

Lipid Profile Alterations in Pregnancy and Gestational Diabetes Mellitus: Pathophysiology, Clinical Significance and Pregnancy Outcomes

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Abstract

Aim:

To review the alterations in lipid profile during normal pregnancy and gestational diabetes mellitus (GDM), with emphasis on their underlying pathophysiology, clinical significance, and association with maternal and fetal pregnancy outcomes. These findings are particularly relevant to maternal health.

Materials and Methods:

A narrative review of published literature was conducted using major biomedical databases, including PubMed, Scopus, and Google Scholar. Relevant studies published predominantly between 2015 and 2026 were reviewed using keywords such as *pregnancy*, *gestational diabetes mellitus*, *lipid profile*, *triglycerides*, *total cholesterol*, *LDL-C*, *HDL-C*, *dyslipidemia*, and *pregnancy outcomes*. Studies evaluating lipid alterations, insulin resistance, GDM, and maternal or fetal outcomes were included. Relevant findings were critically synthesized to assess the relationship between maternal lipid abnormalities and GDM.

Results:

Pregnancy is associated with physiological increases in total cholesterol, LDL-C, HDL-C, triglycerides, and free fatty acids, particularly during the second and third trimesters. These changes become more pronounced in GDM because of increased insulin resistance, enhanced adipose-tissue lipolysis, increased free fatty-acid availability, and hepatic VLDL and triglyceride synthesis. Among lipid parameters, elevated triglycerides showed the most consistent association with GDM and adverse pregnancy outcomes. Reduced HDL-C and increased TG/HDL-C ratio were also associated with an insulin-resistant metabolic phenotype. Maternal dyslipidemia, particularly hypertriglyceridemia, has been associated with preeclampsia, gestational hypertension, preterm birth, macrosomia, large-for-gestational-age infants, and other adverse outcomes. Emerging evidence suggests that early-pregnancy lipid parameters and indices such as TG/HDL-C and triglyceride-glucose index may have potential value for early identification of women at increased risk of GDM.

Conclusion:

Alterations in lipid metabolism are an important component of the metabolic changes occurring during pregnancy and are more pronounced in women with GDM. Maternal hypertriglyceridemia appears to be the most clinically relevant lipid abnormality and may serve as an important marker of metabolic dysfunction and adverse pregnancy outcomes. Incorporating lipid parameters with conventional glucose-based assessment may improve early metabolic

risk stratification; however, standardized gestational-age-specific reference ranges and prospective studies are required before routine lipid-based screening can be recommended.

Keywords:

Pregnancy; Gestational diabetes mellitus; Lipid profile; Dyslipidemia; Triglycerides; Total cholesterol; LDL cholesterol; HDL cholesterol; Insulin resistance; Pregnancy outcomes.

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INTRODUCTION

Pregnancy is accompanied by substantial physiological adaptations in carbohydrate and lipid metabolism that ensure adequate energy availability for the mother, placenta, and developing fetus. Maternal concentrations of triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) progressively change throughout gestation, with the most prominent alterations generally occurring during the second and third trimesters. These changes represent an important component of normal maternal metabolic adaptation; however, excessive lipid elevation may indicate underlying metabolic dysfunction and may be associated with adverse pregnancy outcomes (1,2).

Gestational diabetes mellitus (GDM) is one of the most common metabolic complications of pregnancy and develops when pregnancy-induced insulin resistance exceeds pancreatic β -cell compensatory capacity. Insulin resistance promotes adipose-tissue lipolysis, increases circulating free fatty acids, and enhances hepatic synthesis of triglyceride-rich lipoproteins. Consequently, women with GDM frequently demonstrate an altered lipid profile characterized particularly by elevated TG and, in some studies, reduced HDL-C. A systematic review and meta-analysis involving 292 studies and 97,880 pregnant women demonstrated that TG concentrations were approximately 20% higher in women with GDM than in women without GDM, with differences detectable from the first trimester and persisting throughout pregnancy (3). Similar findings from another meta-analysis confirmed significantly higher TG and lower HDL-C concentrations among women with GDM (4).

The relationship between dyslipidemia and GDM is complex and potentially bidirectional. Increased circulating free fatty acids can interfere with insulin signaling and aggravate insulin resistance, while

hyperinsulinemia and altered hepatic lipid metabolism can further increase triglyceride synthesis and VLDL secretion. This interaction may create a metabolic cycle involving insulin resistance, hyperglycemia, increased lipolysis, and dyslipidemia. The triglyceride-glucose (TyG) index and TG/HDL-C ratio have therefore attracted interest as surrogate markers of insulin resistance and potential predictors of GDM, particularly when measured during early pregnancy (5,6).

Among the different lipid parameters, maternal hypertriglyceridemia appears to have the most consistent association with GDM and adverse pregnancy outcomes. Elevated TG concentrations have been associated with excessive fetal growth, macrosomia, large-for-gestational-age (LGA) birth, hypertensive disorders, and preterm delivery. In a recent prospective study of 32,411 pregnant women, higher early-pregnancy TG, TC, and remnant cholesterol concentrations were positively associated with subsequent GDM, while the TG/HDL-C ratio was also associated with preeclampsia (7). These findings suggest that lipid abnormalities may become evident before the conventional diagnosis of GDM and could potentially contribute to early metabolic risk assessment.

Maternal dyslipidemia may influence fetal growth through increased availability of fatty acids to the placenta. Placental lipases can hydrolyze maternal triglyceride-rich lipoproteins, facilitating the uptake of free fatty acids for placental and fetal utilization. Excessive lipid availability, particularly in combination with maternal hyperglycemia, may promote fetal adiposity and excessive fetal growth. Recent cohort evidence has demonstrated that first-trimester maternal dyslipidemia was associated with increased risks of GDM, preterm birth, and LGA birth (8).

The association between dyslipidemia and hypertensive pregnancy complications is also

clinically important. Hypertriglyceridemia, oxidative stress, systemic inflammation, endothelial dysfunction, and abnormal placental vascular adaptation share several pathological pathways with preeclampsia. In women with established GDM, elevated TG concentrations have recently been reported as independent risk factors for preeclampsia, preterm birth, macrosomia, postpartum hemorrhage, and fetal distress, even among women receiving adequate glycemic control (9).

Interpretation of maternal lipid concentrations requires particular caution because pregnancy itself produces physiological increases in circulating lipids. Application of non-pregnant reference ranges may therefore lead to inappropriate classification of normal pregnancy-related changes as pathological dyslipidemia. Recent large cohort data support the use of trimester-specific reference intervals for TC, TG, LDL-C, HDL-C, non-HDL-C, apolipoproteins, and related lipid measures, emphasizing the importance of gestational-age-specific interpretation (10).

Increasing evidence consequently supports consideration of maternal lipid metabolism as an important component of the pathophysiology of GDM rather than an isolated biochemical abnormality. Nevertheless, lipid parameters currently complement rather than replace established glucose-based diagnostic criteria for GDM. Further prospective studies are required to establish standardized gestational-age-specific thresholds, determine the predictive value of lipid-derived indices, and clarify whether early identification and modification of maternal dyslipidemia can improve maternal and fetal outcomes. The broader implications are also relevant to public health.

The present review therefore focuses on the physiological alterations in maternal lipid metabolism during pregnancy, mechanisms underlying dyslipidemia in GDM, clinical significance of individual lipid parameters and lipid-derived indices, and their association with maternal and fetal pregnancy outcomes.

MATERIALS AND METHODS

A narrative review was conducted to evaluate alterations in lipid profile during pregnancy and their association with gestational diabetes mellitus (GDM), maternal complications, and pregnancy outcomes. A literature search was performed using

PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar for studies published mainly between **2015 and 2026**.

The search strategy included combinations of the keywords: **“pregnancy,” “gestational diabetes mellitus,” “GDM,” “lipid profile,” “triglycerides,” “total cholesterol,” “LDL-C,” “HDL-C,” “dyslipidemia,” “insulin resistance,” “preeclampsia,” “macrosomia,” and “pregnancy outcomes.”** Original research articles, systematic reviews, meta-analyses, and relevant review articles were considered.

Inclusion Criteria

- Studies conducted in **pregnant women**.
- Studies evaluating **lipid profile and/or GDM**.
- Studies reporting **TG, TC, LDL-C, HDL-C** or related lipid parameters.
- Studies assessing **maternal or fetal pregnancy outcomes**.
- Articles published in **English** during the selected study period.

Exclusion Criteria

- Studies unrelated to **pregnancy or GDM**.
- Animal studies and laboratory-only studies.
- Case reports, conference abstracts, and duplicate publications.
- Studies with insufficient or unavailable relevant data.

Studies evaluating maternal lipid parameters during pregnancy, particularly **triglycerides, total cholesterol, LDL-C, HDL-C, VLDL, and lipid-derived indices**, and their relationship with GDM or maternal and fetal outcomes were included. Articles unrelated to pregnancy or GDM, duplicate publications, case reports, and studies with insufficient relevant information were excluded.

Relevant data regarding **study population, gestational age, lipid parameters, GDM status, metabolic associations, and maternal and fetal outcomes** were extracted and narratively synthesized. Because of substantial heterogeneity in study populations, gestational age at lipid assessment, diagnostic criteria, and reported lipid cut-offs, a qualitative synthesis rather than quantitative meta-analysis was performed.

RESULTS

The findings of the **10 key references** used in the review are summarized below.

Table 1. Summary of major studies evaluating lipid profile and GDM

Re f.	Study Year	Study / design & Major population findings	Key conclusion
1	Formisa et al., 2024	Narrative review of dyslipidemia in pregnancy	Pregnancy produces progressive physiological increases in TG, TC and LDL-C, with important changes in lipoprotein metabolism. Severe abnormalities may become clinically significant.
2	Mulder et al., 2024	Narrative review	Maternal lipid metabolism changes substantially throughout pregnancy; both TG and other lipid fractions increase as pregnancy progresses. Maternal
3	Hu et al., 2021	Systematic review and meta-analysis; 292 studies, 97,880 women	dyslipidemia may influence placental and fetal lipid metabolism. Women with GDM had approximately 20% higher TG than women without GDM; pooled difference was 0.388 mmol/L. GDM was associated with higher TC (SMD 0.23), markedly higher TG (SMD 1.14), higher VLDL (SMD 0.99) and TG/HDL ratio (SMD 0.65), while
4	Rahneim et al., 2021/22	Systematic review and meta-analysis; 33 studies, 23,792 women	TG showed the strongest lipid association with GDM.

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Re Study f.	Year	Study / design & Major population findings	Key conclusion	Re Study f.	Year	Study / design & Major population findings	Key conclusion
		HDL was lower (SMD -0.35). LDL-C difference was not statistically significant.				significantly higher (p=0.019). TG was significantly higher in GDM throughout all three trimesters (WMD 30.9, 95% CI 25.4–36.4). Hypertriglyceridemia is a consistent feature of GDM across the second pregnancy and third trimesters. No significant overall differences were found for TC or LDL-C.	
5	2021	Observational study in obese pregnant women	Among women who developed GDM, TG was higher than in women without GDM (144.57 vs 115.14 mg/dL), although the TG difference was not statistically significant. HDL-C was significantly lower in the GDM group (56.32 vs 66.18 mg/dL; p=0.038), while TyG index was		6	Systematic review by Ryckman et al., and meta-analysis; 60 studies	
			HDL-C and TyG may provide additional information regarding early metabolic risk in obese pregnant women.				Highest vs lowest TG quartile Early lipid measurements may help identify women at increased risk of GDM and preeclampsia.
				7	2025	Early-pregnancy lipid cohort study, Prospective cohort; 32,411 pregnant women	

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Re f.	Study Year	Study / design & Major population findings	Key conclusion	Re f.	Study Year	Study / design & Major population findings	Key conclusion
8	Liu et al., 2025	Prospective Birth Cohort; 10,215 offspring	(OR 1.396). TG/HDL-C was strongly associated with preeclampsia (OR 2.451). First-trimester maternal dyslipidemia was associated with GDM (adjusted RR 1.36), Early maternal dyslipidemia is associated with important adverse maternal and neonatal outcomes. No significant association was found with gestational hypertension or SGA after adjustment.	10	Yang et al., 2025	women TC (5.52 control vs 5.41 adequate. mmol/L), LDL-C (2.71 vs 2.63 mmol/L) and lower HDL-C (1.88 vs 2.00 mmol/L). High TG independently predicted preeclampsia, preterm birth, macrosomia, postpartum hemorrhage and fetal distress. Established trimester-specific reference intervals. TG increased approximately 2.5-fold from the first trimester to delivery, while TC	was adequate. mmol/L), LDL-C (2.71 vs 2.63 mmol/L) and lower HDL-C (1.88 vs 2.00 mmol/L). High TG independe ntly predicted preeclamp sia, preterm birth, macrosomi a, postpartum hemorrhag e and fetal distress. Gestational-age-specific lipid reference ranges are important for interpreting maternal dyslipidemia.
9	Zhao et al., 2025	Retrospective study; 1,001 NGT and 1,078 GDM	GDM women had higher TG (2.18 vs 1.82 mmol/L), TG remained an important predictor of adverse outcomes even when glycemic				

Re Study f. Year	Study / design & Major population findings	Key conclusion	Lipid parameter	Findings across studies	Clinical interpretation
		and LDL-C increased approximately 1.5-fold. Lipid levels outside the pregnancy-specific reference intervals were associated with adverse pregnancy outcomes.	HDL-C	Frequently lower in May GDM, particularly increased in later pregnancy	reflect increased insulin resistance
			VLDL-C	Increased in GDM	Reflects increased hepatic TG-rich lipoprotein production
			TG/HDL-C ratio	Increased in GDM and associated with preeclampsia	Potential surrogate marker of insulin resistance
			TyG index	Higher in women at increased metabolic/GDM risk	Potential early predictor of insulin resistance
			Remnant cholesterol	Higher early in pregnancy associated with GDM	Emerging biomarker with requiring further validation

Table 2. Overall lipid-profile pattern reported across the references

Lipid parameter	Findings across studies	Clinical interpretation
Triglycerides (TG)	Consistently increased in GDM; strongest and most reproducible association	Most important lipid marker associated with GDM and adverse outcomes
Total cholesterol (TC)	Generally increased in GDM and progressively rises during pregnancy	May contribute to metabolic risk but is less specific than TG
LDL-C	Results are inconsistent; physiological pregnancy-related increase complicates	Should be interpreted according to trimester

Across these 10 references, **hypertriglyceridemia emerged as the most consistent lipid abnormality associated with GDM**. The evidence also supports an association between maternal dyslipidemia—particularly elevated TG—and **preeclampsia, preterm birth, macrosomia and LGA birth**. However, because lipid concentrations physiologically increase during pregnancy, **trimester-specific interpretation is essential**.

DISCUSSION

The present review demonstrates that alterations in maternal lipid metabolism are closely associated with gestational diabetes mellitus (GDM) and may contribute to adverse maternal and fetal outcomes. Although pregnancy itself produces physiological increases in circulating lipids, the available evidence suggests that women with GDM exhibit a more pronounced metabolic disturbance, particularly characterized by elevated triglycerides (TG), altered

HDL-C, and increased lipid-derived indices. The following discussion integrates the findings of references 1–10 with additional recent evidence from references 11–20.

Association between triglycerides and GDM

Among all lipid parameters, TG showed the most consistent association with GDM. Jin et al., in a large systematic review and meta-analysis involving **292 studies and 97,880 pregnant women**, reported approximately 20% higher TG concentrations in women with GDM, with the difference already detectable during the first trimester (3). This finding is particularly important because it suggests that lipid abnormalities may precede the conventional diagnosis of GDM.

Rahnemaei et al. similarly reported that TG demonstrated the largest pooled difference between women with GDM and normal pregnant women, with an SMD of **1.14**, substantially greater than the differences observed for TC, HDL-C, or LDL-C (4). These findings support the concept that hypertriglyceridemia is not simply a consequence of late pregnancy but may reflect an underlying metabolic phenotype associated with GDM.

Ryckman et al. also demonstrated that TG concentrations were significantly higher in women with GDM throughout all three trimesters, with a pooled weighted mean difference of approximately **30.9 mg/dL** (6). Thus, the consistency of findings across different populations and study designs strengthens the association between hypertriglyceridemia and GDM.

Pathophysiological link between insulin resistance and dyslipidemia

The association between GDM and dyslipidemia can be explained largely by pregnancy-associated insulin resistance. As gestation progresses, placental hormones reduce insulin sensitivity, particularly in adipose tissue and skeletal muscle. In women who develop GDM, this physiological insulin resistance becomes excessive relative to β -cell compensatory capacity.

Reduced insulin-mediated suppression of hormone-sensitive lipase increases adipose-tissue lipolysis and releases free fatty acids into the circulation. Increased hepatic uptake of fatty acids subsequently promotes triglyceride synthesis and VLDL secretion. This

mechanism provides a biological explanation for the consistently elevated TG concentrations observed in women with GDM (1–4).

The relationship may also be bidirectional. Excess circulating free fatty acids can impair insulin signaling and promote oxidative stress, thereby worsening insulin resistance. Consequently, dyslipidemia may not simply be a biochemical consequence of GDM but may participate in the progression of metabolic dysfunction.

Importance of trimester-specific lipid assessment

An important finding emerging from recent evidence is that lipid abnormalities should be interpreted according to gestational age. A recent trimester-specific systematic review and meta-analysis demonstrated that TG and the TG/HDL-C ratio were significantly elevated in GDM during all three trimesters. TC and LDL-C showed significant differences mainly during the first and second trimesters, whereas HDL-C was generally lower in GDM pregnancies (12).

These observations are consistent with the earlier findings of Ryckman et al. (6) and Jin et al. (3). They also emphasize why conventional non-pregnant lipid reference ranges may be inappropriate during pregnancy.

A recent systematic review and meta-analysis specifically addressing pregnancy-specific lipid reference ranges emphasized that maternal lipid concentrations increase physiologically throughout gestation and that trimester-specific reference intervals are necessary to avoid misclassification of normal pregnancy-related changes as pathological dyslipidemia (13).

Early pregnancy lipid abnormalities and prediction of GDM

One of the most clinically promising findings is that dyslipidemia may be detectable before GDM is conventionally diagnosed. Liu et al. reported that first-trimester maternal dyslipidemia was associated with a **36% higher risk of GDM** after adjustment for potential confounders (8). The same study found increased risks of preterm birth and LGA birth, suggesting that early lipid abnormalities may identify women with an unfavorable metabolic phenotype.

Similarly, a large 2025 cohort study demonstrated significant associations between early-pregnancy TG, TC, remnant cholesterol, and subsequent GDM (14). The TG/HDL-C ratio was also associated with preeclampsia, further supporting the potential value of lipid-derived markers for early risk stratification.

However, these findings should not yet be interpreted as evidence that lipid testing can replace the oral glucose tolerance test. Rather, lipid parameters may eventually complement established clinical and glucose-based risk assessment. Such early identification may have value within the wider health system.

TG/HDL-C ratio and insulin resistance

The TG/HDL-C ratio has gained increasing attention because it incorporates two metabolically interconnected lipid fractions. Higher TG together with lower HDL-C generally reflects a more insulin-resistant and atherogenic metabolic phenotype.

Rahnemaei et al. reported a significantly higher TG/HDL-C ratio in women with GDM (4). More recent evidence has reinforced this association. A 2026 meta-analysis involving **23 studies and more than 180,000 participants** found that elevated TG/HDL-C was associated with GDM and LGA, while elevated TyG was associated with GDM, preeclampsia, gestational hypertension, preterm birth, and LGA (15).

Nevertheless, the clinical utility of TG/HDL-C depends on population-specific thresholds and standardized laboratory measurements. Therefore, it should currently be considered an adjunctive risk marker rather than a diagnostic test.

Triglyceride-glucose index and GDM

The TyG index combines fasting TG and glucose and has emerged as a surrogate marker of insulin resistance. A systematic review and meta-analysis reported that TyG was significantly higher among women with GDM, although heterogeneity between studies was substantial (16).

A subsequent umbrella review of meta-analyses found a significant association between elevated TyG and GDM, with an OR of approximately **2.41**, although the authors noted that the overall epidemiological evidence remained limited (17).

The advantage of TyG is that it combines two routinely available biochemical parameters. However, differences in fasting status, gestational age, diagnostic criteria, and population characteristics remain major limitations. Larger prospective studies are needed before TyG can be incorporated into routine antenatal screening algorithms.

Association with fetal growth and macrosomia

The relationship between maternal dyslipidemia and fetal growth is biologically plausible. The fetus depends substantially on maternal lipid-derived substrates, while placental lipases facilitate the hydrolysis of maternal triglyceride-rich lipoproteins and release fatty acids for placental and fetal utilization.

In women with GDM, the combination of maternal hyperglycemia and hypertriglyceridemia may therefore provide an increased nutrient supply to the fetus. This may contribute to excessive fetal adiposity and macrosomia.

Shi et al. found that in women with GDM, every 1 mmol/L increase in second-trimester TG was associated with higher odds of LGA and macrosomia, and the associations were even stronger during the third trimester (18).

Similarly, Song et al. demonstrated that GDM and high TG levels contributed to the relationship between pre-pregnancy overweight/obesity and macrosomia (19). These findings suggest that maternal glucose and lipid abnormalities may act together rather than independently in determining fetal growth.

Association with adverse maternal and neonatal outcomes

The clinical significance of maternal dyslipidemia extends beyond GDM and fetal overgrowth. Zhao et al. reported that among women with GDM, elevated TG was associated with several adverse outcomes, including preeclampsia, preterm birth, macrosomia, postpartum hemorrhage, and fetal distress (10).

The findings of Shi et al. further demonstrated associations between higher TG levels and cesarean delivery, LGA, macrosomia, and neonatal unit admission (18). These associations remained significant after adjustment for relevant confounding factors.

A 2025 prospective cohort study also found that first-trimester maternal dyslipidemia increased the risks of GDM, preterm birth, and LGA birth, although significant associations were not observed for all pregnancy outcomes (8). This variation highlights that lipid-related risk is multifactorial and may depend on the specific lipid fraction, timing of measurement, maternal BMI, glycemic control, and other clinical factors.

CONCLUSION

Pregnancy is associated with substantial physiological alterations in lipid metabolism, but these changes become more pronounced and clinically relevant in women with gestational diabetes mellitus (GDM). Among the lipid parameters, **elevated triglycerides appear to be the most consistent abnormality associated with GDM**, while reduced HDL-C and increased TG/HDL-C and TyG indices may further reflect underlying insulin resistance. Maternal dyslipidemia, particularly hypertriglyceridemia, has been associated with **preeclampsia, preterm birth, macrosomia, large-for-gestational-age infants, and other adverse pregnancy outcomes**. Early-pregnancy lipid abnormalities may therefore have potential value for identifying women at increased metabolic risk before conventional GDM diagnosis. However, physiological gestational changes necessitate **trimester-specific interpretation**, and lipid parameters should currently complement rather than replace established glucose-based diagnostic criteria. Further large, prospective studies are required to establish standardized lipid cut-offs and determine whether early identification and targeted management of dyslipidemia can improve maternal and fetal outcomes.

Limitations

Most available evidence is observational and heterogeneous regarding gestational age, population characteristics, diagnostic criteria, and lipid cut-offs. Further large, prospective multicenter studies are needed to establish standardized trimester-specific lipid thresholds and confirm causal relationships with pregnancy outcomes. These considerations may ultimately contribute to improved maternal and fetal outcomes and child wellbeing.

Future Prospects

Future research should focus on establishing **trimester-specific lipid reference ranges**

and validated cut-off values for early prediction of GDM and adverse pregnancy outcomes. Large prospective studies should evaluate the predictive value of **triglycerides, TG/HDL-C ratio, TyG index, and remnant cholesterol**, while investigating whether early lifestyle or targeted metabolic interventions can improve maternal and fetal outcomes. Future research should also evaluate the role of healthy lifestyle interventions alongside targeted metabolic strategies.

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