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Original Research Article

Evaluation of Maternal Serum Lipid Profile in the Second Trimester as a Predictor of Preeclampsia: A Prospective Observational Study

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Abstract

Background: Preeclampsia is a major hypertensive disorder of pregnancy associated with significant maternal and perinatal morbidity and mortality. Early identification of women at risk allows timely preventive interventions and improved pregnancy outcomes. Abnormal maternal lipid metabolism has been implicated in endothelial dysfunction and placental vascular abnormalities, suggesting a potential role of lipid profile assessment as an early predictor of preeclampsia.

Aim: To evaluate the association between maternal serum lipid profile measured during the second trimester and subsequent development of preeclampsia.

Methods: This prospective observational study included 200 pregnant women between 14 and 20 weeks of gestation who were followed until delivery. Maternal serum lipid parameters, including total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, VLDL cholesterol, and TC/HDL ratio, were assessed at enrollment. Participants were categorized into preeclampsia and non-preeclampsia groups based on the development of hypertensive disorder during pregnancy. Lipid parameters were compared between groups, and ROC curve analysis was performed to evaluate their predictive ability.

Results: Among 200 participants, 24 (12.0%) developed preeclampsia. Women with preeclampsia had significantly higher levels of total cholesterol (205.42 ± 32.18 vs 174.36 ± 28.74 mg/dL), triglycerides (184.26 ± 42.35 vs 142.58 ± 36.21 mg/dL), LDL-C (128.74 ± 28.56 vs 108.32 ± 24.18 mg/dL), VLDL-C, and TC/HDL ratio, with significantly lower HDL-C levels (42.18 ± 6.42 vs 48.26 ± 7.18 mg/dL) compared with the non-preeclampsia group. ROC analysis showed triglycerides had the highest predictive performance (AUC 0.82) for predicting preeclampsia.

Conclusion: Second-trimester maternal serum lipid abnormalities are significantly associated with the development of preeclampsia. Lipid profile assessment may serve as a simple, accessible, and cost-effective screening tool for early risk prediction and improved antenatal surveillance.

Keywords: Preeclampsia; Pregnancy; Lipid profile; Triglycerides; Dyslipidemia; Second trimester; Predictive marker.

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Introduction

Preeclampsia is one of the most important hypertensive disorders of pregnancy and remains a major cause of maternal and perinatal morbidity and mortality worldwide. It is characterized by new-onset hypertension after 20 weeks of gestation, with or without proteinuria and/or maternal organ dysfunction [1]. Hypertensive disorders affect approximately 10% of pregnancies globally, while preeclampsia occurs in nearly 2–8% of pregnancies and is associated with complications such as fetal growth restriction, preterm birth, placental abruption, cerebrovascular events, renal impairment, and increased long-term cardiovascular risk [2,3]. The pathogenesis of preeclampsia involves multiple mechanisms, including abnormal placentation, defective spiral artery remodeling, impaired uteroplacental perfusion, oxidative stress, systemic inflammation, endothelial dysfunction, and imbalance between angiogenic and antiangiogenic factors [4].

Abnormal placental development leads to placental ischemia and release of circulating factors causing widespread endothelial injury and vascular dysfunction. Hence, early identification of high-risk women is essential for preventive interventions, close surveillance, and improved maternal and fetal outcomes [3].

According to the International Society for the Study of Hypertension in Pregnancy (ISSHP), hypertension in pregnancy is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg confirmed on repeated measurements. Early prediction of preeclampsia has become increasingly important due to the potential benefits of preventive measures such as low-dose aspirin therapy in high-risk women, which may reduce early-onset preeclampsia, fetal growth restriction, and preterm delivery [3]. Several clinical, biochemical, and biophysical markers, including mean arterial pressure, serum uric acid, pregnancy-associated plasma protein-A (PAPP-A), β-human chorionic gonadotropin (β-hCG), inflammatory markers, angiogenic factors, and uterine artery Doppler indices, have been investigated for prediction of preeclampsia [4–8]. However, many of these markers are expensive and require specialized facilities, limiting their routine clinical application[9].Previous studies have demonstrated that vascular changes, abnormal biochemical profiles, and impaired uteroplacental blood flow may precede the clinical onset of preeclampsia [10,1]. Therefore, there is a need for simple, inexpensive, and easily accessible biomarkers for early risk assessment.

Pregnancy is associated with physiological alterations in lipid metabolism, including increased levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C), with changes in high-density lipoprotein cholesterol (HDL-C) to meet fetal growth requirements [10]. However, excessive maternal dyslipidemia may contribute to preeclampsia through oxidative stress, endothelial dysfunction, vascular inflammation, and impaired placental function [10].

Elevated triglycerides and abnormal lipoprotein metabolism may promote lipid oxidation, endothelial injury, increased vascular resistance, and inflammatory responses, which are important mechanisms involved in the development of hypertension and proteinuria in preeclampsia [11].Several studies have reported that women who develop preeclampsia show higher levels of triglycerides, total cholesterol, and LDL-C, along with reduced HDL-C levels, even before clinical disease manifestation.

These findings suggest that lipid abnormalities may play a role in disease development; however, variations in population characteristics and study methodologies have resulted in inconsistent conclusions.[10,11]The second trimester provides a valuable window for identifying pregnancies at increased risk, as metabolic abnormalities associated with future preeclampsia may become detectable before clinical symptoms appear. Maternal serum lipid profile assessment during this period is simple, minimally invasive, cost-effective, and widely available for routine antenatal care.

Therefore, the present prospective Study was planned to Evaluation of Maternal Serum Lipid Profile in the Second Trimester as a Predictor of Preeclampsia

Material and Methods

The present study was conducted as a prospective observational study to evaluate the association between maternal serum lipid profile measured during the second trimester and the subsequent development of preeclampsia. All participants were followed prospectively from the second trimester until delivery for the development of preeclampsia and assessment of maternal and pregnancy outcomes. The study was carried out in the Department of Obstetrics and Gynaecology at a tertiary care healthcare center providing antenatal and obstetric services to pregnant women. The study population consisted of pregnant women attending the antenatal outpatient department for routine pregnancy care.

Study Setting and Duration: The study was conducted in the Department of Obstetrics and Gynaecology, ESIC Medical College, PGIMSR and Hospital, Kalaburagi, Karnataka, from January 2025 to August2025.

Study Population: The study included pregnant women presenting for antenatal care during the second trimester of pregnancy. A total of 200 pregnant women fulfilling the predefined eligibility criteria were enrolled in the study. All eligible participants were assessed at the time of recruitment, and maternal serum lipid profile was evaluated between 14 and 20 weeks of gestation. The enrolled women were prospectively followed throughout pregnancy until delivery to identify the development of preeclampsia. A total sample size of 200 pregnant women was included in the present study.

Inclusion Criteria

Pregnant women fulfilling the following criteria were included in the study:

- Pregnant women aged 18 years or above.
- Singleton pregnancy.
- Gestational age between 14 and 20 weeks at the time of enrollment.
- Women attending routine antenatal care.

- Women willing to participate in the study and provide written informed consent.
- Women available for regular antenatal follow-up until delivery.

Exclusion Criteria

Participants were excluded from the study if they had:

- History of chronic hypertension before pregnancy.
- Previous history of preeclampsia or eclampsia.
- Pre-existing diabetes mellitus or gestational diabetes diagnosed before enrollment.
- Chronic renal disease.
- Cardiovascular disease.
- Known thyroid disorders or endocrine disorders affecting lipid metabolism.
- Liver disease.
- Multiple pregnancy.
- Known autoimmune disorders.
- Current use of lipid-lowering medications.
- Any medical condition likely to affect pregnancy outcome or lipid profile interpretation.
- Women who were lost to follow-up during the study period.

Study Procedure

Baseline Assessment: After obtaining written informed consent, detailed demographic and clinical information was collected from all enrolled participants.

Baseline assessment included:

- Maternal age
- Gravida and parity status
- Gestational age
- Body mass index (BMI)
- Medical and obstetric history
- Family history of hypertension or metabolic disorders
- Blood pressure measurement
- General physical examination

Gestational age was confirmed using the last menstrual period and/or first-trimester ultrasonography findings.

Blood Pressure Assessment: Blood pressure was measured using a standardized technique with the participant in a comfortable sitting position after adequate rest. Blood pressure measurements were obtained using an appropriately sized cuff, and systolic and diastolic blood pressure values were recorded. Participants were monitored during subsequent antenatal visits for the development of hypertension. Preeclampsia was diagnosed according to standard criteria as the development of new-onset hypertension after 20 weeks of gestation with associated proteinuria and/or maternal organ dysfunction.

Assessment of Maternal Serum Lipid Profile

Sample Collection: Venous blood samples were collected from all participants during the second trimester between 14 and 20 weeks of gestation. Participants were advised overnight fasting before blood collection. Approximately 5 mL of venous blood was collected under aseptic precautions and transferred into appropriate sample containers. The collected blood samples were processed in the institutional laboratory for estimation of lipid parameters.

Lipid Profile Analysis: Maternal serum lipid profile was assessed using standard biochemical methods.

The following lipid parameters were evaluated:

- Total cholesterol (TC)
- Triglycerides (TG)
- High-density lipoprotein cholesterol (HDL-C)
- Low-density lipoprotein cholesterol (LDL-C)

All laboratory investigations were performed according to standard operating procedures of the institutional laboratory.

Follow-up and Outcome Assessment: All enrolled participants were followed prospectively during routine antenatal visits until delivery.

During follow-up, participants were assessed for:

- Development of gestational hypertension
- Development of preeclampsia
- Severity of preeclampsia
- Gestational age at delivery
- Mode of delivery
- Maternal complications
- Neonatal outcomes

Participants were categorized into:

1. Preeclampsia group – women who developed preeclampsia during pregnancy.
2. Non-preeclampsia group – women who remained normotensive throughout pregnancy.

Maternal lipid profile values were compared between both groups to evaluate their association with the development of preeclampsia.

Statistical Analysis: The collected data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 26 statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on the distribution of data. Categorical variables were presented as frequencies and percentages. Comparison of continuous variables between groups was performed using the Student's t-test for normally

distributed data or the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the Chi-square test or Fisher's exact test wherever appropriate. The association between maternal lipid parameters and development of preeclampsia was evaluated using appropriate statistical tests. Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive ability and optimal cut-off values of lipid parameters for predicting preeclampsia. A p-value <0.05 was considered statistically significant.

Results

A total of 200 pregnant women were enrolled in the present prospective observational study and were followed until delivery for the development of preeclampsia. The mean maternal age of the study participants was 26.84 ± 4.12 years. Majority of the participants belonged to the 20–29 years age group (142; 71.0%), followed by women aged ≥30 years (40; 20.0%), while 18 (9.0%) participants were below 20 years of age. Regarding parity distribution, 118 (59.0%) women were primigravida, whereas 82 (41.0%) were multigravida. The mean gestational age at enrollment was 16.82 ± 1.94 weeks, with more than half of the participants enrolled between 14–16 weeks of gestation (112; 56.0%), while 88 (44.0%) participants were enrolled between 17–20 weeks. The mean BMI of the study population was 24.18 ± 3.21 kg/m². Most women had normal BMI (<25 kg/m²) (128; 64.0%), whereas 54 (27.0%) were overweight and 18 (9.0%) were obese. A positive family history of hypertension was present in 34 (17.0%) participants, while a family history of diabetes/metabolic disease was reported in 26 (13.0%) women (Table 1).The overall distribution of baseline maternal characteristics of the study participants is depicted in Figure 1.Among the 200 enrolled women, 24 (12.0%) developed preeclampsia, while 176 (88.0%) remained normotensive throughout pregnancy. Comparison of second-trimester maternal serum lipid parameters demonstrated significant differences between women who developed preeclampsia and those who did not. The mean serum total cholesterol level was significantly higher among women who developed preeclampsia (205.42 ± 32.18 mg/dL) compared with the non-preeclampsia group (174.36 ± 28.74 mg/dL; p<0.001). Similarly, serum triglyceride levels were significantly elevated in the preeclampsia group (184.26 ± 42.35 mg/dL) compared with women without preeclampsia (142.58 ± 36.21 mg/dL; p<0.001).The mean LDL cholesterol level was also significantly higher among women with preeclampsia (128.74 ± 28.56 mg/dL) compared with the non-preeclampsia group (108.32 ± 24.18 mg/dL; p=0.001). In contrast, HDL cholesterol levels were significantly lower among women who developed preeclampsia (42.18 ± 6.42 mg/dL) compared with women without preeclampsia (48.26 ± 7.18 mg/dL; p<0.001). Additionally, VLDL cholesterol and TC/HDL ratio were significantly higher in the preeclampsia group (p<0.001). These findings suggest a significant association between abnormal second-trimester lipid profile and subsequent development of preeclampsia (Table 2).The comparison of individual lipid parameters between the preeclampsia and non-preeclampsia groups is illustrated in Figure 2.The association between abnormal maternal lipid parameters and occurrence of preeclampsia was evaluated among the study participants. Women with raised total cholesterol levels showed a significantly higher frequency of preeclampsia compared with those having normal cholesterol levels. Among women with raised total cholesterol, 14 (7.0%) developed preeclampsia, whereas only 10 (5.0%) cases of preeclampsia were observed among women with normal cholesterol levels (p<0.001). Similarly, elevated triglyceride levels were significantly associated with increased occurrence of preeclampsia. Among women with raised triglycerides, 16 (8.0%) developed preeclampsia, compared with 8 (4.0%) among women with normal triglyceride levels (p<0.001).Raised LDL-C levels were also associated with higher incidence of preeclampsia, with 13 (6.5%) women developing preeclampsia in the raised LDL-C group compared with 11 (5.5%) women in the normal LDL-C group (p=0.001). Furthermore, reduced HDL-C levels were significantly associated with preeclampsia, as 15 (7.5%) women with low HDL-C developed preeclampsia compared with 9 (4.5%) women with normal HDL-C levels (p<0.001) (Table 3).Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive ability of individual lipid parameters for development of preeclampsia. Serum triglyceride levels demonstrated the highest predictive performance among all evaluated lipid parameters, with an area under the curve (AUC) of 0.82 (95% CI: 0.74–0.90) at a cut-off value of >165 mg/dL, providing a sensitivity of 79.2% and specificity of 80.1% (p<0.001). Total cholesterol showed good predictive ability with an AUC of 0.78 (95% CI: 0.69–0.87) at a cut-off value of >190 mg/dL, with sensitivity and specificity of 75.0% and 76.7%, respectively. LDL-C demonstrated an AUC of 0.74 (95% CI: 0.64–0.84) at a cut-off value of >120 mg/dL, with sensitivity of 70.8% and specificity of 72.2%. HDL-C showed comparatively lower predictive performance, with an AUC of 0.71 (95% CI: 0.61–0.81) at a cut-off value of <45 mg/dL, sensitivity of 66.7%, and specificity of 70.5% (Table 4).

Table 1: Baseline Maternal Characteristics of Study Participants (n=200)

Variables	n (%) / Mean ± SD
Maternal age (years)	
Mean ± SD	26.84 ± 4.12
Age group (years)	
<20 years	18 (9.0%)
20–29 years	142 (71.0%)
≥30 years	40 (20.0%)
Parity	
Primigravida	118 (59.0%)
Multigravida	82 (41.0%)
Gestational age at enrollment (weeks)	
Mean ± SD	16.82 ± 1.94
14–16 weeks	112 (56.0%)
17–20 weeks	88 (44.0%)
BMI (kg/m²)	
Mean ± SD	24.18 ± 3.21
Normal BMI (<25 kg/m²)	128 (64.0%)
Overweight (25–29.9 kg/m²)	54 (27.0%)
Obese (≥30 kg/m²)	18 (9.0%)
Family history of hypertension	34 (17.0%)
Family history of diabetes/metabolic disease	26 (13.0%)

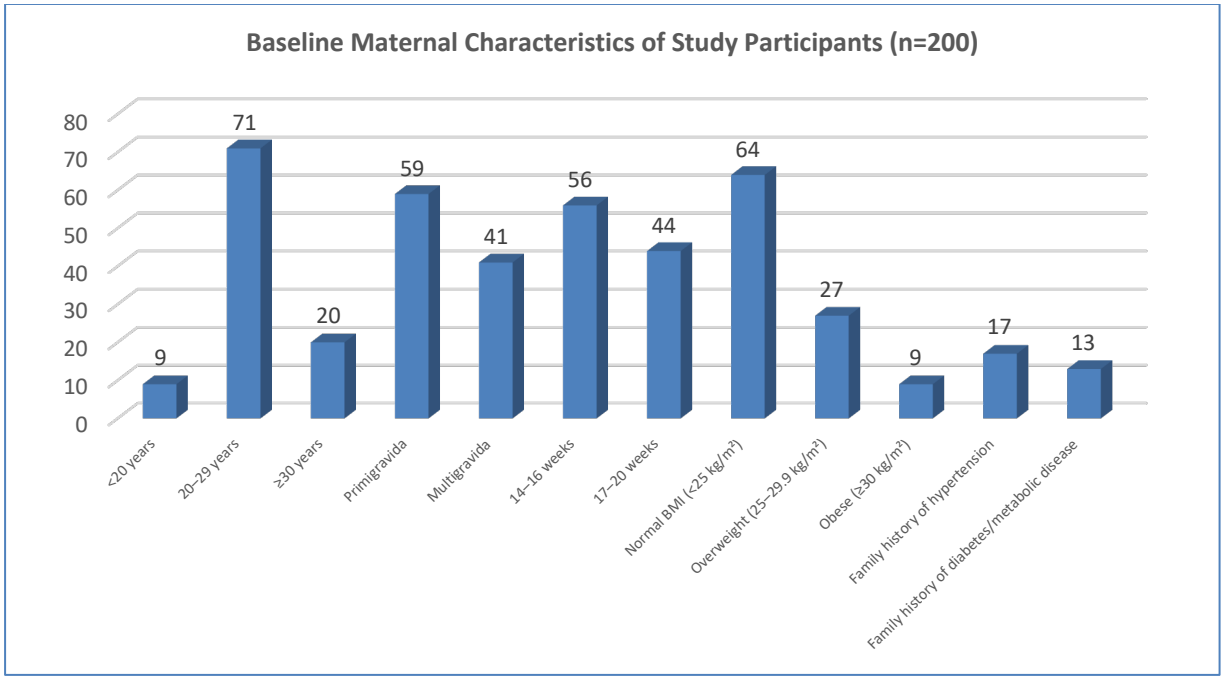

Figure 1: Baseline Maternal Characteristics of Study Participants (n=200)

Table 2: Comparison of Second Trimester Maternal Serum Lipid Profile between Preeclampsia and Non-Preeclampsia Groups

Lipid Parameters	Preeclampsia Group (n=24) Mean ± SD	Non-Preeclampsia Group (n=176) Mean ± SD	p-value
Total cholesterol (mg/dL)	205.42 ± 32.18	174.36 ± 28.74	<0.001*
Triglycerides (mg/dL)	184.26 ± 42.35	142.58 ± 36.21	<0.001*
LDL cholesterol (mg/dL)	128.74 ± 28.56	108.32 ± 24.18	0.001*
HDL cholesterol (mg/dL)	42.18 ± 6.42	48.26 ± 7.18	<0.001*
VLDL cholesterol (mg/dL)	36.84 ± 8.47	28.52 ± 7.24	<0.001*
TC/HDL ratio	4.92 ± 0.86	3.72 ± 0.74	<0.001*

***Statistically significant**

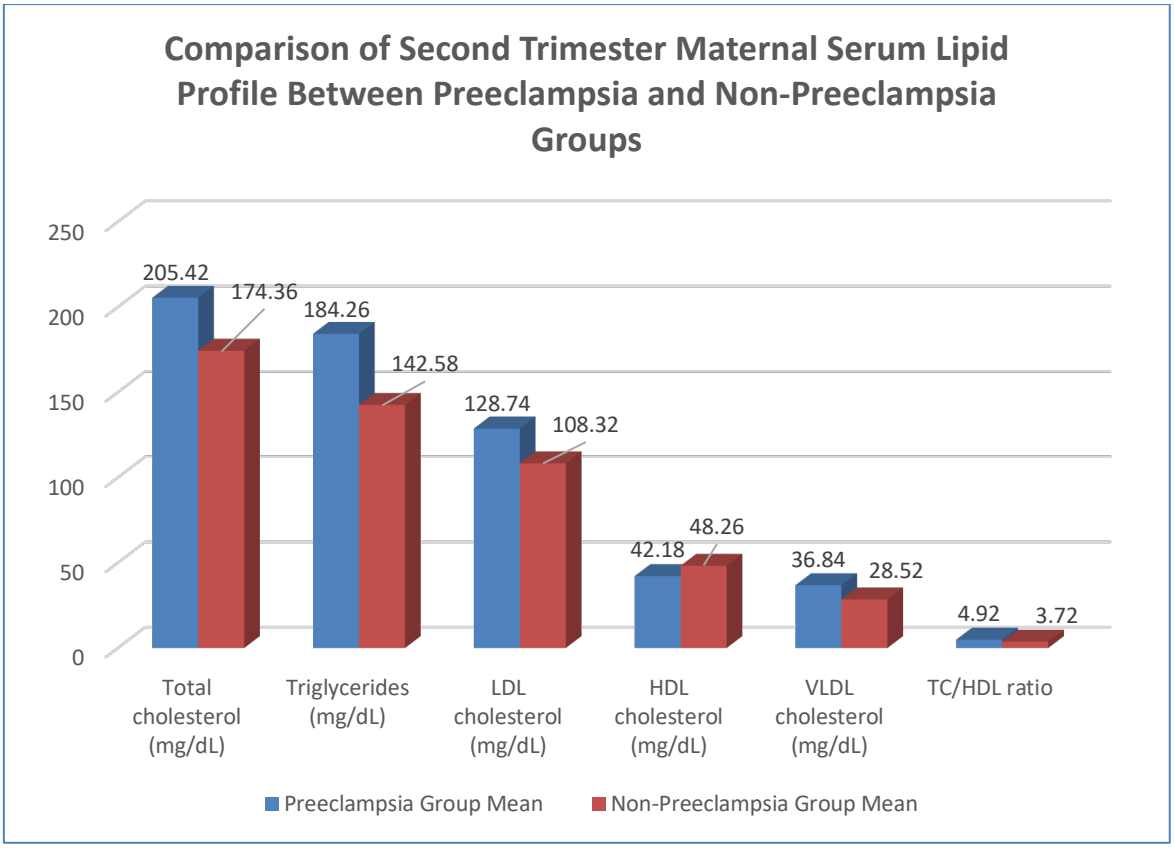

Figure 2: Comparison of Second Trimester Maternal Serum Lipid Profile between Preeclampsia and Non-Preeclampsia Groups

Table 3: Association between Abnormal Lipid Profile Parameters and Development of Preeclampsia (n=200)

Lipid Parameter	Lipid Status	Preeclampsia Present n (%)	Preeclampsia Absent n (%)	p-value
Total cholesterol	Normal	10 (5.0%)	150 (75.0%)	
	Raised	14 (7.0%)	26 (13.0%)	<0.001*
Triglycerides	Normal	8 (4.0%)	148 (74.0%)	
	Raised	16 (8.0%)	28 (14.0%)	<0.001*
LDL-C	Normal	11 (5.5%)	151 (75.5%)	
	Raised	13 (6.5%)	25 (12.5%)	0.001*
HDL-C	Normal	9 (4.5%)	142 (71.0%)	
	Reduced	15 (7.5%)	34 (17.0%)	<0.001*

Table 4: ROC Curve Analysis of Maternal Serum Lipid Parameters for Prediction of Preeclampsia

Parameter	Cut-off value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	p-value
Total cholesterol	>190 mg/dL	0.78 (0.69–0.87)	75.0	76.7	<0.001
Triglycerides	>165 mg/dL	0.82 (0.74–0.90)	79.2	80.1	<0.001
LDL-C	>120 mg/dL	0.74 (0.64–0.84)	70.8	72.2	<0.001
HDL-C	<45 mg/dL	0.71 (0.61–0.81)	66.7	70.5	<0.001

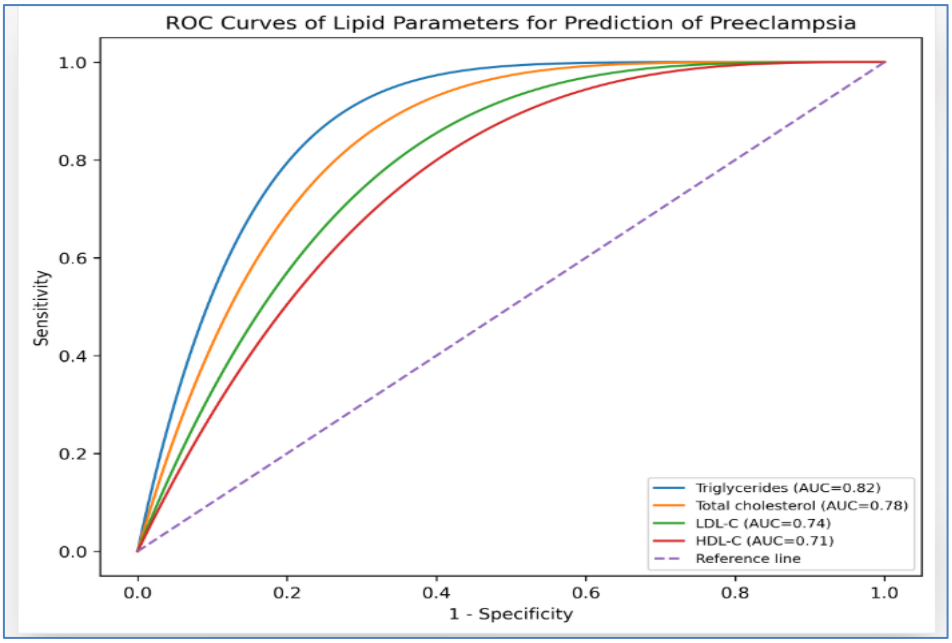

Figure 3: ROC Curve Analysis of Maternal Serum Lipid Parameters for Prediction of Preeclampsia

Discussion

The present prospective observational study evaluated the role of maternal serum lipid profile measured during the second trimester (14–20 weeks) as a predictor of subsequent preeclampsia. Among 200 pregnant women, 24 (12.0%) developed preeclampsia. Women who developed preeclampsia showed significantly adverse lipid profiles, including higher total cholesterol, triglycerides, LDL-C, VLDL-C, TC/HDL ratio and lower HDL-C levels, suggesting that lipid abnormalities precede clinical disease and may serve as early predictive markers. The study population had a mean maternal age of 26.84 ± 4.12 years, with 71.0% women aged 20–29 years. Primigravida women constituted 59.0%, and lipid assessment was performed at a mean gestational age of 16.82 ± 1.94 weeks. Most women had normal BMI (64.0%), indicating that the observed lipid alterations were not solely related to advanced maternal age or obesity. Women who developed preeclampsia had significantly higher total cholesterol levels than normotensive women (205.42 ± 32.18 vs 174.36 ± 28.74 mg/dL, p<0.001). Elevated total cholesterol was associated with increased preeclampsia risk, and ROC analysis showed that cholesterol >190 mg/dL predicted preeclampsia with an AUC of 0.78, sensitivity of 75.0% and specificity of 76.7%. Similar findings were reported by Li et al.[11], who observed significantly elevated second-trimester total cholesterol, triglycerides and LDL-C levels among women who developed preeclampsia. Yadav et al.[12] also demonstrated the usefulness of second-trimester lipid profiling as an early predictor of pregnancy-induced hypertension. Triglycerides showed the strongest association with preeclampsia in the present study, with significantly higher levels in affected women (184.26 ± 42.35 vs 142.58 ± 36.21 mg/dL, p<0.001). Triglyceride levels >165 mg/dL predicted preeclampsia with an AUC of 0.82, sensitivity of 79.2% and specificity of 80.1%. These findings are consistent with Tesfa et al.[13], who reported that elevated triglycerides, total cholesterol, LDL-C and VLDL-C were significantly associated with increased preeclampsia risk. Liu et al.[14] also highlighted second-trimester triglyceride elevation as an important predictor of late-onset preeclampsia. LDL-C levels were significantly higher among women with preeclampsia (128.74 ± 28.56 vs 108.32 ± 24.18 mg/dL, p=0.001), with LDL-C >120 mg/dL predicting preeclampsia (AUC 0.74, sensitivity 70.8%, specificity 72.2%). Li et al.[11] and Tesfa et al.[13] similarly reported significant associations between elevated LDL-C and preeclampsia development. VLDL-C was also significantly increased in the preeclampsia group (36.84 ± 8.47 vs 28.52 ± 7.24 mg/dL, p<0.001), supporting its role in vascular dysfunction through oxidative stress and inflammation.

Conversely, HDL-C levels were significantly lower among women who developed preeclampsia (42.18 ± 6.42 vs 48.26 ± 7.18 mg/dL, p<0.001). HDL-C <45 mg/dL predicted preeclampsia with an AUC of 0.71. Li et al.[11] and Tesfa et al.[13] also reported reduced HDL-C levels in preeclamptic women. Additionally, increased TC/HDL ratio (4.92 ± 0.86 vs 3.72 ± 0.74, p<0.001) indicated a more atherogenic lipid profile. ROC analysis demonstrated that triglycerides had the highest predictive accuracy (AUC 0.82), followed by total cholesterol (AUC 0.78), LDL-C (AUC 0.74) and

HDL-C (AUC 0.71). Overall, the findings confirm that abnormal maternal lipid metabolism during early second trimester is strongly associated with subsequent preeclampsia, with triglycerides emerging as the most promising predictive marker. Routine lipid assessment may therefore assist in early risk stratification and preventive management of high-risk pregnancies.

Limitations of the Study

The present study was conducted at a single center with a relatively limited sample size, which may affect the generalizability of the findings to a larger population. Although maternal lipid profile was assessed during the second trimester, other potential biochemical and angiogenic markers of preeclampsia were not evaluated for comparison.

Long-term maternal and neonatal outcomes beyond the delivery period were also not assessed. Further multicentric studies with larger sample sizes are required to validate the predictive role of lipid parameters in preeclampsia.

Conclusion

The present study demonstrated that abnormal maternal serum lipid profile during the second trimester was significantly associated with subsequent development of preeclampsia.

Women who developed preeclampsia showed higher levels of total cholesterol, triglycerides, LDL-C, VLDL-C, and TC/HDL ratio, along with lower HDL-C levels compared with normotensive women. Among the evaluated lipid parameters, triglycerides showed the highest predictive ability for preeclampsia. Second-trimester lipid profile assessment may therefore serve as a simple, cost-effective, and clinically useful tool for early identification of women at increased risk of developing preeclampsia. Further studies with larger populations are required to confirm its role in routine antenatal screening.

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