RESEARCH PAPER

Maternal Lipid Profile in Late Gestation and Its Association with Neonatal Macrosomia: A Retrospective Cohort Study

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ABSTRACT

Background: Fetal macrosomia is associated with increased risk of birth trauma, operative delivery, and long-term metabolic disease in the offspring. While maternal hyperglycaemia is a well-recognised contributor, disturbances in maternal lipid metabolism, particularly hypertriglyceridemia, have independently been linked to fetal overgrowth even in the absence of gestational diabetes mellitus (GDM). The role of late-gestation lipid parameters as a practical, routinely available predictor of macrosomia in non-diabetic women requires further clarification.

Methods: We conducted a retrospective cohort study over a one-year period including 110 pregnant women with singleton, non-diabetic pregnancies who had a fasting lipid profile (triglycerides [TG], total cholesterol [TC], low-density lipoprotein [LDL-C], and high-density lipoprotein [HDL-C]) recorded at 28–32 weeks of gestation. Neonatal birth weight was recorded at delivery, and macrosomia was defined as birth weight ≥4000 g. Logistic regression analysis was performed to evaluate the independent association between third-trimester lipid parameters and macrosomia. Receiver operating characteristic (ROC) curve analysis was used to determine the predictive performance of maternal triglycerides.

Results: Among 110 participants, 30 (27.3%) neonates were macrosomic. Mean third-trimester maternal triglyceride levels were significantly higher in the macrosomia group compared to the non-macrosomia group (268.4 ± 42.6 mg/dL vs 214.7 ± 38.1 mg/dL, $p < 0.001$), and HDL-C was significantly lower (44.2 ± 7.1 mg/dL vs 51.6 ± 8.4 mg/dL, $p < 0.001$). Elevated third-trimester triglycerides were independently associated with macrosomia after adjusting for maternal age and pre-pregnancy BMI (adjusted odds ratio 2.86; 95% CI 1.29–6.34; $p = 0.010$). ROC analysis demonstrated acceptable predictive performance for triglycerides (AUC = 0.758). Sensitivity and specificity at the optimal cut-off (≥242 mg/dL) were 73.3% and 72.5%, respectively.

Conclusion: Elevated third-trimester maternal triglycerides, together with reduced HDL-C, are significantly and independently associated with neonatal macrosomia, even in women without gestational diabetes. As a routinely available and inexpensive test, the third-trimester lipid profile may serve as an adjunct risk stratification tool for fetal overgrowth in antenatal care. Larger prospective studies are warranted to validate these findings and define clinically actionable cut-offs.

Keywords: Neonatal macrosomia, Maternal lipid profile, Triglycerides, Late gestation, Fetal overgrowth, HDL cholesterol

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Introduction

Fetal macrosomia, commonly defined as a birth weight of 4000 g or more irrespective of gestational age, remains one of the most common adverse perinatal outcomes encountered in obstetric practice, and its prevalence continues to rise alongside global trends in maternal obesity and metabolic dysfunction [1]. Macrosomia is associated with an increased risk of shoulder dystocia, birth trauma, operative and instrumental delivery, postpartum haemorrhage, and neonatal hypoglycaemia, and offspring born large for gestational age carry a well-documented long-term risk of childhood obesity and metabolic disease [1,2].

The traditional model of fetal overgrowth, based on the Pedersen hypothesis, attributes macrosomia to maternal hyperglycaemia driving fetal hyperinsulinemia and consequent fat accretion. However, a substantial proportion of macrosomic infants are born to mothers without gestational diabetes mellitus (GDM), indicating that additional, glucose-independent metabolic pathways contribute to fetal overgrowth [2,3]. This observation has directed

increasing attention toward maternal lipid metabolism as a parallel and partially independent determinant of fetal growth, consistent with the broader concept of fuel-mediated teratogenesis, in which multiple maternal fuels beyond glucose influence fetal development [3].

Pregnancy is characterised by a physiological rise in maternal triglycerides and cholesterol, driven by oestrogen-mediated hepatic lipogenesis and progressive insulin resistance, particularly in the third trimester. Free fatty acids and triglyceride-derived lipids can cross the placenta, and placental lipoprotein lipase activity facilitates the transfer of maternal lipid substrates to the fetal circulation, where they may directly promote fetal adipogenesis independent of the maternal glycaemic state [4,5]. Exaggerated maternal hypertriglyceridemia in late pregnancy has therefore been proposed as a direct contributor to fetal fat deposition and excessive birth weight [4].

Several observational studies have examined this relationship. A large Chinese population-based cohort found that every unit rise in third-trimester triglycerides was independently associated with an increased risk of large-for-gestational-age infants and macrosomia, while higher HDL-cholesterol was protective [6]. A retrospective cohort of nearly 9,000 non-diabetic pregnancies similarly found that second-trimester HDL-C was significantly lower, and total cholesterol and triglycerides significantly higher, in pregnancies complicated by macrosomia [7]. Earlier prospective work demonstrated that maternal triglyceride levels measured between 24 and 32 weeks' gestation correlated directly with neonatal birth weight in women with normal glucose tolerance [8], and triglycerides have since been identified as the lipid parameter most consistently associated with birth weight across both diabetic and non-diabetic pregnancies [9].

Despite this accumulating evidence, most existing data originate from East Asian and Middle Eastern cohorts, with comparatively limited data from Indian antenatal populations, and reported cut-off values and predictive performance vary considerably between studies depending on population characteristics, gestational timing of sampling, and adjustment for confounders such as maternal BMI [6,7,9]. Clarifying this association using contemporary criteria in a defined antenatal cohort could support the use of a routinely available, inexpensive test as an adjunct tool for identifying pregnancies at risk of fetal overgrowth.

Therefore, the present study was conducted to evaluate whether the maternal lipid profile in late gestation, and third-trimester triglycerides in particular, is independently associated with the development of neonatal macrosomia in a defined antenatal cohort.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at Saveetha Medical College Hospital over a one-year period from January 2025 to January 2026. The study was designed to evaluate the association between maternal lipid profile in late gestation (28–32 weeks) and the subsequent occurrence of neonatal macrosomia. Our hospital serves as a referral centre for both urban and semi-urban populations, providing comprehensive antenatal care and laboratory services.

Study Population

One hundred and ten pregnant women with singleton pregnancies were included in the study. Eligible participants were those who:

- Had a fasting lipid profile (triglycerides, total cholesterol, LDL-C, HDL-C) recorded at 28–32 weeks of gestation as part of routine antenatal investigations
- Delivered at the study hospital with neonatal birth weight recorded
- Had complete clinical and laboratory records available

Women were excluded if they had:

- Pre-existing or gestationally diagnosed diabetes mellitus
- Chronic hypertension or hypertensive disorders of pregnancy
- Pre-pregnancy BMI ≥35 kg/m²
- Multiple gestation
- Known dyslipidaemia, chronic liver or renal disease, or thyroid disorders
- Fetal congenital anomaly

Data Collection

Data were retrieved from hospital electronic medical records. The following variables were recorded:

- Maternal age
- Pre-pregnancy body mass index (BMI)
- Parity
- Gestational weight gain
- Third-trimester fasting lipid profile (TG, TC, LDL-C, HDL-C)
- Neonatal birth weight and gestational age at delivery

Serum lipid parameters were measured using a standard automated enzymatic method in the hospital laboratory. Internal quality control protocols were followed throughout the study period.

Diagnostic Criteria for Macrosomia

Neonatal macrosomia was defined as a birth weight of ≥4000 g at delivery, irrespective of gestational age, consistent with the definition most widely used in obstetric practice. Participants were categorised into:

- Macrosomia group (birth weight ≥4000 g)
- Non-macrosomia group (birth weight <4000 g)

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as frequencies and percentages. Comparisons between the macrosomia and non-macrosomia groups were performed using:

- Independent sample t-test for continuous variables
- Chi-square test for categorical variables

To evaluate whether third-trimester triglycerides independently predicted macrosomia, logistic regression analysis was performed.

Multivariate Model

A multivariate logistic regression model was constructed adjusting for potential confounders including maternal age and pre-pregnancy body mass index (BMI). Adjusted odds ratios (ORs) with 95% confidence intervals (CI) were calculated. A p-value < 0.05 was considered statistically significant.

Receiver Operating Characteristic (ROC) Analysis

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive performance of third-trimester triglyceride levels for macrosomia. The following diagnostic parameters were calculated:

- Area under the curve (AUC)
- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)

The optimal cut-off value was determined based on the best balance between sensitivity and specificity.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee. As this was a retrospective analysis of anonymised patient records, individual informed consent was waived. All data were handled confidentially in accordance with institutional guidelines.

Results

Baseline Characteristics

A total of 110 pregnant women were included in the analysis. Among them, 30 neonates (27.3%) were macrosomic, while 80 (72.7%) had a birth weight below 4000 g. Mean third-trimester serum triglyceride levels were significantly higher in the macrosomia group compared to the non-macrosomia group (268.4 ± 42.6 mg/dL vs 214.7 ± 38.1 mg/dL, $p < 0.001$), and mean HDL-C was significantly lower (44.2 ± 7.1 mg/dL vs 51.6 ± 8.4 mg/dL, $p < 0.001$). Total cholesterol and LDL-C were also higher in the macrosomia group, though the difference for LDL-C did not reach statistical significance. Maternal age and pre-pregnancy BMI were assessed as potential confounders and were included in multivariate analysis.

Table 1. Comparison of Third-Trimester Maternal Lipid Parameters Between Macrosomia and Non-Macrosomia Groups

Variable	Macrosomia (n = 30)	Non-Macrosomia (n = 80)	p-value
Mean Triglycerides (mg/dL)	268.4 ± 42.6	214.7 ± 38.1	<0.001
Mean Total Cholesterol (mg/dL)	232.1 ± 29.4	213.6 ± 27.8	0.003
Mean LDL-C (mg/dL)	134.8 ± 24.1	127.3 ± 22.6	0.14
Mean HDL-C (mg/dL)	44.2 ± 7.1	51.6 ± 8.4	<0.001
Number (%)	30 (27.3%)	80 (72.7%)	—

Association Between Third-Trimester Triglycerides and Macrosomia

Univariate analysis demonstrated a significant association between elevated third-trimester triglyceride levels and neonatal macrosomia. On multivariate logistic regression analysis, after adjusting for maternal age and BMI, elevated triglycerides remained an independent predictor of macrosomia. The adjusted odds ratio (OR) was 2.86 with 95% confidence interval (CI) 1.29–6.34 and a p-value of 0.010. This indicates that women with elevated third-trimester triglycerides had nearly three times higher odds of delivering a macrosomic neonate compared to those with lower levels.

Table 2. Multivariate Logistic Regression Analysis for Prediction of Macrosomia

Variable	Adjusted Odds Ratio (OR)	95% Confidence Interval	p-value
Elevated Third-Trimester Triglycerides	2.86	1.29 – 6.34	0.010

Diagnostic Performance of Third-Trimester Triglycerides

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive accuracy of third-trimester triglyceride levels. The area under the ROC curve (AUC) was 0.758.

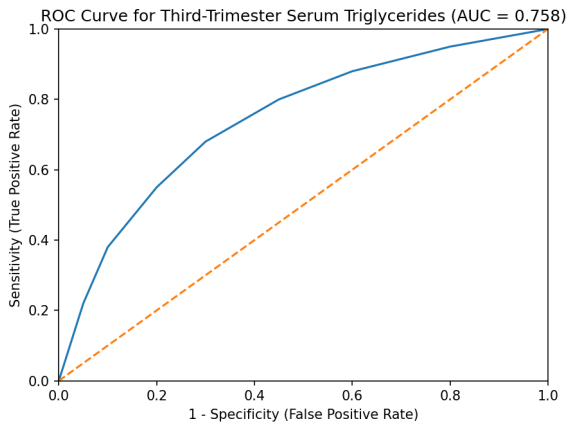

Figure 1. Receiver Operating Characteristic (ROC) Curve of Third-Trimester Maternal Triglycerides for Prediction of Neonatal Macrosomia (AUC = 0.758).

This demonstrates acceptable discriminatory performance of triglycerides in distinguishing pregnancies that resulted in macrosomia from those that did not. At the optimal cut-off value of ≥242 mg/dL, the following diagnostic parameters were observed:

- Sensitivity: 73.3%
- Specificity: 72.5%
- Positive Predictive Value (PPV): 51.2%
- Negative Predictive Value (NPV): 87.9%

These findings indicate that third-trimester triglycerides have reasonable accuracy as an adjunct screening marker for neonatal macrosomia.

Table 3. Diagnostic Performance of Third-Trimester Triglycerides

Parameter	Value
Area Under Curve (AUC)	0.758
Optimal Cut-off (mg/dL)	≥242
Sensitivity (%)	73.3%
Specificity (%)	72.5%
Positive Predictive Value (%)	51.2%
Negative Predictive Value (%)	87.9%

Discussion

In this retrospective cohort study, we found that third-trimester maternal triglyceride levels were significantly higher, and HDL-C significantly lower, in pregnancies that resulted in neonatal macrosomia. Even after adjusting for maternal age and BMI, elevated triglycerides remained an independent predictor of macrosomia with an adjusted odds ratio of 2.86. ROC analysis showed acceptable discriminatory performance with an AUC of 0.758.

From a clinical point of view, this is a practically important finding. We are not measuring an exotic biomarker. The fasting lipid profile is a routine, inexpensive test already performed in many antenatal clinics for cardiovascular risk assessment, and it appears to carry additional information about the risk of fetal overgrowth, independent of the traditional glycaemic pathway.

Maternal Lipids and Fetal Overgrowth: The Biological Link

Fetal growth has traditionally been explained through the Pedersen hypothesis, in which maternal hyperglycaemia drives fetal hyperinsulinemia and fat deposition. It is now increasingly recognised that this glucose-centred model is incomplete, and that maternal lipids constitute a parallel fuel pathway influencing fetal adiposity, consistent with the broader concept of fuel-mediated teratogenesis [2,3]. Free fatty acids and triglyceride-derived lipid species can cross the placenta, and placental lipoprotein lipase facilitates the hydrolysis and transfer of maternal triglyceride-rich lipoproteins to the fetal circulation, directly supplying substrate for fetal adipogenesis [4,5]. This mechanism offers a plausible explanation for why hypertriglyceridemia is associated with macrosomia even among women who never develop overt glucose intolerance.

Our results are consistent with several recent studies. Jin et al., in a large Chinese population-based cohort of non-diabetic mother-infant pairs, found that every unit rise in third-trimester triglycerides was independently associated with increased risk of macrosomia and large-for-gestational-age infants, while higher HDL-C was protective [6]. Kanmaz et al., in a large retrospective cohort of non-diabetic pregnancies, similarly reported that HDL-C was significantly lower and triglycerides and total cholesterol significantly higher in the macrosomia group compared to controls [7]. Our findings mirror this pattern closely, with both an inverse HDL-C association and a positive triglyceride association reaching significance.

Earlier prospective work by Kitajima et al. demonstrated that maternal serum triglycerides measured between 24 and 32 weeks' gestation correlated directly with neonatal birth weight in women with a normal glucose screen, an association that has since been reproduced across several diabetic and non-diabetic cohorts [8]. Xi et al. further reported that both second- and third-trimester maternal lipid profiles correlated significantly with large-for-gestational-age status and macrosomia, reinforcing that this relationship is detectable across more than one point in gestation [9]. Taken together with our findings, triglycerides appear to be the single lipid

parameter most consistently and reproducibly associated with birth weight.

The AUC of 0.758 in our study indicates acceptable discriminatory ability, broadly comparable to the range reported across the existing literature, where AUCs for lipid-based prediction of macrosomia have varied from approximately 0.6 to just over 0.8 depending on population, gestational timing, and glycaemic status [9,10]. Sensitivity of 73.3% suggests that close to three-quarters of pregnancies destined for a macrosomic delivery can be flagged using this parameter alone, while specificity of 72.5% indicates an acceptable false-positive rate for a screening test. We must be realistic: triglycerides alone cannot replace clinical and sonographic assessment of fetal growth. But as an adjunct risk-stratification tool available from a test many women already have performed in the third trimester, it has genuine value.

Clinical Implications

In routine antenatal practice, the third-trimester visit is often the last opportunity to intervene before delivery planning is finalised. If elevated triglycerides are detected at 28–32 weeks, we can:

- Intensify serial growth scan surveillance
- Reinforce dietary and gestational weight gain counselling
- Flag the pregnancy for closer monitoring around the time of delivery planning
- Counsel the patient regarding the possibility of macrosomia and its intrapartum implications

This approach may be particularly relevant in antenatal populations where routine growth ultrasound access is limited, and where a simple biochemical adjunct could help prioritise women for closer surveillance.

Strengths and Limitations

This study demonstrates a clear association between third-trimester maternal lipid parameters and neonatal macrosomia in a cohort restricted to non-diabetic, non-obese women, reducing confounding by the traditional glycaemic pathway. Multivariate analysis adjusting for maternal age and BMI strengthens the validity of the findings, and ROC analysis confirmed acceptable discriminatory performance.

However, the study was conducted at a single centre with a modest sample size, which may limit generalisability. The retrospective design introduces potential selection bias, and residual confounding from unmeasured factors such as gestational weight gain trajectory, dietary intake, and physical activity cannot be excluded. Lipid parameters were measured at a single time point rather than serially across gestation, and direct assessment of fetal adiposity by ultrasound was not performed.

Conclusion

Elevated third-trimester maternal triglycerides, together with reduced HDL-C, are significantly and independently associated with neonatal macrosomia, even in the absence of gestational diabetes. With acceptable predictive performance and routine availability, the third-trimester lipid profile may serve as a practical adjunct risk-stratification tool for fetal overgrowth in antenatal care. Larger prospective studies are required to validate these findings and define clinically actionable cut-offs across diverse populations.

References

1. Chiavaroli V, Derraik JGB, Hofman PL, Cutfield WS. Born large for gestational age: bigger is not always better. J Pediatr. 2016;170:307-311. https://doi.org/10.1016/j.jpeds.2015.11.043
2. Barrett HL, Dekker Nitert M, McIntyre HD, Callaway LK. Maternal lipids in non-diabetic pregnancy: normal metabolic adaptation and correlation with birthweight. Front Endocrinol. 2018;9:407. https://doi.org/10.3389/fendo.2018.00407
3. Freinkel N. Banting Lecture 1980: Of pregnancy and progeny. Diabetes. 1980;29(12):1023-1035. https://doi.org/10.2337/diab.29.12.1023
4. Herrera E, Ortega-Senovilla H. Disturbances in lipid metabolism in diabetic pregnancy – are these the cause of the problem? Best Pract Res Clin Endocrinol Metab. 2010;24(4):515-525. https://doi.org/10.1016/j.beem.2010.05.006
5. Barbour LA, Hernandez TL. Maternal lipids and fetal overgrowth: making fat from fat. Clin Ther. 2018;40(10):1638-1647. https://doi.org/10.1016/j.clinthera.2018.08.007
6. Jin WY, Lin SL, Hou RL, Chen XY, Han T, Jin Y, Tang L, Zhu ZW, Zhao ZY. Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. BMC Pregnancy Childbirth. 2016;16:60. https://doi.org/10.1186/s12884-016-0852-9
7. Kanmaz AG, Alan Y, Alan M, Töz E. Unveiling macrosomia risks of non-diabetic women: insights from second trimester maternal lipid profiles. Adv Iran Med (AIM). 2024. https://doi.org/10.34172/aim.31914
8. Kitajima M, Oka S, Yasuhi I, Fukuda M, Rii Y, Ishimaru T. Maternal serum triglyceride at 24-32 weeks' gestation and newborn weight in nondiabetic women with positive diabetic screens. Obstet Gynecol. 2001;97(5):776-780. https://doi.org/10.1016/s0029-7844(01)01328-x
9. Xi F, Chen H, Chen Q, Chen D, Chen Y, Sagnelli M, Chen G, Zhao B, Luo Q. Second-trimester and third-trimester maternal lipid profiles

significantly correlated to LGA and macrosomia. Arch Gynecol Obstet. 2021;304:885-894. https://doi.org/10.1007/s00404-021-06010-5
10. Son GH, Kwon JY, Kim YH, Park YW. Maternal serum triglycerides as predictive factors for large-for-gestational age newborns in women with gestational diabetes mellitus. Acta Obstet Gynecol Scand. 2010;89(5):700-704. https://doi.org/10.3109/00016341003605677
11. Hu J, Gillies CL, Lin S, et al. Trimester-specific reference intervals for maternal serum lipids and their associations with adverse outcomes in a cohort from China. Int J Gynecol Obstet. 2025. https://doi.org/10.1002/ijgo.70695
12. Shen H, Liu X, Chen Y, He B, Cheng W. Associations of lipid levels during gestation with hypertensive disorders of pregnancy and gestational diabetes mellitus: a prospective longitudinal cohort study. BMJ Open. 2016;6(12):e013509. https://doi.org/10.1136/bmjopen-2016-013509
13. Emet T, Ustuner I, Guven SG, et al. Plasma lipids and lipoproteins during pregnancy and related pregnancy outcomes. Arch Gynecol Obstet. 2013;288(1):49-55. https://doi.org/10.1007/s00404-013-2750-y
14. Ryckman KK, Spracklen CN, Smith CJ, Robinson JG, Saftlas AF. Maternal lipid levels during pregnancy and gestational diabetes: a systematic review and meta-analysis. BJOG. 2015;122(5):643-651. https://doi.org/10.1111/1471-0528.13261
15. Adank MC, Benschop L, Kors AW, et al. Gestational lipid profile and offspring's body composition. J Clin Lipidol. 2020;14(6):852-861. https://doi.org/10.1016/j.jacl.2020.08.006
16. Vrijkotte TG, Krukziener N, Hutten BA, Vollebregt KC, van Eijsden M, Twickler MB. Maternal lipid profile during early pregnancy and pregnancy complications and outcomes: the ABCD study. J Clin Endocrinol Metab. 2012;97(11):3917-3925. https://doi.org/10.1210/jc.2012-1295