.1 mmol/L for fasting glucose, 10.0 mmol/L at 1 h, and 8.5 mmol/L at 2 h [31].

Assessment of inflammatory factors and metabolic indicators

Seven inflammatory factors, including TNF- α , IFN- γ , IL-1 β , IL-6, IL-10, IL-12p70, IL-17 A, in the serum of participants from the third-trimester were measured by multi-bead enzyme-free analyzer (MILLIPLEX[®] MAP, Merck Millipore, Germany) using customized Human High Sensitivity Serum Factor Kit (MilliporeMAT Kit, Cat. No. HSTCMAG-28SK) between December 2018 and October 2019 [32]. The data were analyzed by Milliplex Analyst 5.1.

Participants' fasting blood was collected by trained staff during a 6-year postpartum follow-up. The metabolic indicators were detected by the automatic biochemical analyzer (BECKMAN LX20, Beckman Coulter, Inc., USA), including fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), hemoglobin F (HbF), insulin (RI), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), Low-density lipoprotein (LDL), total protein (TP), albumin (ALB), apolipoprotein A (ApoA), apolipoprotein B (ApoB), uric acid (UA), blood urea nitrogen (BUN), serum creatinine (SCR) and cystatin (CYS).

Abnormal FPG was defined as $FPG \geq 6.1$ mmol/L and abnormal HbA1c was defined as $HbA1c \geq 6.5\%$ [33]. Dyslipidemia was divided into 4 categories [34]: Hypercholesterolemia ($TC \geq 5.2$ mmol/L); Hypertriglyceridemia ($TG \geq 1.7$ mmol/L); Hypo-HDLemia ($HDL \leq 5.2$ mmol/L); Hyper-LDLemia ($LDL \geq 3.4$

mmol/L). Metabolic syndrome (MetS) was diagnosed if 3 or more of the following 5 items were met [33]: (1) central obesity with WC (female) ≥ 85 cm; (2) FPG ≥ 6.1 mmol/L or 2 h PG ≥ 7.8 mmol/L or confirmed DM; (3) SBP/DBP $\geq 130/85$ mmHg or confirmed hypertension; (4) fasting TG ≥ 1.70 mmol/L; and (5) fasting HDL-C < 1.04 mmol/L (female).

Calculation of integrated metabolic index

Two integrated metabolic indices, the triglyceride-glucose (TyG) index and the Simple Method for Quantifying Metabolic Syndrome (siMS) score, were calculated. The TyG index was calculated from the levels of TG and FPG detected 6 years postpartum [35] with the following formula:

$$\text{TyG} = \ln\left(\frac{\text{TG} \times \text{FPG}}{2}\right)$$

The siMS score was calculated from WC, height, FPG, TG, systolic blood pressure (SBP), and HDL measured 6 years postpartum [36], which was calculated as follows:

$$\text{siMSscore} = \frac{2 \times \text{WC}}{\text{height}} + \frac{\text{FPG}}{5.6} + \frac{\text{TG}}{1.7} + \frac{\text{SBP}}{130} - \frac{\text{HDL}}{1.28}$$

Statistical analysis

Categorical variables are represented by frequencies and percentages, and continuous data are expressed as the mean \pm standard deviation. The third-trimester inflammatory factors were log-transformed with a base of 2, so that the transformed distribution approximated a normal distribution for subsequent analysis [37]. If the concentrations of inflammatory factors were below the limit of detection (LOD), LOD / $\sqrt{2}$ was used instead. First, the chi-square test and the t-test were used to evaluate differences in characteristics between the GDM and non-GDM groups. Adjusted covariates were selected based on biological plausibility and the results of t-tests and chi-square tests, of which *p*-values less than 0.1 were included. Second, linear regression was used to determine the association between GDM and metabolic indicators at 6 years postpartum, and binary logistics was used to analyze the association between GDM and the risks of metabolic abnormalities at 6 years postpartum. Besides linear regression was also used to determine the association between GDM and seven third-trimester inflammatory factors, and the association between third-trimester inflammatory factors and metabolic indicators at 6 years postpartum. Based on the results, we use the PROCESS 3.3 plugin to analyze the moderating and mediating effect of third-trimester inflammatory factors

in the association between GDM and significant metabolic indicators.

To account for multiple testing, two-sided *p* values were adjusted according to the Benjamini/Hochberg (B/H) method to control the false discovery rate (FDR). A statistically significant association was determined if its corresponding B/H-adjusted *p* value was less than 0.05, corresponding to an FDR of 5%. Risks are described as unadjusted and adjusted Relative risks (RRs) with 95% confidence intervals (CIs). The adjusted RRs and its 95% CIs were transformed from adjusted odd ratios (ORs) and 95% CIs calculated by binary logistic regression model using the formula from previous study [38]. All tests were two-sided, and *p*-values below 0.05 indicated significance. All statistical analyses were performed using SPSS version 23.0.

Results

From July 2021 to August 2022, of 360 women who received our invitations for follow-up, 335 agreed to participate and have been successfully followed. Since 10 women without GDM in the index pregnancy developed GDM during subsequent pregnancies, these 10 women were transferred to the GDM group. After excluding women with pre-pregnancy hepatorenal diseases (*n*=11), thyroid diseases (*n*=9), cardiovascular diseases (*n*=5), and 3 without complete information, our current study included a final 99 women in the GDM group and 208 women in the non-GDM group. The flowchart is shown in Fig. 1.

Table 1 shows the 6-year postpartum characteristics of the participants, comparing those with prior GDM history and those without it. Compared with women without GDM, those with prior GDM were older, had higher pre-pregnancy BMI and current BMI, and had a higher proportion of DM family history.

Table 2 shows the association between GDM history and metabolic indicators at 6 years postpartum. After adjusting for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history in model 1, compared with women without GDM, those with prior GDM had significantly higher levels of FPG ($\beta=0.39$, 95% CI: 0.18 to 0.61, $P_{\text{FDR}} < 0.001$), HbA1c ($\beta=0.22$, 95% CI: 0.10 to 0.34, $P_{\text{FDR}} < 0.001$), and TyG ($\beta=0.23$, 95% CI: 0.08 to 0.38, $P_{\text{FDR}} = 0.012$) at 6 years postpartum with corrected P_{FDR} below 0.05. While the association between GDM history and TG ($\beta=0.22$, 95% CI: 0.02 to 0.43, $P_{\text{FDR}} = 0.110$), HbF ($\beta=0.07$, 95% CI: 0.00 to 0.14, $P_{\text{FDR}} = 0.110$), RI ($\beta=1.81$, 95% CI: 0.05 to 3.57, $P_{\text{FDR}} = 0.110$), ApoA ($\beta=0.05$, 95% CI: 0.00 to 0.10, $P_{\text{FDR}} = 0.110$), and siMS ($\beta=0.23$, 95% CI: 0.03 to 0.42, $P_{\text{FDR}} = 0.104$) only reached nominal significance level. Based on Model 1, Model 2 further adjusted for sleeping quality, physical activity, and red meat consumption, the association between GDM

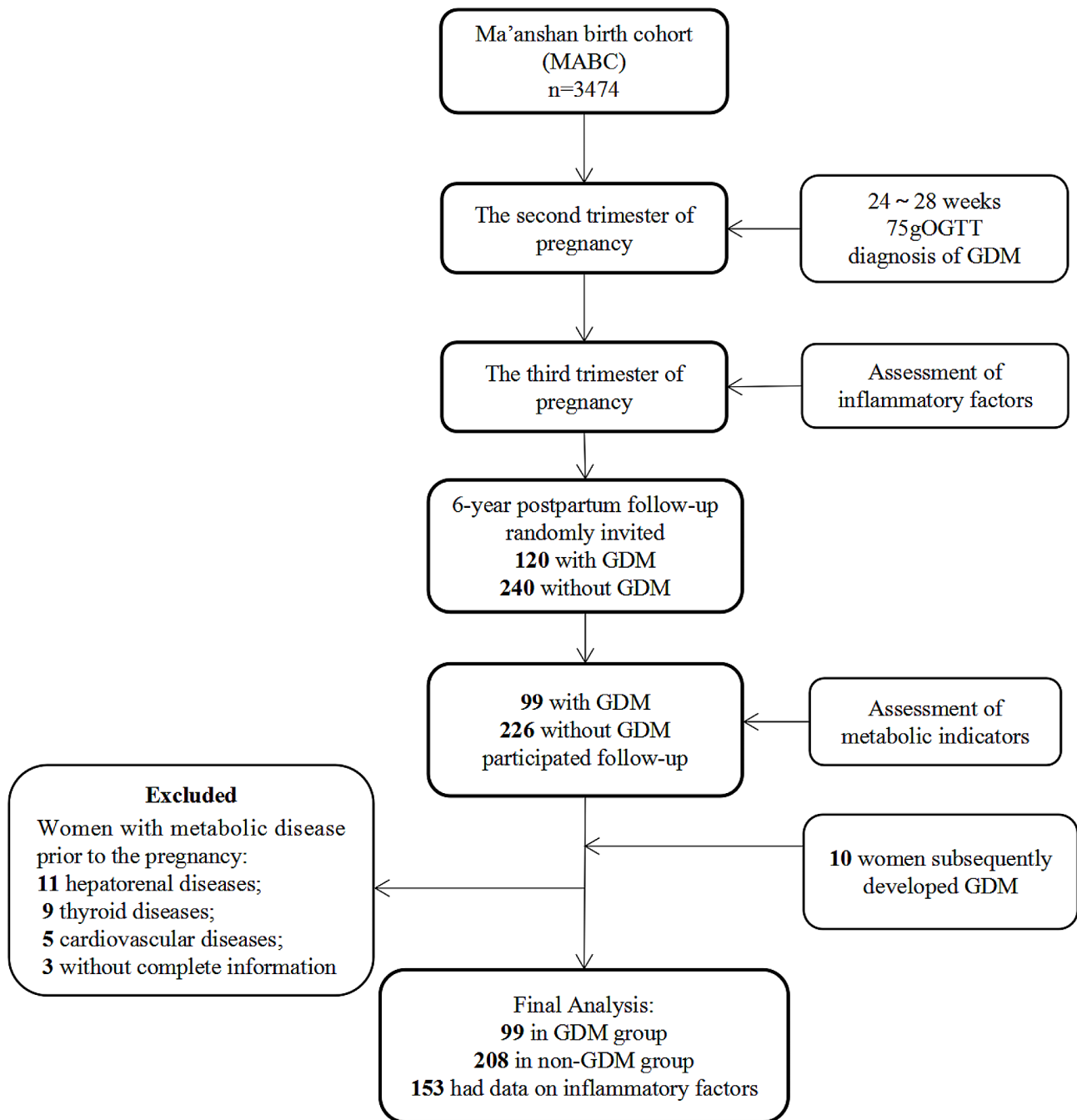


Fig. 1 The flowchart of study

history and 6-year postpartum FPG ($\beta=0.40$, 95% CI: 0.18 to 0.62, $P_{FDR}<0.001$), HbA1c ($\beta=0.22$, 95% CI: 0.09 to 0.34, $P_{FDR} = 0.009$), TyG ($\beta=0.22$, 95% CI: 0.07 to 0.37, $P_{FDR} = 0.024$) remained significant. Still, the association between GDM history and ApoA ($\beta=0.06$, 95% CI: 0.01 to 0.12, $P_{FDR} = 0.090$), SCR ($\beta=2.43$, 95% CI: 0.02 to 4.85, $P_{FDR} = 0.144$), siMS ($\beta=0.20$, 95% CI: 0.01 to 0.40, $P_{FDR} = 0.144$) only reached nominal significance level.

Table 3 shows the associations between GDM history and metabolic abnormalities at 6 years postpartum.

Adjusted model 1 revealed that the association between GDM history and FPG abnormality ($RR=6.95$, 95% CI: 1.34 to 29.48, $P_{FDR} = 0.077$), hypo-HDLemia ($RR=6.58$, 95% CI: 1.52 to 20.07, $P_{FDR} = 0.077$) only reached nominal significance level. Model 2 also showed that the association between GDM history and FPG abnormality ($RR=7.68$, 95% CI: 1.33 to 34.25, $P_{FDR} = 0.081$), MetS ($RR=4.46$, 95% CI: 1.01 to 15.21, $P_{FDR} = 0.112$), hypo-HDLemia ($RR=5.94$, 95% CI: 1.37 to 18.71, $P_{FDR} = 0.081$) only reached nominal significance.

Table 1 Comparison of 6-year postpartum characteristics between the GDM and Non-GDM groups

| Characteristics | Total sample (n = 307) | Non-GDM (n = 208) | GDM (n = 99) | P |
|---|---------------------------|----------------------|-----------------|---------|
| Age (years), mean (SD) | 35.82 (4.11) | 35.15 (3.88) | 37.22 (4.27) | < 0.001 |
| Pre-pregnancy BMI, mean (SD) | 21.04 (3.19) | 20.52 (2.89) | 22.14 (3.52) | < 0.001 |
| Current BMI, mean (SD) | 23.38 (3.73) | 22.77 (3.49) | 24.63 (4.02) | < 0.001 |
| Gravidity, n (%) | | | | 0.718 |
| 1 | 95 (30.9) | 63 (30.3) | 32 (32.3) | |
| ≥ 2 | 212 (69.1) | 145 (69.7) | 67 (67.7) | |
| Parity, n (%) | | | | 0.216 |
| 1 | 207 (67.4) | 145 (69.7) | 62 (62.6) | |
| ≥ 2 | 100 (32.6) | 63 (30.3) | 37 (37.4) | |
| Marital status, n (%) | | | | 0.141 |
| Married | 293 (95.4) | 196 (94.2) | 97 (98.0) | |
| Unmarried or others | 14 (4.6) | 12 (5.8) | 2 (2.0) | |
| Income (10k CNY/year), n (%) | | | | 0.553 |
| < 5 | 45 (14.7) | 31 (14.9) | 14 (14.1) | |
| 5 ~ 9.99 | 118 (38.4) | 76 (36.5) | 42 (42.4) | |
| 10 ~ 19.99 | 97 (31.6) | 65 (31.3) | 32 (32.3) | |
| 20 ~ 29.99 | 27 (8.8) | 22 (10.6) | 5 (5.1) | |
| ≥ 30 | 20 (6.5) | 14 (6.7) | 6 (6.1) | |
| Education, n (%) | | | | 0.628 |
| Middle school / below | 42 (13.7) | 26 (12.5) | 16 (16.2) | |
| High school | 110 (35.8) | 74 (35.6) | 36 (36.4) | |
| Junior college / above | 155 (50.5) | 108 (51.9) | 47 (47.4) | |
| Employment situation, n (%) | | | | 0.588 |
| Unemployed | 108 (35.2) | 70 (33.7) | 38 (38.4) | |
| Mental labor | 165 (53.7) | 116 (55.8) | 49 (49.5) | |
| Manual labor | 34 (11.1) | 22 (10.6) | 12 (12.1) | |
| Abnormal childbearing history, n (%) | | | | 0.475 |
| Yes | 38 (12.4) | 24 (11.5) | 14 (14.1) | |
| No | 269 (87.6) | 184 (99.5) | 85 (85.9) | |
| DM family history, n (%) ^a | | | | < 0.001 |
| Yes | 102 (36.4) | 57 (29.4) | 45 (52.3) | |
| No | 178 (63.6) | 137 (70.6) | 41 (47.7) | |
| CVD family history, n (%) ^b | | | | 0.183 |
| Yes | 81 (30.9) | 52 (28.4) | 29 (36.7) | |
| No | 181 (69.1) | 131 (71.6) | 50 (63.3) | |
| Drinking history, n (%) | | | | 0.328 |
| Yes | 92 (30.0) | 66 (31.7) | 26 (28.3) | |
| No | 215 (70.0) | 142 (68.3) | 73 (73.7) | |
| Smoking history, n (%) | | | | 0.624 |
| Yes | 13 (4.2) | 8 (3.8) | 5 (5.1) | |
| No | 294 (95.8) | 200 (96.2) | 94 (94.9) | |
| Classification of physical activity, n (%) ^c | | | | 0.667 |
| Low | 56 (18.5) | 37 (18.0) | 19 (19.6) | |
| Moderate | 117 (38.6) | 77 (37.4) | 40 (41.2) | |
| High | 130 (42.9) | 92 (44.7) | 38 (39.2) | |
| Classification of sleep quality, n (%) | | | | 0.137 |
| Excellent | 178 (58.0) | 127 (61.1) | 51 (51.5) | |
| Average | 119 (38.8) | 73 (35.1) | 46 (46.5) | |
| Poor | 10 (3.3) | 8 (3.8) | 2 (2.0) | |
| Red meat intake (grams/day), mean (SD) | 75.52 (103.23) | 64.76 (52.15) | 98.14(163.61) | 0.050 |

^a: 27 cases with unclear DM family history were treated as missing values;

^b: 45 cases with unclear CVD family history were treated as missing values.

^c: 6 cases with unclear physical activity were treated as missing values.

Table 2 Association between GDM history and 6-year postpartum metabolic indicators

| Metabolic indicators | Non-GDM (n = 208) | GDM (n = 99) | Model 1 ^a | | | Model 2 ^b | | |
|----------------------|----------------------|-----------------|-----------------------|-------------------------|------------------|------------------------|-------------------------|------------------|
| | | | β (95%CI) | $P_{\text{unadjusted}}$ | P_{FDR} | β (95%CI) | $P_{\text{unadjusted}}$ | P_{FDR} |
| FPG (mmol/L) | 4.69 (0.73) | 5.40 (1.52) | 0.39 (0.18 to 0.61) | <0.001 | <0.001 | 0.40 (0.18 to 0.62) | <0.001 | <0.001 |
| TC (mmol/L) | 4.27 (0.88) | 4.52 (0.78) | 0.10 (-0.15 to 0.34) | 0.430 | 0.595 | 0.12 (-0.13 to 0.37) | 0.356 | 0.534 |
| TG (mmol/L) | 0.97 (0.54) | 1.34 (0.98) | 0.22 (0.02 to 0.43) | 0.035 | 0.110 | 0.20 (-0.01 to 0.41) | 0.068 | 0.175 |
| HDL (mmol/L) | 1.49 (0.30) | 1.42 (0.33) | -0.02 (-0.10 to 0.07) | 0.710 | 0.887 | -0.01 (-0.09 to 0.08) | 0.864 | 0.901 |
| LDL (mmol/L) | 2.52 (0.80) | 2.71 (0.70) | -0.01 (-0.23 to 0.21) | 0.959 | 0.959 | 0.01 (-0.21 to 0.24) | 0.901 | 0.901 |
| HbA1c (%) | 5.26 (0.43) | 5.68 (0.87) | 0.22(0.10 to 0.34) | <0.001 | <0.001 | 0.22 (0.09 to 0.34) | 0.001 | 0.009 |
| HbF (%) | 0.41 (0.24) | 0.46 (0.25) | 0.07(0.00 to 0.14) | 0.049 | 0.110 | 0.06 (-0.01 to 0.13) | 0.082 | 0.182 |
| RI (μ U/mL) | 10.17 (5.86) | 12.91 (7.75) | 1.81(0.05 to 3.57) | 0.044 | 0.110 | 1.53 (-0.28 to 3.34) | 0.098 | 0.182 |
| TP (g/L) | 72.85 (3.76) | 73.75 (3.89) | 0.68(-0.35 to 1.72) | 0.195 | 0.319 | 0.55 (-0.51 to 1.61) | 0.304 | 0.497 |
| ALB (g/L) | 46.70 (2.35) | 46.68 (2.26) | 0.11(-0.54 to 0.77) | 0.739 | 0.887 | 0.34 (-0.43 to 0.91) | 0.484 | 0.622 |
| ApoA (g/L) | 1.12 (0.19) | 1.14 (0.21) | 0.05(0.00 to 0.10) | 0.048 | 0.110 | 0.06 (0.01 to 0.12) | 0.020 | 0.090 |
| ApoB (g/L) | 0.71 (0.17) | 0.77 (0.16) | 0.01(-0.04 to 0.05) | 0.820 | 0.923 | 0.01 (-0.04 to 0.06) | 0.759 | 0.901 |
| BUN (μ mol/L) | 4.59 (1.05) | 4.60 (1.10) | 0.02(-0.28 to 0.32) | 0.887 | 0.939 | 0.02 (-0.29 to 0.33) | 0.890 | 0.901 |
| SCR (μ mol/L) | 56.97 (7.85) | 59.08 (9.36) | 2.00(-0.33 to 4.34) | 0.093 | 0.167 | 2.43 (0.02 to 4.85) | 0.048 | 0.144 |
| UA (μ mol/L) | 270.70 (67.75) | 292.53 (74.79) | 19.07(-0.83 to 38.98) | 0.060 | 0.120 | 16.89 (-3.29 to 37.06) | 0.101 | 0.182 |
| CYS (mg/L) | 0.71 (0.12) | 0.71 (0.13) | -0.02(-0.05 to 0.01) | 0.257 | 0.386 | -0.01 (-0.05 to 0.02) | 0.404 | 0.559 |
| siMS | 1.98 (0.65) | 2.46 (0.93) | 0.23 (0.03 to 0.42) | 0.023 | 0.104 | 0.20 (0.01 to 0.40) | 0.045 | 0.144 |
| TyG | 8.08 (0.52) | 8.47 (0.62) | 0.23(0.08 to 0.38) | 0.002 | 0.012 | 0.22 (0.07 to 0.37) | 0.004 | 0.024 |

Continuous variables are expressed as mean (standard deviation),

^a:model 1 adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history;

^b:Model 2 adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history, sleeping quality, physical activity, red meat consumption.

Table 3 Associations between GDM history and 6-year postpartum metabolic abnormalities

| Metabolic abnormalities | Non-GDM (n = 208) | GDM (n = 99) | Model 1 ^a | | | Model 2 ^b | | |
|-------------------------|----------------------|-----------------|------------------------|-------------------------|------------------|------------------------|-------------------------|------------------|
| | | | RR (95%CI) | $P_{\text{unadjusted}}$ | P_{FDR} | RR (95%CI) | $P_{\text{unadjusted}}$ | P_{FDR} |
| Classification of FPG | | | | 0.022 | 0.077 | | 0.023 | 0.081 |
| Normal | 206 (99.0) | 85 (85.9) | 1.00 | | | 1.00 | | |
| abnormal | 2 (1.0) | 14 (14.1) | 6.95 (1.34 to 29.48) | | | 7.68 (1.33 to 34.25) | | |
| Classification of HbA1c | | | | 0.100 | 0.175 | | 0.235 | 0.274 |
| Normal | 207 (99.5) | 93 (93.9) | 1.00 | | | 1.00 | | |
| abnormal | 1 (0.5) | 6 (6.1) | 16.93 (0.57 to 153.93) | | | 95.06 (0.04 to 207.95) | | |
| MetS | | | | 0.076 | 0.175 | | 0.048 | 0.112 |
| No | 203 (97.6) | 85 (85.9) | 1.00 | | | 1.00 | | |
| Yes | 5 (2.4) | 14 (14.1) | 3.60 (0.87 to 12.29) | | | 4.46 (1.01 to 15.21) | | |
| Hypercholesterolemia | | | | 0.304 | 0.355 | | 0.210 | 0.274 |
| No | 189 (90.9) | 81 (81.8) | 1.00 | | | 1.00 | | |
| Yes | 19 (9.1) | 18 (18.2) | 1.48 (0.69 to 2.93) | | | 1.63 (0.75 to 3.22) | | |
| Hypertriglyceridemia | | | | 0.257 | 0.355 | | 0.230 | 0.274 |
| No | 190 (91.3) | 77 (77.8) | 1.00 | | | 1.00 | | |
| Yes | 18 (8.7) | 22 (22.2) | 1.55 (0.72 to 3.10) | | | 1.60 (0.74 to 3.20) | | |
| Hypo-HDLemia | | | | 0.013 | 0.077 | | 0.019 | 0.081 |
| No | 203 (97.6) | 90 (90.9) | 1.00 | | | 1.00 | | |
| Yes | 5 (2.4) | 9 (9.1) | 6.58 (1.52 to 20.07) | | | 5.94 (1.37 to 18.71) | | |
| Hyper-LDLemia | | | | 0.806 | 0.806 | | 0.935 | 0.935 |
| No | 192 (92.3) | 86 (86.9) | 1.00 | | | 1.00 | | |
| Yes | 16 (7.7) | 13 (13.1) | 0.89 (0.34 to 2.17) | | | 0.96 (0.37 to 2.36) | | |

Categorical variables are expressed as number of cases (ratio),

^a:model 1 adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history;

^b:Model 2 adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history, sleeping quality, physical activity, red meat consumption.

Of the 307 participants included in the analysis, 153 had data on inflammatory factors in the third trimester of pregnancy, and 39 of these had a prior history of GDM. As shown in Table 4, after adjusting for age, pre-pregnant BMI, education, income, parity, DM family history, and CVD family history, a significant inverse association was observed between GDM and the third-trimester level of IL-17 A ($\beta = -0.58$, 95% CI: -0.99 to -0.18, $P_{FDR} = 0.035$) and an inverse association between GDM and IFN- γ ($\beta = -0.46$, 95% CI: -0.85 to -0.07, $P_{FDR} = 0.07$) was observed, but the corrected P value only reached a nominal significance level.

Table 5 shows the association between inflammatory factors in the third trimester and metabolic indicators at 6 years postpartum. No statistically significant association was found between any of the inflammatory factors and 6-year postpartum metabolic indicators.

Based on the above results, since GDM was significantly associated with 6-year postpartum FPG, HbA1c, and TyG, we only presented the results of the mediating and moderating effect analysis of the third-trimester inflammatory factors in linking these associations in eTable 1 and eTable 2 (Supplement). Still, neither of the seven inflammatory factors was observed to have any mediating or moderating effect.

Discussion

Our study found that prior GDM history was significantly associated with 6-year postpartum metabolic indicators FPG, HbA1c, and TyG, indicating that GDM history could influence women's glucose and lipid metabolism in early postpartum, emphasizing the importance of surveillance of those indicators. However, there was no significant effect of the third-trimester inflammatory factors in mediating or moderating these associations, suggesting novel mechanisms should be explored to understand how GDM history influences cardiovascular health.

Consistent with previous findings [15, 39–43], our study revealed that a prior history of GDM was associated with elevated levels of FPG, HbA1c, and the

composite index TyG at 6 years postpartum. Regarding postpartum lipid metabolism indicators, previous studies and our study exhibited mixed results [44–48], with some finding positive associations [44–46] and others null associations [47, 48]. Explanations for the differences might firstly be attributed to the sample size, with small sample sizes in studies from Hungary and Natong [44, 46], and larger in studies from Iran and Louisiana [47, 48]. Secondly, the mentioned studies [44, 46] differed in the time point of follow-up, with some even having obvious between-group differences. For example, in the study of Hungary [44], the GDM and control groups were followed at (3.5±0.6) and (8.2±5.1) years ($P < 0.001$), respectively. The women in the study of Nantong [46] were followed at 1 year postpartum, however they were followed at over 7 years postpartum in Iranian and Louisiana studies [47, 48], and in our study were at over 6 years postpartum. Besides, both Hungary and Nantong studies missed important potential confounders such as sleep, physical activity, and dietary intake, which have been shown to have influences on lipid metabolism and risk of CVD [29, 49, 50]. Moreover, different GDM diagnostic criteria applied in different studies might be another explanation. Therefore, based on the existing studies, the association between GDM history and postpartum lipid metabolism could not be determined. Future studies with larger sample sizes, longer follow-up periods, and more comprehensive adjustments for confounding variables were needed.

Metabolic indicators of liver and kidney functions, which were influenced by endocrine disorders and could reflect the nutrition and protein metabolism, could be used to reflect the pathophysiological process of CVD [19]. Studies in the general population have shown that decreased ALB [17], increased UA [18] and BUN [19], which are indicators reflecting kidney function, were associated with an increased risk of CVD. Two studies [51, 52] from Poland and China showed among women with prior GDM, the levels of UA were positively associated with the risk of T2DM and prediabetes, which is also

Table 4 Association between GDM history and the third-trimester inflammatory factors

| Inflammatory factors | Non-GDM (n = 114) | GDM (n = 39) | Model 1 ^a | | | Model 2 ^b | | |
|----------------------|---------------------|---------------------|------------------------|------------------|-----------|------------------------|------------------|--------------|
| | | | β (95% CI) | $P_{unadjusted}$ | P_{FDR} | β (95% CI) | $P_{unadjusted}$ | P_{FDR} |
| IFN- γ | 6.76 (4.29, 11.77) | 4.99 (3.47, 9.35) | -0.33 (-0.66 to 0.00) | 0.050 | 0.175 | -0.46 (-0.85 to -0.07) | 0.020 | 0.07 |
| IL-1B | 1.07 (0.78, 1.56) | 0.91 (0.67, 1.67) | -0.13 (-0.39 to 0.14) | 0.340 | 0.567 | -0.23 (-0.54 to 0.08) | 0.137 | 0.243 |
| IL-6 | 3.06 (2.29, 4.93) | 2.93 (1.65, 6.67) | 0.18 (-0.25 to 0.60) | 0.405 | 0.567 | 0.16 (-0.35 to 0.67) | 0.530 | 0.618 |
| IL-10 | 12.24 (8.43, 16.66) | 14.24 (7.25, 20.14) | -0.03 (-0.37 to 0.31) | 0.867 | 0.867 | -0.23 (-0.65 to 0.19) | 0.273 | 0.382 |
| IL-12 | 2.47 (1.75, 4.26) | 1.98 (1.42, 3.25) | -0.22 (-0.54 to 0.10) | 0.182 | 0.425 | -0.28 (-0.66 to 0.09) | 0.139 | 0.243 |
| IL-17 A | 8.29 (4.74, 14.09) | 5.73 (3.86, 9.04) | -0.39 (-0.74 to -0.05) | 0.027 | 0.175 | -0.58 (-0.99 to -0.18) | 0.005 | 0.035 |
| TNF- α | 5.22 (3.98, 8.49) | 6.00 (3.65, 10.10) | 0.06 (-0.24 to 0.36) | 0.700 | 0.817 | 0.03 (-0.33 to 0.39) | 0.866 | 0.866 |

Concentration of inflammatory factors are expressed as median (interquartile range);

^a:model 1 was unadjusted;

^b:Model 2 adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history.

Table 5 Association between third-trimester inflammatory factors and 6-year postpartum metabolic indicators

| Metabolic indicators | β (95% CI) | IFN- γ | IL-1B | IL-6 | IL-10 | IL-12 | IL-17 A | TNF- α |
|----------------------|-----------------------|------------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------|---------------|
| FPG | 0.09 (-0.01 to 0.18) | 0.00 (-0.12 to 0.12) | -0.01 (-0.08 to 0.06) | 0.07 (-0.02 to 0.16) | 0.02 (-0.08 to 0.11) | 0.06 (-0.03 to 0.14) | 0.04 (-0.07 to 0.14) | |
| TC | 0.01 (-0.17 to 0.19) | 0.07 (-0.16 to 0.29) | 0.08 (-0.06 to 0.22) | 0.00 (-0.17 to 0.17) | 0.01 (-0.17 to 0.19) | 0.02 (-0.15 to 0.18) | 0.04 (-0.15 to 0.24) | |
| TG | 0.06 (-0.08 to 0.21) | 0.11 (-0.08 to 0.30) | 0.04 (-0.07 to 0.16) | 0.12 (-0.02 to 0.26) | 0.09 (-0.07 to 0.24) | 0.10 (-0.04 to 0.24) | 0.08 (-0.09 to 0.24) | |
| HDL | 0.01 (-0.04 to 0.06) | 0.01 (-0.05 to 0.08) | 0.00 (-0.04 to 0.04) | 0.05 (0.00 to 0.09) | 0.00 (-0.05 to 0.06) | -0.01 (-0.06 to 0.04) | -0.02 (-0.08 to 0.03) | |
| LDL | -0.02 (-0.18 to 0.15) | 0.01 (-0.20 to 0.21) | 0.03 (-0.10 to 0.16) | -0.08 (-0.23 to 0.07) | -0.02 (-0.19 to 0.15) | -0.01 (-0.16 to 0.14) | 0.02 (-0.16 to 0.20) | |
| HbA1c | -0.02 (-0.06 to 0.03) | -0.04 (-0.10 to 0.02) | -0.01 (-0.05 to 0.02) | 0.01 (-0.04 to 0.05) | -0.03 (-0.08 to 0.01) | -0.02 (-0.07 to 0.02) | -0.02 (-0.07 to 0.03) | |
| HbF | 0.00 (-0.05 to 0.05) | -0.02 (-0.08 to 0.04) | 0.00 (-0.03 to 0.04) | 0.01 (-0.04 to 0.05) | 0.00 (-0.05 to 0.05) | 0.00 (-0.05 to 0.05) | 0.00 (-0.06 to 0.05) | |
| RI | 0.47 (-0.67 to 1.61) | -0.17 (-1.62 to 1.28) | -0.07 (-0.97 to 0.82) | 0.29 (-0.79 to 1.37) | 0.73 (-0.45 to 1.91) | 0.84 (-0.24 to 1.91) | 1.24 (0.00 to 2.49) | |
| TP | 0.43 (-0.21 to 1.06) | 0.38 (-1.18 to 0.43) | -0.28 (-0.77 to 0.22) | -0.49 (-1.09 to 0.11) | 0.21 (-0.45 to 0.87) | -0.08 (-0.69 to 0.52) | 0.53 (-0.17 to 1.23) | |
| ALB | 0.34 (-0.04 to 0.73) | 0.12 (-0.37 to 0.61) | 0.19 (-0.11 to 0.49) | -0.13 (-0.49 to 0.24) | 0.17 (-0.24 to 0.57) | 0.14 (-0.23 to 0.51) | 0.37 (-0.05 to 0.80) | |
| ApoA | 0.02 (-0.02 to 0.05) | 0.00 (-0.04 to 0.05) | 0.00 (-0.02 to 0.03) | 0.03 (0.00 to 0.06) | 0.01 (-0.02 to 0.05) | 0.00 (-0.04 to 0.03) | 0.00 (-0.04 to 0.03) | |
| ApoB | 0.00 (-0.04 to 0.03) | -0.01 (-0.05 to 0.04) | 0.00 (-0.02 to 0.03) | -0.01 (-0.05 to 0.02) | 0.00 (-0.04 to 0.04) | 0.00 (-0.04 to 0.03) | 0.01 (-0.03 to 0.05) | |
| BUN | 0.02 (-0.17 to 0.21) | -0.09 (-0.33 to 0.15) | 0.01 (-0.14 to 0.16) | -0.02 (-0.20 to 0.16) | 0.01 (-0.19 to 0.20) | -0.03 (-0.21 to 0.15) | -0.11 (-0.32 to 0.10) | |
| Scr | 0.41 (-1.00 to 1.83) | 0.62 (-1.17 to 2.41) | -0.06 (-1.16 to 1.05) | -0.06 (-1.40 to 1.28) | 0.09 (-1.38 to 1.56) | 0.36 (-0.98 to 1.70) | 0.41 (-1.16 to 1.97) | |
| UA | 3.65 (-9.34 to 16.63) | 2.75 (-13.71 to 19.21) | 4.31 (-5.80 to 14.41) | 5.50 (-6.74 to 17.74) | 3.54 (-9.95 to 17.04) | 2.38 (-9.93 to 14.69) | 12.62 (-1.61 to 26.85) | |
| Cys | -0.02 (-0.04 to 0.00) | -0.01 (-0.03 to 0.02) | -0.01 (-0.03 to 0.01) | -0.01 (-0.03 to 0.01) | -0.02 (-0.04 to 0.00) | 0.00 (-0.02 to 0.02) | -0.01 (-0.03 to 0.01) | |
| sIMS | 0.05 (-0.08 to 0.18) | 0.05 (-0.11 to 0.21) | 0.02 (-0.08 to 0.12) | 0.06 (-0.06 to 0.18) | 0.07 (-0.07 to 0.20) | 0.09 (-0.03 to 0.20) | 0.08 (-0.06 to 0.22) | |
| TyG | 0.06 (-0.04 to 0.15) | 0.02 (-0.10 to 0.13) | 0.00 (-0.07 to 0.08) | 0.07 (-0.02 to 0.16) | 0.05 (-0.04 to 0.15) | 0.06 (-0.03 to 0.15) | 0.06 (-0.04 to 0.17) | |

The model adjusted for age, pre-pregnant BMI, education, income, parity, DM family history, CVD family history, sleeping quality, physical activity, red meat consumption.

an important risk factor for CVD. Our study has shown that the original P value for SCR ($P=0.048$), an indicator of kidney function, was significant. Even though the corrected P values of SCR ($P=0.048$, $P_{FDR} = 0.144$) and ApoA ($P=0.020$, $P_{FDR} = 0.09$) in our study were not significant after multiple testing corrections, the between-group differences in the levels of SCR and ApoA at 6 years postpartum still preliminarily hints that GDM might be associated with liver and kidney metabolic indicators postpartum, however the exact relationship remains to be further investigated.

To our surprise, our study found significantly lower levels of third-trimester IL-17 A in the GDM group than in the non-GDM group. There were no previous studies exploring the relationship between GDM and third-trimester IL-17 A, but a few descriptive studies have reported higher levels of other third-trimester inflammatory factors in the GDM groups [53, 54]. For example, a study in Hohhot, China, showed that IL-6 and IL-8 during pregnancy were higher in the GDM group ($n=60$) compared with the non-GDM group ($n=60$) [53], and an Indian study also showed differences in IL-6 and TNF- α in late pregnancy between the GDM group ($n=35$) and the control group ($n=30$) [54]. However, another study reported an insignificant association between GDM and third-trimester inflammatory factors, for example, a meta-analysis found TNF- α was slightly higher in the GDM group than in the control group but without significance [55]. Thus, due to the varied methods of measuring inflammatory factors and the small sample size of all existing studies, the incidence of GDM could impact the level of maternal inflammatory factors still needs further investigation.

Although pro-inflammatory factors such as TNF- α , IL-1, and IL-6 were found to contribute to the development of atherosclerosis by affecting vascular endothelial cell function, oxidized LDL, heat shock protein and HDL levels, etc., leading to the development of atherosclerosis [56], and were shown to participate in the glucose metabolism by involving in the insulin signaling pathways [57–59]. No association was found between any of the seven third-trimester inflammatory factors and metabolic indicators 6 years postpartum in our study. To our knowledge, no study has attempted to explore the association between maternal inflammatory factors and postpartum metabolic indicators in humans. Only animal experiments indicated that postnatal glucose metabolism alterations were associated with an inflammatory state during pregnancy in rats [60]. Accordingly, there is no moderating or mediating effect of the third-trimester inflammatory factors in any association between GDM and FPG, HbA1c, or TyG at 6 years postpartum either.

Our study has several strengths. First, a set of comprehensive metabolic indicators was examined, particularly

for liver and renal functions, and two integrated metabolic indices, TyG and siMS score. Second, a range of lifestyle factors such as sleep, physical activity, and dietary intake were adjusted for, increasing the reliability of our results. More importantly, we innovatively explored the role of maternal inflammatory factors in these associations. However, some limitations should also be acknowledged. First, only seven third-trimester inflammatory factors were assayed, other important inflammatory indicators, such as IL-4 and C-reactive protein, were not included. Second, the long-term storage of serum samples might affect the accuracy of inflammatory factors assays, but all samples were stored under the same storage conditions and underwent a similar number of freeze-thaw cycles before being tested, the variability between samples was not altered. Third, the small sample size might affect the statistical power in detecting differences in this study. Fourth, we did not collect blood glucose indicators to objectively reflect glycemic control during late pregnancy, despite we have investigated treatments for GDM during pregnancy, and all participants reported only controlled dietary therapies. Fifth, we did not perform the OGTT to diagnose whether participants had developed T2DM during follow-up.

Conclusion

A prior history of GDM was significantly associated with elevated FPG, HbA1c, and TyG at 6 years postpartum, whereas third-trimester inflammatory factors had no role in mediating or moderating these associations. Our findings remain to be further validated in a prospective study with a large sample size.

Abbreviations

| | |
|-------|---|
| GDM | Gestational diabetes mellitus |
| MABC | Ma'anshan birth cohort |
| CVD | Cardiovascular disease |
| PSQI | The Pittsburgh sleep quality index |
| IPAQ | The international physical activity questionnaire |
| FFQ | The food frequency questionnaire |
| WC | Waists circumference |
| OGTT | Oral glucose tolerance test |
| FPG | Fasting plasma glucose |
| HbA1c | glycosylated hemoglobin |
| HbF | hemoglobin F |
| RI | Insulin |
| TG | Triglycerides |
| TC | Total cholesterol |
| HDL | High-density lipoprotein |
| LDL | Low-density lipoprotein |
| TP | Total protein |
| ALB | Albumin |
| ApoA | Apolipoprotein A |
| ApoB | Apolipoprotein B |
| UA | Uric acid |
| BUN | Blood urea nitrogen |
| SCR | Serum creatinine |
| CYS | Cystatin |
| MetS | Metabolic syndrome |
| TyG | triglyceride-glucose index |
| siMS | Quantifying metabolic syndrome score |

LOD The limit of detection
CI Confidence interval
RR Relative risk

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12884-024-06563-3>.

Supplementary Material 1

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Author contributions

FT, BZ conceived and designed the study. XY, WQ, KG, YC conducted the study and implemented the data collection. XY performed the analysis and drafted the manuscript. BZ made critical contributions to the interpretation of the data and substantively revised the manuscript. All authors read and approved the final manuscript and agreed both to be personally accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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Data availability

Data are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study obtained ethics approval from the ethics committee of Anhui Medical University (20131195, 20210732). Written informed consent was obtained from all participating women.

Consent for publication

All authors approved the final manuscript and the submission to this journal.

Competing interests

The authors declare no competing interests.

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References

1. Saravanan P, Diabetes in Pregnancy Working Group; Maternal Medicine Clinical Study Group. Royal College of Obstetricians and gynaecologists, UK.

- Gestational diabetes: opportunities for improving maternal and child health. *Lancet Diabetes Endocrinol.* 2020;8(9):793–800. [https://doi.org/10.1016/S2213-8587\(20\)30161-3](https://doi.org/10.1016/S2213-8587(20)30161-3).
2. McIntyre HD, Catalano P, Zhang C, et al. Gestational diabetes mellitus. *Nat Rev Dis Primers.* 2019;5(1):47. <https://doi.org/10.1038/s41572-019-0098-8>.
3. Metzger BE, Coustan DR, Trimble ER. Hyperglycemia and adverse pregnancy outcomes. *Clin Chem.* 2019;65(7):937–8. <https://doi.org/10.1373/clinchem.2019.303990>.
4. Retnakaran R, Shah BR. Glucose screening in pregnancy and future risk of cardiovascular disease in women: a retrospective, population-based cohort study. *Lancet Diabetes Endocrinol.* 2019;7(5):378–84. [https://doi.org/10.1016/S2213-8587\(19\)30077-4](https://doi.org/10.1016/S2213-8587(19)30077-4).
5. Tobias DK, Stuart JJ, Li S, et al. Association of History of Gestational Diabetes with Long-Term Cardiovascular Disease Risk in a large prospective cohort of US women. *JAMA Intern Med.* 2017;177(12):1735–42. <https://doi.org/10.1001/jamainternmed.2017.2790>.
6. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 update: a Report from the American Heart Association. *Circulation.* 2017;135(10):e146–603. <https://doi.org/10.1161/CIR.0000000000000485>.
7. Zhao D, Liu J, Wang M, et al. Epidemiology of cardiovascular disease in China: current features and implications. *Nat Rev Cardiol.* 2019;16(4):203–12. <https://doi.org/10.1038/s41569-018-0119-4>.
8. Echouffo-Tcheugui JB, Chen H, Kalyani RR, et al. Glycemic markers and subclinical Cardiovascular Disease: the Jackson Heart Study. *Circ Cardiovasc Imaging.* 2019;12(3):e008641. <https://doi.org/10.1161/CIRCIMAGING.118.008641>.
9. Willeit P, Ridker PM, Nestel PJ, et al. Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. *Lancet.* 2018;392(10155):1311–20. [https://doi.org/10.1016/S0140-6736\(18\)31652-0](https://doi.org/10.1016/S0140-6736(18)31652-0).
10. Koide Y, Miyoshi T, Nishihara T, et al. The Association of Triglyceride to High-Density Lipoprotein Cholesterol Ratio with high-risk coronary plaque characteristics determined by CT angiography and its risk of Coronary Heart Disease. *J Cardiovasc Dev Dis.* 2022;9(10):329. <https://doi.org/10.3390/jcdd9100329>.
11. Yu H, Li Y, Tao L, et al. Trajectories of lipid Profile and Risk of Carotid atherosclerosis progression: a longitudinal cohort study. *Nutrients.* 2022;14(15):3243. <https://doi.org/10.3390/nu14153243>.
12. Tao LC, Xu JN, Wang TT, et al. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. *Cardiovasc Diabetol.* 2022;21(1):68. <https://doi.org/10.1186/s12933-022-01511-x>.
13. Jang YN, Lee JH, Moon JS, et al. Metabolic syndrome severity score for Predicting Cardiovascular events: a Nationwide Population-based study from Korea. *Diabetes Metab J.* 2021;45(4):569–77. <https://doi.org/10.4093/dmj.2020.0103>.
14. Pathirana MM, Lassi Z, Ali A, et al. Cardiovascular risk factors in women with previous gestational diabetes mellitus: a systematic review and meta-analysis. *Rev Endocr Metab Disord.* 2021;22(4):729–61. <https://doi.org/10.1007/s11154-020-09587-0>.
15. Banerjee M, Anderson SG, Malik RA, et al. Small artery function 2 years postpartum in women with altered glycaemic distributions in their preceding pregnancy. *Clin Sci (Lond).* 2012;122(2):53–61. <https://doi.org/10.1042/CS20110033>.
16. Mai C, Wang B, Wen J, et al. Lipoprotein-associated phospholipase A2 and AGEs are associated with cardiovascular risk factors in women with history of gestational diabetes mellitus. *Gynecol Endocrinol.* 2014;30(3):241–4. <https://doi.org/10.3109/09513590.2013.871522>.
17. Chen S, Chen L, Jiang H. Prognosis and risk factors of chronic kidney disease progression in patients with diabetic kidney disease and non-diabetic kidney disease: a prospective cohort CKD-ROUTE study. *Ren Fail.* 2022;44(1):1309–18. <https://doi.org/10.1080/0886022X.2022.2106872>.
18. Ndrepepa G. Uric acid and cardiovascular disease. *Clin Chim Acta.* 2018;484:150–63. <https://doi.org/10.1016/j.cca.2018.05.046>.
19. Lan Q, Zheng L, Zhou X, et al. The Value of Blood Urea Nitrogen in the prediction of risks of Cardiovascular Disease in an older Population. *Front Cardiovasc Med.* 2021;8:614117. <https://doi.org/10.3389/fcvm.2021.614117>.
20. Kramer CK, Campbell S, Retnakaran R. Gestational diabetes and the risk of cardiovascular disease in women: a systematic review and meta-analysis. *Diabetologia.* 2019;62(6):905–14. <https://doi.org/10.1007/s00125-019-4840-2>.
21. Samad F, Ruf W. Inflammation, obesity, and thrombosis. *Blood.* 2013;122(20):3415–22. <https://doi.org/10.1182/blood-2013-05-427708>.

22. Haybar H, Shokuhian M, Bagheri M, et al. Involvement of circulating inflammatory factors in prognosis and risk of cardiovascular disease. *J Mol Cell Cardiol.* 2019;132:110–9. <https://doi.org/10.1016/j.jmcc.2019.05.010>.
23. Liu W, Yin Y, Zhou Z, et al. OxLDL-induced IL-1 beta secretion promoting foam cells formation was mainly via CD36 mediated ROS production leading to NLRP3 inflammasome activation. *Inflamm Res.* 2014;63(1):33–43. <https://doi.org/10.1007/s00011-013-0667-3>.
24. Zhang C, Xu X, Potter BJ, et al. TNF- α contributes to endothelial dysfunction in ischemia/reperfusion injury. *Arterioscler Thromb Vasc Biol.* 2006;26(3):475–80. <https://doi.org/10.1161/01.ATV.0000201932.32678.7e>.
25. Moss JW, Ramji DP. Cytokines: roles in atherosclerosis disease progression and potential therapeutic targets. *Future Med Chem.* 2016;8(11):1317–30. <https://doi.org/10.4155/fmc-2016-0072>.
26. Gao H, Zhu YD, Xu YY, et al. Season-dependent concentrations of urinary phthalate metabolites among Chinese pregnant women: repeated measures analysis. *Environ Int.* 2017;104:110–7. <https://doi.org/10.1016/j.envint.2017.03.021>.
27. Tsai PS, Wang SY, Wang MY, et al. Psychometric evaluation of the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) in primary insomnia and control subjects. *Qual Life Res.* 2005;14(8):1943–52. <https://doi.org/10.1007/s11136-005-4346-x>.
28. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28(2):193–213. [https://doi.org/10.1016/0165-1781\(89\)90047-4](https://doi.org/10.1016/0165-1781(89)90047-4).
29. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35(8):1381–95. <https://doi.org/10.1249/01.MSS.0000078924.61453.FB>.
30. Zhong VW, Van Horn L, Greenland P, et al. Associations of processed meat, unprocessed Red Meat, Poultry, or Fish Intake With Incident Cardiovascular Disease and all-cause mortality. *JAMA Intern Med.* 2020;180(4):503–12. <https://doi.org/10.1001/jamainternmed.2019.6969>.
31. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2019. *Diabetes Care.* 2019;42(Suppl 1):S13–S28. <https://doi.org/10.2337/dc19-S002>.
32. Wang YF. The role of inflammation markers in the association between excessive gestational weight gain and social-emotional status in children: a birth cohort study. *Anhui Med Univ.* 2020. <https://doi.org/10.26921/d.cnki.ganyu.2020.000027>.
33. Chinese Diabetes Society. Guidelines for the prevention and control of type 2 diabetes in China (2017 Edition). *Chin J Practical Intern Med.* 2018;38(04):292–344. <https://doi.org/10.19538/j.nk2018040108>.
34. Zhu JR, Gao RL, Zhao SP, et al. Guidelines for the prevention and treatment of dyslipidemia in Chinese adults (2016 Edition). *Chin Circulation J.* 2016;31(10):937–53. <https://doi.org/10.3969/j.issn.1000-3614.2016.10.001>.
35. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord.* 2008;6(4):299–304. <https://doi.org/10.1089/met.2008.0034>.
36. Soldatovic I, Vukovic R, Culafic D, et al. siMS score: simple method for quantifying metabolic syndrome. *PLoS ONE.* 2016;11(1):e0146143. <https://doi.org/10.1371/journal.pone.0146143>.
37. Graham AM, Rasmussen JM, Rudolph MD, et al. Maternal systemic interleukin-6 during pregnancy is associated with newborn amygdala phenotypes and subsequent behavior at 2 years of age. *Biol Psychiatry.* 2018;83(2):109–19. <https://doi.org/10.1016/j.biopsych.2017.05.027>.
38. Viera AJ. Odds ratios and risk ratios: what's the difference and why does it matter? *South Med J.* 2008;101(7):730–4. <https://doi.org/10.1097/SMJ.0b013e31817a7ee4>.
39. Shen Y, Wang P, Wang L, et al. Gestational diabetes with diabetes and prediabetes risks: a large observational study. *Eur J Endocrinol.* 2018;179(1):51–8. <https://doi.org/10.1530/EJE-18-0130>.
40. Lekva T, Bollerslev J, Godang K, et al. β -cell dysfunction in women with previous gestational diabetes is associated with visceral adipose tissue distribution. *Eur J Endocrinol.* 2015;173(1):63–70. <https://doi.org/10.1530/EJE-15-0153>.
41. Hakkarainen H, Huopio H, Cederberg H, et al. The risk of metabolic syndrome in women with previous GDM in a long-term follow-up. *Gynecol Endocrinol.* 2016;32(11):920–5. <https://doi.org/10.1080/09513590.2016.1198764>.
42. Gunderson EP, Chiang V, Pletcher MJ, et al. History of gestational diabetes mellitus and future risk of atherosclerosis in mid-life: the coronary artery risk development in young adults study. *J Am Heart Assoc.* 2014;3(2):e000490. <https://doi.org/10.1161/JAHA.113.000490>.
43. Krishnaveni GV, Hill JC, Veena SR, et al. Gestational diabetes and the incidence of diabetes in the 5 years following the index pregnancy in South Indian women. *Diabetes Res Clin Pract.* 2007;78(3):398–404. <https://doi.org/10.1016/j.diabres.2007.06.002>.
44. Madarász E, Tamás G, Tabák AG, et al. Carbohydrate metabolism and cardiovascular risk factors 4 years after a pregnancy complicated by gestational diabetes. *Diabetes Res Clin Pract.* 2009;85(2):197–202. <https://doi.org/10.1016/j.diabres.2009.05.001>.
45. Stuebe AM, Mantzoros C, Kleinman K, et al. Gestational glucose tolerance and maternal metabolic profile at 3 years postpartum. *Obstet Gynecol.* 2011;118(5):1065–73. <https://doi.org/10.1097/AOG.0b013e3182325f5a>.
46. Wang YM, Zhao LH, Su JB, et al. Glycemic variability in normal glucose tolerance women with the previous gestational diabetes mellitus. *Diabetol Metab Syndr.* 2015;7:82. <https://doi.org/10.1186/s13098-015-0077-5>.
47. Minooee S, Ramezani Tehrani F, Rahmati M, et al. Dyslipidemia incidence and the trend of lipid parameters changes in women with history of gestational diabetes: a 15-year follow-up study. *Endocrine.* 2017;58(2):228–35. <https://doi.org/10.1007/s12020-017-1413-3>.
48. Shostrom DCV, Sun Y, Oleson JJ, et al. History of gestational diabetes Mellitus in Relation to Cardiovascular Disease and Cardiovascular Risk factors in US women. *Front Endocrinol (Lausanne).* 2017;8:144. <https://doi.org/10.3389/fendo.2017.00144>.
49. Javaheri S, Redline S. Insomnia and risk of Cardiovascular Disease. *Chest.* 2017;152(2):435–44. <https://doi.org/10.1016/j.chest.2017.01.026>.
50. Stamatakis E, Gale J, Bauman A, et al. Sitting time, physical activity, and risk of mortality in adults. *J Am Coll Cardiol.* 2019;73(16):2062–72. <https://doi.org/10.1016/j.jacc.2019.02.031>.
51. Molęda P, Fronczyk A, Safranow K, et al. Is uric acid a Missing Link between previous gestational diabetes Mellitus and the development of type 2 diabetes at a later time of life? *PLoS ONE.* 2016;11(5):e0154921. <https://doi.org/10.1371/journal.pone.0154921>.
52. Leng J, Wang L, Wang J, et al. Uric acid and diabetes risk among Chinese women with a history of gestational diabetes mellitus. *Diabetes Res Clin Pract.* 2017;134:72–9. <https://doi.org/10.1016/j.diabres.2017.09.015>.
53. Zhang J, Chi H, Xiao H, et al. Interleukin 6 (IL-6) and tumor necrosis factor α (TNF- α) single nucleotide polymorphisms (SNPs), inflammation and metabolism in gestational diabetes Mellitus in Inner Mongolia. *Med Sci Monit.* 2017;23:4149–57. <https://doi.org/10.12659/msm.903565>.
54. Banerjee S, Bhattacharjee R, Sur A, et al. A study of serum growth differentiation factor 15 in Indian women with and without gestational diabetes mellitus in the third trimester of pregnancy and its association with pro-inflammatory markers and glucose metabolism. *Diabetol Int.* 2020;12(3):254–9. <https://doi.org/10.1007/s13340-020-00478-y>.
55. Gomes CP, Torloni MR, Gueuvoghlian-Silva BY, et al. Cytokine levels in gestational diabetes mellitus: a systematic review of the literature. *Am J Reprod Immunol.* 2013;69(6):545–57. <https://doi.org/10.1111/aji.12088>.
56. Aghamohammadzadeh R, Unwin RD, Greenstein AS, et al. Effects of obesity on perivascular adipose tissue vasorelaxant function: nitric oxide, inflammation and elevated systemic blood pressure. *J Vasc Res.* 2015;52(5):299–305. <https://doi.org/10.1159/000443885>.
57. Wu H, Ballantyne CM. Metabolic inflammation and Insulin Resistance in obesity. *Circ Res.* 2020;126(11):1549–64. <https://doi.org/10.1161/CIRCRESAHA.119.315896>.
58. Akash MSH, Rehman K, Liaqat A. Tumor necrosis Factor-Alpha: role in development of insulin resistance and Pathogenesis of type 2 diabetes Mellitus. *J Cell Biochem.* 2018;119(1):105–10. <https://doi.org/10.1002/jcb.26174>.
59. Wali JA, Thomas HE, Sutherland AP. Linking obesity with type 2 diabetes: the role of T-bet. *Diabetes Metab Syndr Obes.* 2014;7:331–40. <https://doi.org/10.2147/DMSO.S51432>.
60. Ushida T, Macdonald-Goodfellow SK, Quadri A, et al. Persistence of risk factors associated with maternal cardiovascular disease following aberrant inflammation in rat pregnancy. *Biol Reprod.* 2017;97(1):143–52. <https://doi.org/10.1093/biolre/iox072>.

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