Lipids in Health and Disease

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Impact of maternal lipid profiles on offspring birth size in late pregnancy among women with and without gestational diabetes

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Abstract

Background Maternal glucose and lipid levels are known to influence fetal growth. However, data on how maternal lipid profiles affect birth size in women with gestational diabetes (GDM) compared with those without GDM are scarce.

Methods This retrospective study included 10,490 women with singleton pregnancies (2351 with GDM and 8139 without GDM) between December 2016 and July 2022. Maternal serum levels of total cholesterol (TC), triglycerides (TGs), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol were measured at 28–42 weeks of gestation. Maternal glucose levels were determined using the 2-h oral glucose tolerance test. The neonatal birth weight was obtained at delivery and standardized as the birth weight z score according to the INTERGROWTH-21st standards.

Results Compared with women without GDM, those with GDM presented increased mean TG levels and decreased levels of TC, HDL cholesterol, and LDL cholesterol. TG levels were positively associated with birth weight in both the GDM and non-GDM groups, whereas TC, HDL cholesterol, and LDL cholesterol levels were mildly negatively correlated with birth weight. In the GDM group, an increase of 1 mmol/L in maternal TGs correlated with a 28.4 g increase in birth weight (95% CI: 17.8 to 39.1), whereas increases of 1 mmol/L in TC (-19.2 g; 95% CI: -31.9 to -6.5), HDL cholesterol (-120.7 g; 95% CI: -164.8 to -76.6), and LDL cholesterol (-22.2 g; 95% CI: -40.4 to -4) were associated with a decrease in birth weight. Compared with women with GDM with TG levels ≤ the 10th percentile, those with TG levels ≥ the 90th percentile had increased risks of large-for-gestational-age offspring (adjusted OR: 3.09; 95% CI: 1.51–6.30) and macrosomia (adjusted OR: 4.04; 95% CI: 1.37–11.93); this risk was stronger than that in women without GDM.

Conclusions This study provides evidence of a significant association between maternal lipid levels during late pregnancy and offspring birth size. However, the observational nature of the study limits the ability to establish causal relationships regarding the direct impact of lipid levels on birth size. Additionally, the influence of maternal lipid profiles is disproportionately greater in women with GDM than in women without GDM.

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Introduction

Globally, the incidence of gestational diabetes mellitus (GDM) is increasing, leading to an increased risk of various pregnancy complications in affected women [1–3]. Recent clinical research has increasingly emphasized the associations among impaired glucose metabolism, abnormal lipid profiles, and adverse pregnancy outcomes [4]. According to a thorough meta-analysis, compared with women without GDM, those diagnosed with GDM exhibit notably increased serum levels of triglycerides (TGs), total cholesterol (TC), and low-density lipoprotein (LDL) cholesterol and decreased levels of high-density lipoprotein (HDL) cholesterol [5]. Additionally, various studies have indicated that maternal lipid levels can predict adverse birth outcomes, such as large for gestational age (LGA) and macrosomia [6, 7]. Increased maternal TG levels in early pregnancy are associated with increased birth weight and increased risks of LGA [8]. Changes in maternal lipid metabolism are frequently observed during pregnancy and are characterized by slight increases in lipids, particularly TGs, in early pregnancy and substantial increases in later pregnancy [9, 10]. However, there are no standardized guidelines for lipid levels during pregnancy. The intrauterine metabolic environment of maternal glucose and lipid profiles may have an interactive effect on fetal growth [11]. While several studies have explored the associations between lipid metabolism during GDM and non-GDM pregnancies and birth size [12–14], research in this area is limited, particularly in the Chinese population. Therefore, this study aimed to explore the correlation between maternal lipid levels during late pregnancy and newborn birth size, with a particular focus on the differences between women with and without GDM.

Methods

Study population

The data for this retrospective study were sourced from women who delivered at Guangdong Women and Children Hospital from December 2016 to July 2022. This hospital serves as the provincial maternal and child health surveillance center in Guangdong in southern China. Pregnant women who had received prenatal health care since the first trimester and underwent a 2-h oral glucose tolerance test (OGTT) at the hospital were included. The exclusion criteria included multiple pregnancies; stillbirth; type 1 or type 2 diabetes mellitus diagnosed before pregnancy; maternal chronic diseases, including chronic or gestational hypertension; chronic heart, liver or kidney diseases; fetal chromosomal abnormalities; fetal malformations; gestational age at birth < 24 weeks or > 42 weeks; and missing key medical data, such as lipid profiles during pregnancy and birth weight.

Data collection and measures

The data were extracted from the hospital information system. Information related to maternal age, parity, height, prepregnancy weight, weight at delivery, OGTT results, lipid levels, and pregnancy complications was collected from prenatal examination medical records. Data on gestational age at birth, birth weight, birth length, newborn sex, and delivery mode were collected from medical records.

Maternal 75-g OGTT tests were performed at 24–28 weeks of gestation. The glucose thresholds for the 75-g OGTT are as follows: fasting (0 h), 5.1 mmol/L; 1-hour postprandial, 10.0 mmol/L; and 2-hour postprandial, 8.5 mmol/L. The diagnostic criterion for GDM is any single value that is equal to or greater than the specified threshold [15]. To assess glycemic control in the GDM group, HbA1c data were collected in the third trimester.

TC, TG, HDL cholesterol, and LDL cholesterol levels in late pregnancy were measured at 28–42 weeks of gestation. In accordance with the manufacturer's instructions, the parameters were measured in fasting venous blood samples via the colorimetric method and analyzed via an automatic biochemical analyzer (Beckman AU5800, USA).

Outcome definitions

In accordance with the INTERGROWTH-21st standards, birth weight was standardized as a birth weight z score (BWZ) [16]. LGA was defined as a birth weight above the 90th percentile of sex-specific standards, whereas small for gestational age (SGA) was defined as a birth weight below the 10th percentile. Newborns with birth weights between the 10th and 90th percentiles are classified as appropriate for gestational age (AGA). A birth weight exceeding 4000 g is categorized as macrosomia.

Statistical analysis

Continuous variables are presented as the means ± standard deviations, whereas categorical variables are presented as numbers and percentages. To compare differences in continuous variables between GDM and non-GDM women, a t test was employed. For categorical variables, the chi-square test was used to assess differences. The relationships between variables were analyzed via bivariate correlation through Spearman's correlation test. Lipid levels were divided into ≤ 10th percentile, 10th–90th percentile, and ≥ 90th percentile. Linear regression was used to evaluate the associations between lipid levels and offspring birth weight in women with and without GDM. Additionally, the specific associations between different levels of TC, TGs, HDL cholesterol, and LDL cholesterol and the risks of developing LGA, SGA, or macrosomia were quantified with logistic regression models, and the corresponding odds ratios

(ORs) and their 95% confidence intervals (CIs) were calculated. The models were adjusted for maternal age, parity, prepregnancy BMI, and gestational age at birth, with the reference group for each factor defined as the ≤ 10th percentile group. Statistical analysis of the data was conducted with the SPSS software package (version 26, IBM Statistics, Chicago, IL, USA), with a significance level of $P < 0.05$.

Results

Among 10,490 women with singleton pregnancies, 2351 were diagnosed with GDM. Among these women with GDM, HbA1c values were available for 1958 women (with 393 missing); the distribution of HbA1c values is shown in Supplementary Fig. 1. A total of 77.4% of the participants met the HbA1c target of < 6% recommended by the American Diabetes Association, which represents ideal glycemic control for GDM patients. The maternal and neonatal characteristics of the women with GDM and without GDM are shown in Table 1. The average TG concentration was increased in women diagnosed with GDM compared with those without GDM, whereas women with GDM had relatively lower levels of TC, HDL cholesterol, and LDL cholesterol.

Figure 1 shows the correlations among maternal OGTT results and lipid profiles and offspring BWZ in women with GDM and without GDM. Positive correlations were observed between OGTT-0 h blood glucose levels and TG levels ($r = 0.17$ in the GDM group and $r = 0.13$ in the non-GDM group; both $P < 0.01$). OGTT-0 h blood glucose and TG levels were also positively correlated with BWZ in the GDM and non-GDM groups. TC, HDL cholesterol, and LDL cholesterol levels were weakly negatively correlated with BWZ.

In the GDM group, an increase of 1 mmol/L in maternal TG levels correlated with a 28.4 g increase in birth weight (95% CI: 17.8 to 39.1), whereas increases of 1 mmol/L in TC (-19.2 g; 95% CI: -31.9 to -6.5), HDL cholesterol (-120.7 g; 95% CI: -164.8 to -76.6), and LDL cholesterol (-22.2 g; 95% CI: -40.4 to -4) levels were linked to a decrease in birth weight (Table 2). Stratification by lipid level percentile was conducted to further investigate the relationship between birth weight and lipid profiles. Among women with GDM, compared with low lipid

Table 1 Characteristics of the study sample stratified by GDM status

Characteristics	Non-GDM ($n = 8139$)	GDM ($n = 2351$)	*P* value
Maternal age (years)	29.84 ± 4.81	31.99 ± 4.77	< 0.001
Prepregnancy BMI (kg/m^2)	20.87 ± 2.93	22.2 ± 3.34	< 0.001
BMI at delivery (kg/m^2) *	26.40 ± 3.23	26.81 ± 3.60	< 0.001
Parity			
Nulliparous	3893 (47.8)	919 (39.1)	< 0.001
Multiparous	4246 (52.2)	1432 (60.9)	
Delivery mode			
Vaginal delivery	5076 (62.4)	1301 (55.3)	< 0.001
Cesarean section	3063 (37.6)	1050 (44.7)	
OGTT-0 h (mmol/L)	4.37 ± 0.31	4.76 ± 0.56	< 0.001
OGTT-1 h (mmol/L)	7.30 ± 1.36	9.84 ± 1.56	< 0.001
OGTT-2 h (mmol/L)	6.36 ± 1.05	8.60 ± 1.52	< 0.001
TG (mmol/L)	3.03 ± 1.26	3.31 ± 1.50	< 0.001
TC (mmol/L)	6.21 ± 1.24	6.07 ± 1.24	< 0.001
HDL (mmol/L)	1.87 ± 0.36	1.85 ± 0.37	0.021
LDL (mmol/L)	3.27 ± 0.95	3.06 ± 0.90	< 0.001
Gestational age at birth (weeks)	39.16 ± 1.63	38.85 ± 1.81	< 0.001
Preterm birth	500 (6.1)	207 (8.8)	< 0.001
Neonatal sex			
Male	4390 (53.9)	1304 (55.5)	0.190
Female	3749 (46.1)	1047 (44.5)	
Birth weight (kg)	3.20 ± 0.47	3.17 ± 0.52	0.019
BWZ	0.02 ± 0.93	0.07 ± 0.98	0.011
Macrosomia	276 (3.4)	103 (4.4)	0.023
Birth weight for gestational age			
SGA	645 (7.9)	190 (8.1)	0.004
AGA	6803 (83.6)	1910 (81.2)	
LGA	691 (8.5)	251 (10.7)	

Note: Data are expressed as the means ± standard deviations or frequencies (proportions). *Among 535 women with missing information on BMI at delivery, 401 were included in the non-GDM group, and 134 were included in the GDM group

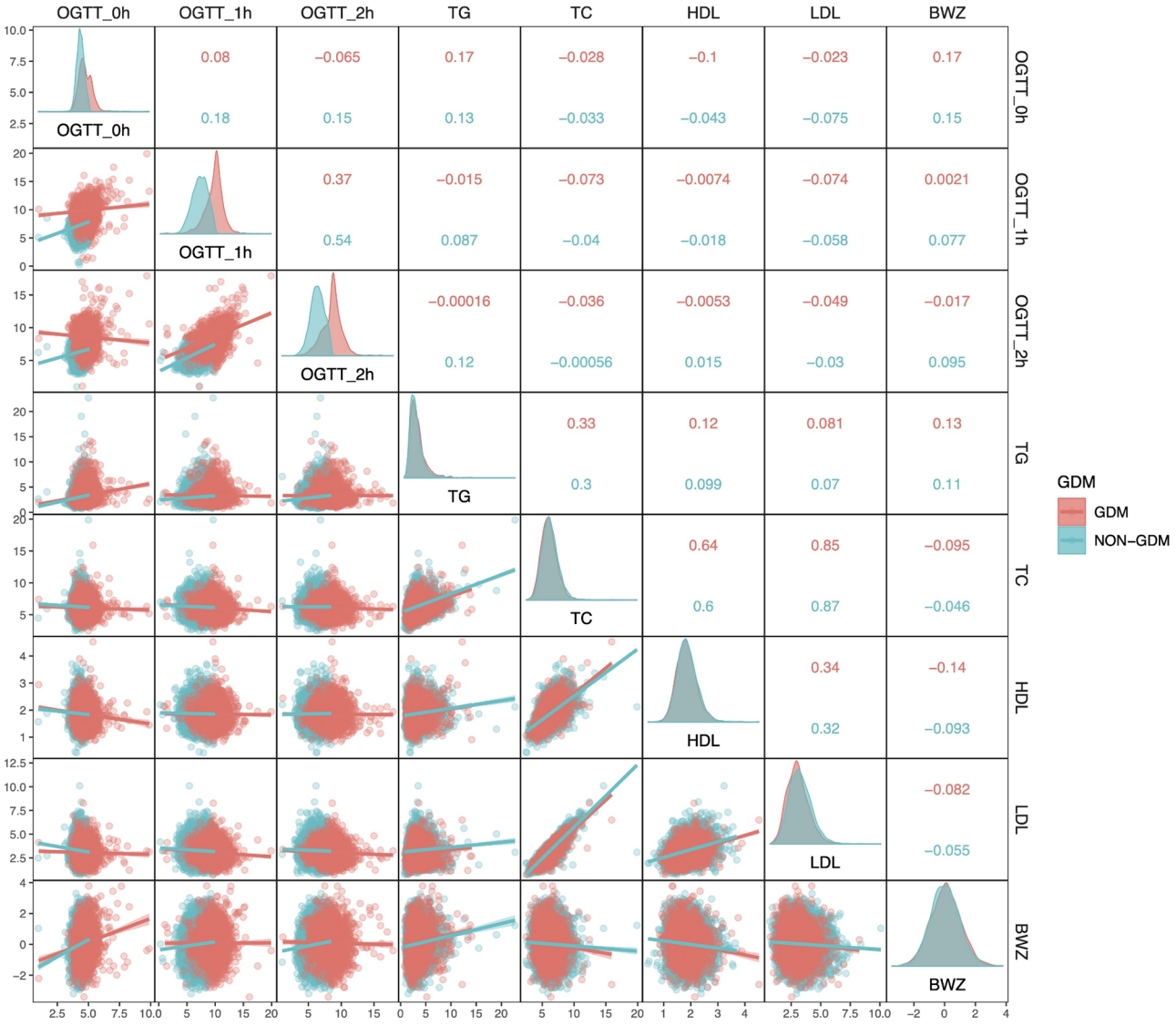

Fig. 1 Correlation analysis among maternal OGTT parameters and lipid profiles and offspring BWZ in pregnant women with and without GDM. In the pairwise comparison matrix, the lower triangle shows the scatter plots for each pair, and the upper triangle displays the Pearson correlation coefficients corresponding to these pairs (GDM, orange; non-GDM, blue). GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; TG, triglyceride; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BWZ, birth weight z score

profiles (≤ 10th percentile), a significant association was observed between high TG levels (≥ 90th percentile) and increased birth weight (156.2 g; 95% CI: 87.8–224.5), and high TC, HDL cholesterol, and LDL cholesterol levels (≥ 90th percentile) were associated with decreased birth weight. Similar results were found for women in the non-GDM group, but the effects were greater in the GDM group.

Logistic regression analysis revealed that in women with GDM, compared with TG levels ≤ the 10th percentile, TG levels ≥ the 90th percentile were associated with increased risks of offspring LGA (adjusted OR: 3.09; 95% CI: 1.51–6.30) and macrosomia (adjusted OR: 4.04; 95% CI: 1.37–11.93), which were greater than those in women without GDM (Table 3; Fig. 2). There was no association between maternal lipid levels in women with GDM and the risk of SGA (Table 4).

Discussion

To accommodate the nutritional needs of pregnant women and fetal growth, as well as postpartum lactation requirements, a physiological increase in blood lipid levels occurs during the gestational period [17]. The lipid levels of TGs, TC, HDL cholesterol, and LDL cholesterol gradually increase throughout pregnancy, peaking in the late stages of gestation [18]. Currently, pregnancy-specific norms for blood lipid levels remain undefined, but increased lipid concentrations during this

Table 2 Associations of the maternal lipid profile in late pregnancy with offspring birth weight (g) in women with and without GDM

Lipid levels and percentile categories	Non-GDM		GDM	
	β (95% CI)	*P* value	β (95% CI)	*P* value
TG (mmol/L)	28.2 (21.9 to 34.5)	< 0.001	28.4 (17.8 to 39.1)	< 0.001
≤ 10th percentile	Reference		Reference	
10th-90th percentile	64.8 (38.4 to 91.1)	< 0.001	78.1 (21.7 to 134.5)	0.007
≥ 90th percentile	136.9 (100.4 to 173.3)	< 0.001	156.2 (87.8 to 224.5)	< 0.001
TC (mmol/L)	-6.3 (-12.8 to 0.2)	0.100	-19.2 (-31.9 to -6.5)	0.003
≤ 10th percentile	Reference		Reference	
10th-90th percentile	-17.9 (-45.3 to 9.4)	0.198	-48.3 (-96.9 to 0.3)	0.051
≥ 90th percentile	-17.3 (-53.2 to 18.6)	0.344	-66.8 (-136.5 to 2.8)	0.060
HDL (mmol/L)	-79.1 (-102.3 to -55.9)	< 0.001	-120.7 (-164.8 to -76.6)	< 0.001
≤ 10th percentile	Reference		Reference	
10th-90th percentile	-51.8 (-80.3 to -23.3)	< 0.001	-97.9 (-150.5 to -45.3)	< 0.001
≥ 90th percentile	-114.3 (-152.0 to -76.6)	< 0.001	-141.2 (-215.1 to -67.4)	< 0.001
LDL (mmol/L)	-9.5 (-18.5 to -0.5)	0.039	-22.2 (-40.4 to -4.0)	0.017
≤ 10th percentile	Reference		Reference	
10th-90th percentile	-31.6 (-61.1 to -2.0)	0.036	-28.2 (-76.2 to 19.9)	0.250
≥ 90th percentile	-35.7 (-73.8 to 2.3)	0.066	-87 (-162.5 to -11.5)	0.024

Note: The models were adjusted for maternal age, parity, BMI before pregnancy, and gestational age at delivery

Table 3 Associations of the maternal lipid profile in late pregnancy with LGA offspring in women with and without GDM

Percentile categories	Non-GDM		GDM	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
TG (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	1.15 (0.85 to 1.54)	0.366	1.93 (1.00 to 3.75)	0.051
≥ 90th percentile	1.81 (1.26 to 2.59)	0.001	3.09 (1.51 to 6.30)	0.002
TC (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	0.91 (0.70 to 1.18)	0.462	0.73 (0.50 to 1.06)	0.096
≥ 90th percentile	0.92 (0.64 to 1.31)	0.625	0.52 (0.27 to 0.99)	0.048
HDL (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	0.62 (0.48 to 0.79)	< 0.001	0.70 (0.47 to 1.05)	0.081
≥ 90th percentile	0.48 (0.33 to 0.70)	< 0.001	0.48 (0.24 to 0.95)	0.034
LDL (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	0.90 (0.68 to 1.19)	0.446	0.78 (0.53 to 1.14)	0.196
≥ 90th percentile	0.95 (0.66 to 1.37)	0.782	0.64 (0.32 to 1.27)	0.197

Note: The models were adjusted for maternal age, parity, BMI before pregnancy, and gestational age at delivery

period present potential risks to both maternal and neonatal health. In this hospital-based study, a comprehensive analysis of maternal lipid profiles in Chinese women from 28 to 42 weeks of gestation was conducted, and the associations between these levels and offspring birth size were explored and compared between women with and without GDM. Notably, women with GDM presented significantly increased TG levels during the third trimester compared with those without GDM. A high TG level (≥ 90th percentile) in women during late pregnancy is associated with increased birth weight, and women with GDM have a greater absolute increase. The findings from the Pune Maternal Nutrition Study revealed that an increase of one standard deviation in maternal TG concentrations at 28 weeks was linked to birth weight increases of 36 g [19], which is consistent with the current results. During pregnancy, TGs exhibit the greatest increase in blood lipid levels, increasing to 50% at 35–42 gestational weeks; TGs serve as the primary source of fetal energy and can promote protein synthesis, reduce fat breakdown, and facilitate the accumulation of nutrients such as fats and glucose in the fetus [20, 21]. There are various hypotheses and supporting evidence regarding the mechanism by which hyperlipidemia affects birth weight. This mechanism may involve several aspects, including changes in placental lipid transport function,

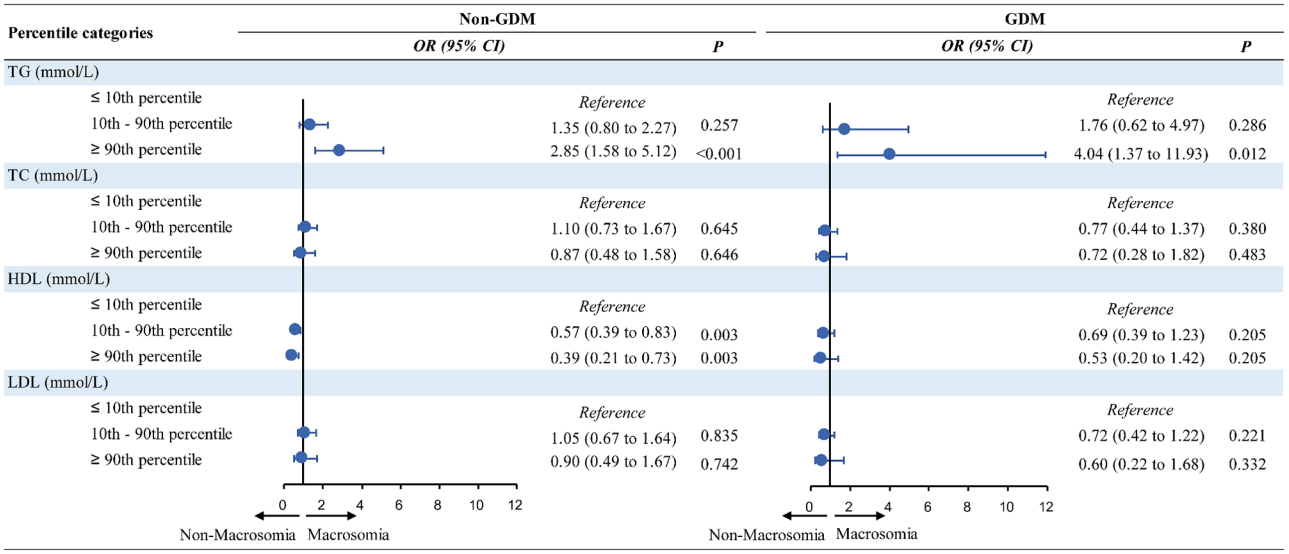

Fig. 2 Odds ratio estimates for the effects of the maternal lipid profile in late pregnancy on macrosomia by maternal GDM status. The lipid levels are divided into the following three categories on the basis of percentile distribution: ≤ 10th percentile, 10th–90th percentile, and ≥ 90th percentile. The lowest 10th percentile group served as the reference group. ORs were adjusted for maternal age, parity, prepregnancy BMI, and gestational age at birth

Table 4 Associations of the maternal lipid profile in late pregnancy with SGA offspring in women with and without GDM

Percentile categories	Non-GDM		GDM	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
TG (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	0.80 (0.62 to 1.03)	0.079	0.82 (0.49 to 1.36)	0.438
≥ 90th percentile	0.53 (0.35 to 0.81)	0.003	0.79 (0.41 to 1.52)	0.484
TC (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	1.00 (0.74 to 1.35)	0.990	1.41 (0.81 to 2.45)	0.219
≥ 90th percentile	1.04 (0.71 to 1.52)	0.849	1.74 (0.86 to 3.50)	0.123
HDL (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	0.96 (0.71 to 1.30)	0.796	1.16 (0.65 to 2.07)	0.607
≥ 90th percentile	1.42 (0.97 to 2.06)	0.069	1.68 (0.82 to 3.48)	0.159
LDL (mmol/L)				
≤ 10th percentile	Reference		Reference	
10th-90th percentile	1.09 (0.78 to 1.52)	0.633	0.98 (0.60 to 1.60)	0.924
≥ 90th percentile	1.28 (0.86 to 1.93)	0.228	1.37 (0.68 to 2.77)	0.386

Note: The models were adjusted for maternal age, parity, BMI before pregnancy, and gestational age at delivery

impacts on fetal insulin sensitivity, and fat metabolism [19]. One possible mechanism is that hyperlipidemia, particularly high TG levels, may influence placental function and the fetal metabolic environment, thereby increasing fetal fat accumulation and birth weight [22]. Hyperlipidemia may alter the lipid transport function of the placenta, allowing more maternal lipids to be transferred to the fetus. Additionally, hyperlipidemia may affect fetal insulin sensitivity and fat metabolism, further promoting fetal fat deposition. This study also revealed that high TG levels (≥ 90th percentile) in pregnant women with and without GDM increased the risk of LGA and macrosomia in offspring, and this risk was greater in women with GDM. The relationship between GDM and hyperlipidemia is well established. However, even when pregnant women with GDM achieved significant progress in blood glucose control, the incidence of LGA and macrosomia did not significantly decrease [23, 24]. Some studies have focused on the relationship between lipid levels in pregnant women with GDM and birth size; the current findings are consistent with the findings of these previous studies [11–13, 25].

The results of this study revealed that high maternal TC, HDL cholesterol, and LDL cholesterol

concentrations were directly associated with decreased birth weight, with greater impact sizes of all these associations in the GDM group than in the non-GDM group. However, the results for these parameters vary among different studies. Limited research is available on pregnancy in diabetic women, but studies of nondiabetic women with varying prepregnancy BMI classifications have reported a negative correlation between HDL levels and offspring birth weight [26, 27]. However, Kulkarni et al. reported that HDL cholesterol levels are unrelated to neonatal birth size [19]. The underlying mechanism for the impact of HDL cholesterol levels on newborn birth weight remains unclear.

Strengths and limitations

Maternal glucose and lipid metabolism are considered the most important determinants of neonatal birth size and are influenced by regional and dietary habits [28, 29]. Research on these factors in China is relatively rare, with a limited focus on the relationship between blood lipid metabolism in pregnant women with GDM and newborn birth size. This study provides valuable contributions to this field, which has been relatively underexplored in southern China. The use of a large hospital-based sample population allows more reliable conclusions to be drawn regarding the relationships among maternal GDM status, maternal lipid concentrations during pregnancy and offspring birth size. A major limitation of this study is its observational design, which restricts the ability to establish causality between the observed associations; studies with an interventional or longitudinal design are needed to confirm causal links and guide targeted interventions. Furthermore, owing to the retrospective study design, certain confounding variables, including gestational lipid levels at different time points during pregnancy, diet, and other factors, could not be investigated or controlled for.

Conclusions

The study provides evidence of a significant association between maternal lipid levels during late pregnancy and offspring birth size. However, the observational nature of the study limits the ability to establish causal relationships regarding the direct impact of lipid levels on birth size. Additionally, the influence of maternal lipid profiles is disproportionately greater in women with GDM than in women without GDM.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02458-0.

Supplementary Material 1: Supplementary Figure 1 Distribution of HbA1c values in late pregnancy in the GDM group

Author contributions

Conception and design: YG, GL and JP. Data collection and analysis: LZ, JJ, HM and YG. The first draft of the manuscript was written by YG, JP and all authors commented on previous versions of the manuscript. All authors reviewed the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval

Ethical approval for this study was obtained from the Medical Ethics Committee at Guangdong Women and Children Hospital (ID: 202201203). The data used in this study were extracted from the hospital information system without personally identifiable information; therefore, informed consent for the retrospective study was waived by the Medical Ethics Committee.

Competing interests

The authors declare no competing interests.

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