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Original Research Article

Fetomaternal outcomes of hyperlipidemia in pregnancy

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ABSTRACT

Background: Maternal lipid levels increase physiologically during pregnancy; however, excessive elevations may be associated with adverse maternal and neonatal outcomes. This study aimed to evaluate maternal lipid profile patterns and their association with fetomaternal outcomes.
Methods: This prospective observational study was conducted on 100 singleton pregnant women with gestational age >28 weeks attending the antenatal clinic and labour room of Pt. B.D. Sharma PGIMS, Rohtak. Detailed history, clinical examination, and body mass index (BMI) assessment were performed. Lipid profiles were analyzed using auto-analyzers. Hyperlipidemia was defined as total cholesterol >200 mg/dL, triglycerides (TGs) ≥150 mg/dL, high-density lipoprotein (HDL-C)≤45 mg/dL, or low-density lipoprotein (LDL)≥130 mg/dL. Participants were followed until delivery and maternal and neonatal outcomes were recorded.
Results: Hyperlipidemia was observed in 98% of the study participants. Elevated TGs were seen in 86% and elevated LDL in 37%. Hypercholesterolemia was significantly associated with induction of labour (35.71%, p=0.024). Pre-eclampsia occurred in 22.45% cases, PROM in 21.43%, intrahepatic cholestasis of pregnancy (IHCP) in 8.16%, fetal growth restriction in 3.06% and gestational diabetes mellitus (GDM) in 1.02%. Low HDL levels were significantly associated with maternal anaemia (p=0.012) and elevated LDL levels with IHCP (p=0.049). Low birth weight was observed in 35% neonates and 26.53% required NICU admission, most commonly due to prematurity.
Conclusions: Maternal hyperlipidemia was associated with increased maternal complications such as pre-eclampsia, IHCP, and anaemia, as well as neonatal prematurity and NICU admissions. Monitoring lipid profiles during pregnancy may help identify women at risk of adverse fetomaternal outcomes.

Keywords: Hyperlipidemia, Pregnancy, Lipid profile, Maternal outcomes, Neonatal outcomes, Preeclampsia

INTRODUCTION

Lipids, including TGs, phospholipids, and steroids, play essential roles in the body such as vitamin absorption, cell membrane formation, and steroid precursor synthesis.[1] Cholesterol and TGs require lipoproteins for plasma transport, with LDL and VLDL facilitating lipid distribution, while HDL mediates reverse cholesterol transport.[2] Dyslipidemia, particularly hyperlipidemia, is characterized by elevated levels of LDL, total cholesterol, or TGs, or reduced HDL levels.[3] Pregnancy-induced hyperlipidemia arises due to hormonal and metabolic changes essential for fetal development.[4]

Maternal hyperlipidemia peaks in the third trimester due to increased estrogen-driven triglyceride synthesis and reduced clearance.[5] Elevated lipid levels have been linked to gestational hypertension (GHTN), preeclampsia, GDM, and IHCP.[6] Hyperlipidemia is also implicated in inflammation and oxidative stress, contributing to preterm labor (PTL). Elevated triglyceride levels predict GDM and

hypertensive disorders, while high LDL and low HDL levels are associated with poor pregnancy outcomes.[7]

Fetal growth and development is also influenced by maternal lipid levels. High maternal triglyceride levels correlate with large-for-gestational-age (LGA) infants and macrosomia, while low levels are linked to small-for-gestational-age (SGA) outcomes. Dyslipidemia contributes to placental insufficiency, affecting nutrient transport and fetal metabolic programming, increasing long-term cardiometabolic risks.[8]

Recent studies have highlighted the role of altered maternal lipid metabolism in the development of adverse pregnancy outcomes such as hypertensive disorders of pregnancy, GDM, and preterm birth.[13,18] Increasing evidence suggests that maternal dyslipidemia may influence placental function, oxidative stress, and inflammatory pathways, thereby contributing to abnormal fetomaternal outcomes.[8] However, data from Indian populations remain limited, necessitating further evaluation of lipid profile patterns and their clinical significance during pregnancy.

This study highlights the need for further research and preventive strategies tailored to populations such as Indian women, where lifestyle changes and dietary patterns contribute to increased dyslipidemia rates. The present study aimed to evaluate maternal lipid profile patterns in late pregnancy and their association with adverse maternal and neonatal outcomes.

METHODS

This prospective observational study was conducted from October 2023 to December 2024 in the Antenatal OPD, Labour Room, and Department of Biochemistry at Pt. B.D. Sharma PGIMS, Rohtak. One hundred singleton pregnant women with >28 weeks gestation visiting the antenatal clinic and labour room were enrolled into our study. Our exclusion criteria were tobacco/alcohol/drug use affecting lipid metabolism, pre-existing diabetes, inherited metabolic or thyroid disorders, and conception via assisted reproductive techniques.

Ethical clearance was obtained, and informed consent was secured. Gestational age was determined via LMP or first-trimester ultrasound. Comprehensive history, general/obstetric examination, and BMI assessment were conducted. Lipid profiles were analyzed using auto-analyzers, and hyperlipidemia was defined as cholesterol >200 mg/dl, TG ≥150 mg/dl, HDL-C ≤45 mg/dl, or LDL ≥130 mg/dl.

Participants were followed every two weeks until 36 weeks, then weekly until delivery and discharge. Pregnancy outcomes included preeclampsia, GDM, preterm birth, cholestasis, and delivery mode. Neonatal outcomes such as birth weight and APGAR scores [9] were recorded.

GDM was identified in them by glucose challenge test (GCT) on those exceeding values of >140 mg/dl at ≥28 weeks of gestation as per DIPSI criteria. [10] Preeclampsia was diagnosed by the presence of new hypertension ≥140/90 after 20 weeks' gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury, liver dysfunction, neurological features, haemolysis or thrombocytopenia, and/or fetal growth restriction, however proteinuria is not mandatory for the diagnosis.[10] Cholestasis was identified clinically based on pruritus and deranged liver function test.[11] Preterm birth was defined as delivery before 37 completed weeks of gestation.[12]

Neonatal birthweight and APGAR Scores were noted post-delivery of all the enrolled patients in this study and those <2500 gm were considered LBW, 2500-3500 normal, >3500 gm LGA and >4000 gm macrosomia. Statistical analysis was performed to assess the effects of maternal hyperlipidemia on pregnancy and neonatal outcomes. Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). A $p<0.05$ was considered statistically significant.

RESULTS

The mean age of the participants was 26.19±5.3 years, with a mean gestational age of 31.92±3.01 weeks at the time of admission. Amongst our study subjects, 41% were primi gravida and 59% were multi gravida. The majority of patients (90%) had a normal BMI, and no significant association between BMI and hyperlipidemia was observed.

Table 1: Demographic characteristics of study participants.

Variables	Values
Mean age (in years)	26.19±5.3
Mean gestational age at recruitment	31.92±3.01 weeks
Primigravida	41%
Multigravida	59%
BMI normal	90%

The majority of participants demonstrated abnormal lipid profiles, with 56% exhibiting deranged total cholesterol (≥200 mg/dL), 86% with elevated TGs (>150 mg/dl), and 96% with high VLDL (>32 mg/dl). Furthermore, 37% of the participants had deranged LDL (>130 mg/dl), and 39% had low HDL (≤45 mg/dl). Overall, 98% of the participants were found to have hyperlipidemia, with only 2% having a normal lipid profile.

The study observed that total cholesterol had the lowest sensitivity (17.91%) and highest specificity (100%) in predicting adverse outcomes, while TGs demonstrated the highest sensitivity (82.09%) but the lowest specificity (36.36%). The highest PPV was found for total cholesterol (100%), and the highest NPV was found for TGs (50%). None of the lipid parameters exhibit strong diagnostic

power (AUC>0.7). Total cholesterol has the weakest predictive ability, while HDL shows slightly better discrimination but remains below the fair threshold. These findings suggest that while lipid levels may contribute to risk assessment, they should not be used as standalone biomarkers for maternal or fetal complications (Table 2).

The chi-square (χ^2) test was applied for comparisons with expected counts ≥5, while Fisher's exact test was used for smaller counts. Significant findings were defined as $p<0.05$. All tools used, including lipid assays and scoring systems, are free to use or licensed for clinical/research purposes.[9]

A significant association was observed between elevated total cholesterol levels (≥200 mg/dL) and induction of labor, with a higher proportion of induced labor among women with deranged cholesterol compared to those with normal levels (35.71% vs. 13.51%; $\chi^2(1)=5.07$, $p=0.024$). Low HDL levels (<50 mg/dL) were also significantly associated with maternal anemia (44.90% vs. 10.20%; $\chi^2(1)=6.30$, $p=0.012$). In addition, elevated LDL levels (>130 mg/dL) showed a significant association with IHCP (18.92% vs. 1.59%; $p=0.049$, Fisher's exact test). No statistically significant associations were found between triglyceride levels and preeclampsia or between total cholesterol levels and pre-eclampsia (Table 3).

Chi-square (χ^2) tests were applied for outcomes with expected counts ≥5, while Fisher's Exact test was used for smaller counts. A $p<0.05$ was considered statistically significant. Lipid assays and scoring systems, including Apgar scoring, are free to use or appropriately licensed for research purposes.[9]

With regards to preterm birth, 32% of the study population experienced premature deliveries, with 21% of cases occurring between 32 and 36 weeks, and 11% between 28 and 31 weeks. Hyperlipidemic women showed a higher incidence of premature rupture of membranes (PROM) (21.43%, $p=1$) and PTL (18.37%, $p=0.345$), although these results were not statistically significant. When considering lipid profiles, total cholesterol and TGs showed comparable results for PROM and PTL.

Neonatal outcomes revealed that 35% of the neonates were classified as low birth weight (LBW), with 13% being very low birth weight (VLBW), and 2% as extremely low birth weight (ELBW). However, no significant association was found between maternal hyperlipidemia and small for gestational age (SGA) neonates, as the distribution of SGA was similar across lipid parameters.

Neonates born to hyperlipidemic mothers showed a 26.53% NICU admission rate, with prematurity being the most common cause (69.23%) (Table 4).

Overall, the findings of the present study suggests that hyperlipidemia in pregnancy, particularly elevated total cholesterol, TGs, and LDL, is associated with a higher incidence of maternal complications such as preeclampsia, IHCP, and anaemia. While there was no significant impact on fetal growth or SGA, there was a notable association with neonatal prematurity and NICU admissions.

The findings highlight the importance of monitoring lipid profiles in pregnant women, particularly in those with abnormal cholesterol and lipid levels, as they are more likely to experience complications.

Table 2: Diagnostic performance of lipid parameters for predicting maternal and fetal outcomes.

Lipid parameters	Outcome type	Outcome	Sensitivity	Specificity	PPV	NPV	Optimal threshold (mg/dl)
Total cholesterol	Maternal	Preeclampsia (≥200 mg/dl)	68%	76%	45%	89%	284.48
Total cholesterol	Fetal	Low birth weight (<2.5 kg) (≥200 mg/dl)	58%	74%	37%	88%	-
TGs	Maternal	PTL (≥150 mg/dl)	72%	69%	39%	89%	183.22
TGs	Fetal	NICU admissions (≥150 mg/dL)	70%	77%	43%	91%	-
LDL	Maternal	IHCP (>130 mg/dl)	77%	82%	46%	95%	89.54
LDL	Fetal	Low Apgar scores (<7 at 5 min) (>130 mg/dl)	64%	80%	35%	92%	-
HDL	Maternal	Labor induction (<40 mg/dl)	61%	85%	51%	89%	56.50
HDL	Fetal	Respiratory distress	4.76%	16.22%	-	-	-
HDL	Fetal	Low Apgar (<7)	7.94%	32.43%	-	-	-

*PPV=Positive predictive value; NPV=Negative predictive value; PTL=Preterm labour; NICU=Neonatal intensive care unit; LDL=Low-density lipoprotein; HDL=High-density lipoprotein; IHCP=Intrahepatic cholestasis of pregnancy. Diagnostic performance parameters were derived from ROC curve analysis; chi-square testing was not applicable. NICU: neonatal intensive care unit and APGAR score.[9]

Table 3: Association between lipid parameters and maternal outcomes.

Lipid parameters	Outcome	Cut-off	Normal, N (%)	Deranged, N (%)	χ^2, (df=1)	P value	Interpretation
Total cholesterol	Preeclampsia	≥200 mg/dl	7 (15.91)	15 (26.79)	1.70	0.192	Not significant
Total cholesterol	Labor induction	≥200 mg/dl	5 (13.51)	15 (35.71)	5.07	0.024	Significant
Total cholesterol	IHCP	≥200 mg/dl	1 (2.27)	7 (12.50)	-	0.075	Borderline
TGs	Preeclampsia	≥150 mg/dl	2 (14.29)	20 (23.26)	-	0.729	Not significant
HDL	Anemia	<50 mg/dl	5 (10.20)	22 (44.90)	6.30	0.012	Significant
LDL	IHCP	>130 mg/dl	1 (1.59)	7 (18.92)	-	0.049	Significant

Table 4: Association between lipid parameters and neonatal outcomes.

Lipid parameter	Outcome	Lipid cutoff	Normal cases (%)	Deranged cases (%)	χ^2 value	P value	Test used	Significant finding
Total cholesterol	Birth weight <1 kg	≥200 mg/dl	0 (0%)	2 (3.57%)	-	0.053	Fisher's exact	Borderline significant
Total cholesterol	Birth weight 2.5-3.5 kg	≥200 mg/dl	15 (34.09%)	32 (57.14%)	5.26	0.022	Chi-square	Yes
LDL	NICU admission	>130 mg/dl	11 (17.46%)	15 (40.54%)	6.46	0.474	Chi-square	No
Any lipid derangement	Respiratory distress	-	3 (4.76%)	6 (16.22%)	-	0.087	Fisher's exact	No
Any lipid derangement	Low Apgar (<7)	-	5 (7.94%)	12 (32.43%)	-	0.072	Fisher's exact	Borderline significant

DISCUSSION

This prospective observational study aimed to evaluate the effects of hyperlipidemia in pregnancy on maternal and fetal outcomes. The study enrolled 100 pregnant women, and we observed various lipid profile abnormalities, including elevated total cholesterol, TGs, LDL cholesterol (LDL-C), and low high-density lipoprotein cholesterol (HDL-C). The results of our study were compared to findings from other studies in order to assess the association of dyslipidemia with maternal and fetal complications.

98% of the participants exhibited hyperlipidemia, with significant proportions of cases showing deranged triglyceride levels (86%), VLDL (96%), and total cholesterol (56%). This is consistent with other studies like, Divyanee et al reported a hyperlipidemia prevalence of 47.8%, while Singh et al found a lower prevalence of 35.5%.[13,14] This suggests a variable but generally high prevalence of lipid abnormalities in pregnancy. The higher prevalence in our study could be due to the inclusion of women with late-stage pregnancies (≥28 weeks of gestation), as lipid levels rise significantly in the second and third trimesters, as evidenced in other research.

This study found that hyperlipidemia was associated with various maternal complications, including preeclampsia (22.45%), PTL (18.37%), anemia (20.51%), intra-hepatic cholestasis of pregnancy (IHCP) (8.16%), and GDM (1.02%). The association of hyperlipidemia with preeclampsia, in particular, has been reported by multiple studies. For example, Kumari et al observed a significant association between total cholesterol and TGs with preeclampsia ($p<0.0001$).[15] However, our study did not find statistically significant associations between hyperlipidemia and preeclampsia ($p=1$), which may be attributable to the small sample size in our study.

The high prevalence of hyperlipidemia observed in our study may reflect the physiological metabolic adaptations of late pregnancy, where increased estrogen levels stimulate hepatic lipid synthesis. However, excessive lipid elevation may contribute to endothelial dysfunction, oxidative stress, and inflammatory responses, which are known mechanisms involved in the development of hypertensive disorders and placental insufficiency. These mechanisms may explain the increased frequency of complications such as preeclampsia and prematurity observed in our study population.

The study also observed an association between high cholesterol levels and intra-hepatic cholestasis of pregnancy (IHCP), where high total cholesterol levels were significantly correlated with the condition ($p=0.049$). This mirrors findings from other research that linked hyperlipidemia to the risk of IHCP, which can lead to severe maternal and fetal outcomes.[16]

Furthermore, a significant correlation between low HDL cholesterol levels and anemia ($p=0.012$) was observed. Low HDL-C has been linked to various hematological disorders, and our study strengthens the notion that dyslipidemia can impair oxygen delivery during pregnancy, exacerbating the risk of anemia. This is especially concerning since anemia is a known risk factor

for PTL and low birth weight, which were also seen in our study.

However, we did not observe a significant association between hyperlipidemia and gestational diabetes mellitus (GDM), which contradicts studies such as Jin et al who found TGs and HDL-C to be significantly associated with GDM.[6]

This study found 35% of neonates were born with LBW, 13% with very low birth weight (VLBW), and 2% with extremely low birth weight (ELBW), there was no significant association between maternal lipid levels and these outcomes. This contrasts with findings from studies by Jin et al who reported a significant association between TGs and birth weight (OR 1.19, 95% CI: 1.02-1.39), and Sharami et al who found a higher risk of FGR in pregnancies complicated by hyperlipidemia.[6,17]

Further, this study did not identify any cases of LGA infants, which aligns with the findings from Singh et al that also did not observe an increased risk of LGA associated with maternal dyslipidemia. However, other studies such as Gulati et al and Parveen reported significant associations between dyslipidemia and fetal growth outcomes, indicating a need for larger studies to validate these findings.[13,14,16]

In this study, 26.53% of neonates born to mothers with hyperlipidemia required NICU admission, with the majority of cases linked to prematurity (69.23%), respiratory distress syndrome (RDS), and meconium aspiration syndrome (MAS). These findings align with those of other studies, including those by Gulati et al which observed a higher incidence of preterm birth and related complications in pregnancies complicated by hyperlipidemia. Although our study did not find a statistically significant association between hypercholesterolemia and low birth weight (p=0.053), the observed trend is consistent with existing literature that suggests maternal hyperlipidemia can adversely affect fetal growth.[13,18]

We also assessed the predictive value of lipid profiles for maternal and fetal outcomes. In our study, total cholesterol demonstrated the highest specificity (100%) and PPV (100%), while TGs showed the highest sensitivity (82.09%) but a lower NPV (50%). These results support findings by Singh et al who also observed that normal lipid profiles had high NPV (88.72%) for maternal complications.[14] However, predictive power of lipid profiles was less definitive in our study, particularly regarding PTL and preeclampsia, as evidenced by lack of statistically significant associations for many lipid parameters.

The findings of the present study contribute to emerging evidence that alterations in maternal lipid metabolism may play an important role in the development of adverse fetomaternal outcomes, particularly in late pregnancy. Early identification of abnormal lipid profiles may help clinicians identify high-risk pregnancies and implement closer monitoring to improve maternal and neonatal outcomes. However, larger multicentric studies are required to further clarify the role of maternal lipid profile as a potential screening marker for predicting adverse pregnancy outcomes.

Limitations

One of the major limitations of our study was the relatively small sample size, which may have influenced the statistical power and could explain the lack of significant associations between lipid derangements and certain maternal and fetal outcomes. Further research with a larger sample size is needed to confirm these results and elucidate the exact role of hyperlipidemia in pregnancy.

CONCLUSION

In conclusion, maternal hyperlipidemia is common during late pregnancy and may be associated with an increased risk of maternal complications such as pre-eclampsia, IHCP, and anaemia, as well as adverse neonatal outcomes including prematurity and NICU admission. Although individual lipid parameters demonstrated limited predictive value, abnormal lipid levels may serve as an early indicator of potential pregnancy complications. Monitoring maternal lipid profiles during pregnancy may therefore assist in identifying high-risk pregnancies and improving fetomaternal outcomes, particularly in resource-limited settings where early risk identification is crucial. Additionally, the exclusion of lipid-lowering medications in our cohort, due to their known teratogenic effects during pregnancy, further limits generalizability of findings. It would be beneficial to explore the effects of controlled lipid-lowering interventions during pregnancy in future studies.

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