



ORIGINAL ARTICLE

Maternal Serum Cholesterol levels in Early Pregnancy as a Predictor for Preterm Delivery

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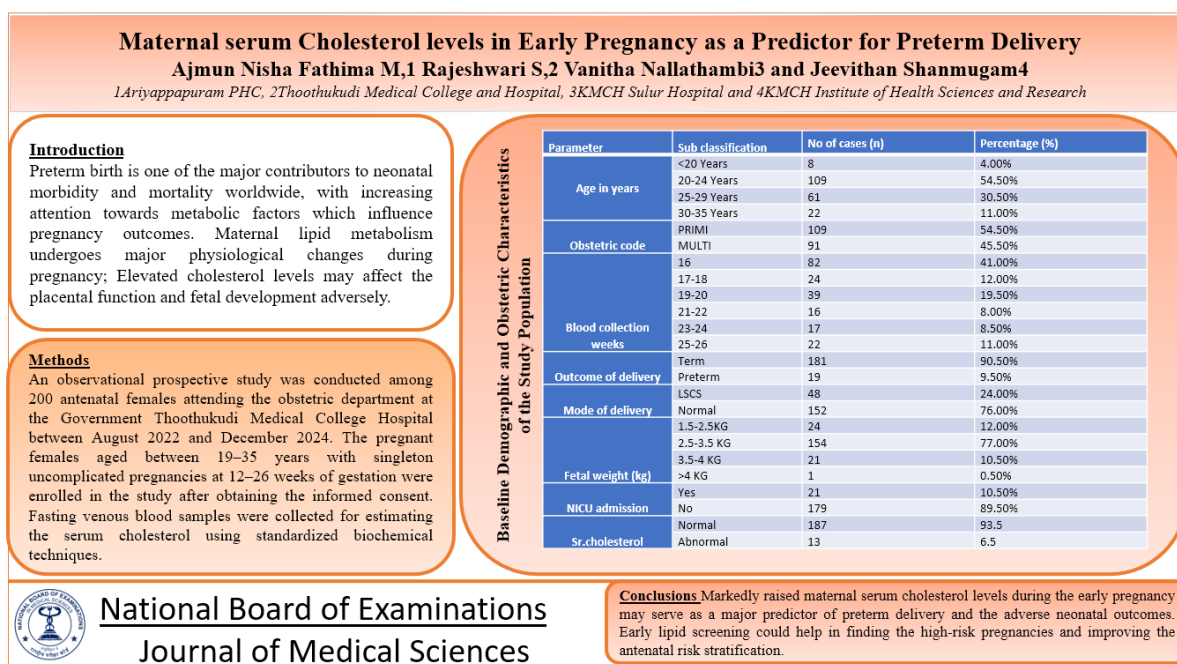
Abstract

Introduction: Preterm birth is one of the major contributors to neonatal morbidity and mortality worldwide, with increasing attention towards metabolic factors which influence pregnancy outcomes. Maternal lipid metabolism undergoes major physiological changes during pregnancy; Elevated cholesterol levels may affect the placental function and fetal development adversely. **Materials and Methods:** An observational prospective study was conducted among 200 antenatal females attending the obstetric department at the Government Thoothukudi Medical College Hospital between August 2022 and December 2024. The pregnant females aged between 19–35 years with singleton uncomplicated pregnancies at 12–26 weeks of gestation were enrolled in the study after obtaining the informed consent. Fasting venous blood samples were collected for estimating the serum cholesterol using standardized biochemical techniques. **Results:** The incidence of preterm delivery was found to be 9.5%. Mothers with serum cholesterol levels exceeding 300 mg/dL showed a higher proportion of preterm births (69.23%) compared to those with lower cholesterol levels ($p < 0.001$). The Mean maternal cholesterol levels were significantly higher in the preterm delivery (277.26 ± 68.90 mg/dL) than in the term delivery group (223.23 ± 43.20 mg/dL). Elevated cholesterol was also linked with a higher proportion of low birth weight infants and increased NICU admissions, while maternal age, gestational age and parity were not significantly associated with the outcome of the delivery. **Conclusion:** Markedly raised maternal serum cholesterol levels during the early pregnancy may serve as a major predictor of preterm delivery and the adverse neonatal outcomes. Early lipid screening could help in finding the high-risk pregnancies and improving the antenatal risk stratification.

Keywords: Pregnancy dyslipidaemia, Maternal cholesterol, Fetal birth weight, Preterm birth, Neonatal outcomes

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Graphical Abstract



Introduction

Preterm birth, is defined as delivery occurring before 37 completed weeks of gestation. It remains as a major global public health concern and it is a major contributor to neonatal morbidity and mortality. Nearly 15 million premature babies are born every year, accounting for a major proportion of neonatal deaths and a long-term neurodevelopmental complication. Prematurity is associated with adverse outcomes like intraventricular haemorrhage, respiratory distress syndrome, necrotizing enterocolitis, and long-term cognitive impairment, thereby causing substantial socioeconomic and emotional burden on healthcare systems and families [1]. Despite the recent advances in obstetric and neonatal care, finding the modifiable risk factors for preterm delivery continues to be a clinical priority.

The aetiology of preterm labor is multifactorial and it involves a complex

interaction of inflammatory, genetic, environmental, and endocrine mechanisms. Risk assessment has focused on the uterine overdistension, maternal infections, cervical insufficiency, and obstetric history. But the recent evidences prove that metabolic alterations during pregnancy, mainly disturbances in lipid metabolism, may play an essential role in triggering early parturition [2-4]. Pregnancy itself induces the physiological hyperlipidaemia, which is characterized by elevated triglycerides, total cholesterol, and lipoproteins. These may support fetal growth and steroid hormone synthesis. The metabolic changes are considered to be adaptive, more elevations in lipid levels may contribute to, oxidative stress, endothelial dysfunction and inflammatory responses within the uteroplacental circulation [3,4].

Cholesterol, is a fundamental lipid molecule which is essential for cell membrane integrity and steroidogenesis. It

assumes vital importance during gestation due to its role in fetal growth and neurodevelopment. The cholesterol metabolism dysfunction has been mentioned in adverse pregnancy outcomes, including the fetal growth restriction, preeclampsia, and preterm birth [3]. Elevated maternal low-density lipoproteins and cholesterol can promote impair vascular inflammation, nitric oxide signalling. It can also induce placental ischemia, which activates pathways involved in uterine contractions and cervical ripening [4,5]. Oxidized lipid particles may stimulate the cytokine synthesis and matrix metalloproteinase activation, which in turn may lead to premature rupture of membranes and early labor initiation [4,5].

Several observational studies have showed an association between preterm delivery and maternal lipid abnormalities. Mudd et al. reported that women with more mid-pregnancy cholesterol levels showed more risk of spontaneous preterm birth, proving that lipid profiling may serve as an essential biomarker for adverse obstetric outcomes [6]. Similarly, Smith et al demonstrated an independent association between higher maternal total cholesterol levels and spontaneous preterm labor reinforcing the hypothesis that lipid metabolism plays an essential role in maintaining duration of pregnancy [7]. Other researchers have also highlighted the contribution of maternal dyslipidaemia to endothelial dysfunction, and altered fetal growth patterns, placental inflammation, further supporting the biological plausibility of this association [3,4,8].

Although evidence from Western and International populations are present, the region-specific data from low and middle-income countries are less. Indian

women are experiencing a greater epidemiological transition characterized by sedentary lifestyle, changing dietary patterns, and growing prevalence of metabolic disorders, which may influence the lipid profiles during pregnancy. Also, routine lipid screening is not incorporated into antenatal care protocols, largely due to insufficient local evidence. Assessing the relationship between preterm delivery and the maternal cholesterol levels within the Indian population is therefore essential for developing cost-effective screening strategies and preventive interventions.

In this context, the present prospective observational study was undertaken to evaluate the association between maternal serum cholesterol levels measured during early to mid-pregnancy and the risk of preterm delivery. By examining both maternal and neonatal outcomes, this study aims to contribute to the growing evidences exploring metabolic determinants of preterm birth and to identify potential markers that may aid in early risk stratification during antenatal care.

Materials and Methods

This prospective observational study was conducted among antenatal mothers attending Government Thoothukudi Medical College Hospital over a study period extending from August 2022 to December 2024. Prior to initiation of the study, approval was obtained from the Institutional Human Ethics Committee, and the study was done in accordance with the ethical principles outlined in the Declaration of Helsinki. Eligible participants were approached during usual antenatal visits and were provided with detailed verbal and written information regarding the procedures, purpose,

confidentiality, potential benefits of the study. Participation was entirely voluntary, and written informed consent was obtained from all mothers before enrolment. The participants were assured that withdrawal at any stage of the study would not affect their routine clinical care.

Pregnant women aged between 19 - 35 years with gestational age of 12–26 weeks and uncomplicated singleton pregnancies were included in the study. Mothers with a previous history of uterine anomalies, preterm delivery, pregnancy-induced hypertension, gestational diabetes mellitus, multiple gestation, cervical incompetence, fetal anomalies, or known chronic illnesses such as cardiac, hepatic, renal, thyroid, or metabolic disorders were excluded to minimize the confounding factors. 200 eligible participants who fulfilled the inclusion criteria were enrolled for the study. After enrolment, a detailed clinical evaluation was conducted, including dietary habits, demographic profile, obstetric history, and general physical examination. Obstetric examination was conducted based on standard antenatal protocols.

An overnight fasting venous blood sample was taken under strict aseptic precautions from each participant during the specified gestational window for estimation of maternal serum cholesterol levels. The analysis of lipid profile was performed using standardized biochemical tests in the institutional laboratory, ensuring quality control measures. The gestational age at blood collection was recorded, and participants were followed prospectively until delivery through routine antenatal follow-up visits and hospital records. Outcomes of Delivery was classified as term or preterm based on the gestational age at the time of birth. In addition, the maternal

and neonatal parameters, including the mode of delivery, requirement for admission in neonatal intensive care unit (NICU) and birth weight of the fetus were documented.

All the clinical procedures were conducted in accordance with the standard obstetric practice, ensuring that there was no invasive intervention or additional risk introduced only for research purposes. Ethical Principles of non-maleficence, voluntary participation, confidentiality in maintenance of medical records, and respect for the patient's autonomy were strictly upheld. All the data collection forms were recorded in order to prevent identification of each participant, and the access to that dataset was restricted to maintain data confidentiality and integrity.

Statistical analysis was performed using SPSS 27. All *continuous variables* were expressed as mean \pm standard deviation, while all *categorical variables* were summarized as percentages and frequencies. Normality of the data was assured with Kolmogorov-Smirnov test. The associations between categorical variables were assessed using the Chi-square test, and comparison of continuous variables between delivery groups (term and preterm) was performed using the independent t-test. A p-value of less than 0.05 was considered as statistically significant. Multivariable logistic regression analysis was not undertaken in this study due to quasi-complete separation observed in the dataset, where increased cholesterol levels strongly predicted the preterm delivery thereby limiting reliable model estimation.

Results

While analysing the baseline characteristics of the study population, predominance of younger antenatal mothers, with 54.5% in the 20–24 years age group and a mean maternal age of 24.55 years was observed. Primigravida women constituted 54.5% of the study participants, while multigravida mothers accounted for 45.5%, showing a relatively balanced obstetric distribution. Blood cholesterol testing was most frequently performed before 16 weeks of gestation (41%),

reflecting need for early antenatal screening practices. Most pregnancies resulted in term delivery (90.5%), whereas preterm birth was seen in 9.5% of cases. Normal vaginal delivery was the frequent mode of birth (76%), with caesarean section conducted in 24% of mothers. Most neonates had weight between 2.5–3.5 kg (77%) at birth, and only 12% of them weighed below 2.5 kg. NICU admission was required in 10.5% of newborns, suggesting the favourable neonatal outcomes in the study cohort (Table 1).

Table 1. Baseline Demographic and Obstetric Characteristics of the Study Population

Parameter	Sub classification	No of cases (n)	Percentage (%)
Age in years	<20	8	4.00%
	20-24	109	54.50%
	25-29	61	30.50%
	30-35	22	11.00%
Obstetric code	PRIMI	109	54.50%
	MULTI	91	45.50%
Blood collection weeks	16	82	41.00%
	17-18	24	12.00%
	19-20	39	19.50%
	21-22	16	8.00%
	23-24	17	8.50%
	25-26	22	11.00%
Outcome of delivery	Term	181	90.50%
	Preterm	19	9.50%
Mode of delivery	LSCS	48	24.00%
	Normal	152	76.00%
Fetal weight (kg)	1.5-2.5	24	12.00%
	2.5-3.5	154	77.00%
	3.5-4	21	10.50%
	>4	1	0.50%
NICU admission	Yes	21	10.50%
	No	179	89.50%
Sr.cholesterol	Normal	187	93.5
	Abnormal	13	6.5

Analysis of maternal serum cholesterol proved a significant association with delivery outcome. Among mothers with cholesterol levels below 200 mg/dL, 91.89% delivered at term, while only 8.11% were delivered as preterm birth. Similarly, in the 200–300 mg/dL category, term delivery became predominant at 96.46%, with preterm delivery was seen in only 3.54% of cases. In contrast, mothers with cholesterol levels exceeding 300 mg/dL showed a markedly different pattern, with

69.23% delivering the preterm and only 30.77% reaching the term gestation. This high-cholesterol group is present in only 6.5% of the total population, it accounted for a disproportionately greater proportion of preterm births. The difference across these cholesterol categories was statistically significant ($p < 0.001$), indicating that elevated maternal cholesterol, especially values above 300 mg/dL, may act as a strong predictor of preterm delivery (Table 2).

Table 2. Association Between Maternal Serum Cholesterol Levels and Delivery Outcome

S.CHOLESTEROL	OUTCOME OF DELIVERY				CSV	P value
	Term		Preterm			
	No of cases (n)	Percentage (%)	No of cases (n)	Percentage (%)		
<200	68	91.89	6	8.11	58.783	<0.001
200-300	109	96.46	4	3.54		
>300	4	30.77	9	69.23		

Maternal serum cholesterol levels proved a significant relationship with neonatal birth weight distribution. In mothers with cholesterol levels below 200 mg/dL, 78.38% of neonates had a birth weight between 2.5–3.5 kg, while only 10.81% weighed less than 2.5 kg. A similar pattern was observed in the 200–300 mg/dL group, where 80.53% of neonates fell within the normal weight range and 12.39% weighed above 3.5 kg. However, among mothers with cholesterol levels exceeding

300 mg/dL, a notable shift toward lower birth weight was observed, with 61.54% of neonates weighing less than 2.5 kg and none exceeding 3.5 kg. This trend suggests that markedly increased maternal cholesterol may influence the fetal growth patterns. The link between fetal weight and cholesterol level was statistically significant ($p < 0.001$), supporting a possible metabolic influence on intrauterine growth (Table 3).

Table 3. Relationship Between Maternal Serum Cholesterol Levels and Fetal Birth Weight

Sr. CHOLESTEROL (mg/dL)	FETAL WEIGHT (kg)			CSV	P Value
	<2.5	2.5-3.5	>3.5		
<200	8 (10.81)	58 (78.38)	8 (10.81)	27.412	<0.001
200-300	8 (7.08)	91 (80.53)	14 (12.39)		
>300	8 (61.54)	5 (38.46)	0		

No significant association was seen between age, outcome of delivery, obstetric code and mode of delivery. Comparison of continuous variables between the preterm and term delivery groups proved a significant difference in the serum cholesterol levels, while the gestational age at blood collection did not differ significantly. The mean serum cholesterol level among mothers delivering at term was 223.23 ± 43.20 mg/dL, whereas mothers with preterm delivery exhibited a higher

mean value of 277.26 ± 68.90 mg/dL, and this difference was statistically significant ($p < 0.001$). In contrast, the mean blood collection week was comparable between term group (18.17 ± 4.83 weeks) and preterm group (17.16 ± 4.49 weeks), with no significant difference observed ($p = 0.383$). These results indicate that elevated maternal cholesterol, rather than timing of lipid assessment, is more strongly linked with the risk of preterm birth (Table 4).

Table 4. Comparison of Continuous Variables Between Term and Preterm Delivery Groups

Parameter	OUTCOME OF DELIVERY				T value	P value
	Term		Preterm			
	Mean	SD	Mean	SD		
BLOOD COLLECTION WEEKS	18.171	4.835	17.158	4.488	0.874	0.383
S.CHOLESTEROL	223.233	43.202	277.263	68.900	-4.856	<0.001

Discussion

The present prospective observational study assessed the association between maternal serum cholesterol levels measured during early to mid-pregnancy and the observed risk of preterm delivery. The overall incidence of preterm delivery in this cohort was 9.5%, which is consistent with previously proven prevalence rates in similar populations [2]. Baseline obstetric and maternal characteristics, including parity, age distribution, gestational age at blood collection, and mode of delivery, did not show a statistically significant association with delivery outcome, suggesting that these variables were unlikely to confound the primary relationship observed between cholesterol levels and preterm birth. In our

study most participants were primigravida, and young mothers aged between 20 and 24 years. Similar results were observed in a study done by Catov et al. where in they demonstrated elevated maternal lipid concentration in early pregnancy were significantly associated with high risk of spontaneous preterm birth [9]. Kramer et al. also reported that mid-trimester maternal lipid concentrations were independently associated with spontaneous preterm birth, indicating that lipid abnormalities during the second trimester may have predictive value for adverse pregnancy outcomes [10].

The important findings observed in this study were the strong association between elevated maternal cholesterol levels and preterm delivery. While most of the mothers with cholesterol levels below

300 mg/dL delivered at term, a considerable proportion of preterm births was seen among those with cholesterol levels exceeding 300 mg/dL. This group (elevated cholesterol) accounts for a disproportionately high number of preterm deliveries, substantiating the potential predictive value of higher cholesterol levels. Similar results have also been reported in prior studies, where in maternal dyslipidaemia was linked with an increased risk of spontaneous preterm labor, possibly mediated through the vascular and inflammatory mechanisms affecting the placental function [3-7]. The significant difference in the mean cholesterol levels between preterm and term in this study further strengthens this association and also appreciates our hypothesis that more maternal lipid levels during pregnancy may play a vital role in the pathophysiology of early parturition. The findings of the present study are in agreement with those of Vrijkotte et al., who observed that abnormal maternal lipid profiles in early pregnancy were associated with adverse outcomes including preterm birth and low birth weight, highlighting the broader impact of lipid metabolism on fetal growth [11]. A meta-analysis by Spracklen et al. further confirmed that maternal hyperlipidemia is significantly associated with an increased risk of preterm birth, reinforcing the importance of lipid abnormalities as a modifiable risk factor in pregnancy [12]. Wiznitzer et al. also demonstrated that elevated maternal lipid levels during pregnancy are associated with multiple adverse obstetric outcomes, suggesting that dyslipidemia may contribute to a spectrum of complications including preterm birth [13].

Physiological hyperlipidaemia during pregnancy is now considered a

normal adaptive mechanism to support the steroid hormone synthesis and fetal growth: however, excessive accumulation of lipids may induce endothelial dysfunction, oxidative stress, and inflammatory responses within the uteroplacental circulation [4,5]. Elevated cholesterol levels can also impair the nitric oxide bioavailability thereby activating cytokine-mediated pathways, and hence promote vascular inflammation, all of which can lead to premature cervical remodelling and uterine contractility [4,5]. These findings align with the hypothesis, that maternal hypercholesterolemia may be an important metabolic trigger in the cascade leading to preterm birth.

Another observation in this study was the association between maternal cholesterol levels and the fetal birth weight. While neonates born to mothers with cholesterol levels below 300 mg/dL had adequate birth weights, a higher proportion of low birth-weight infants were observed among mothers with significantly elevated cholesterol levels. This pattern supports the evidence that maternal lipid imbalance may not only influence the gestational duration but also affects intrauterine growth of the fetus. Earlier studies have also reported that dyslipidaemia during pregnancy may affect the placental lipid transport and thereby lead to inflammatory changes. These changes may reduce the nutrient exchange and thereby affect fetal growth outcomes [3,4].

It was also observed that gestational age at blood collection did not differ significantly between term and preterm groups, indicating that the timing of lipid assessment was unlikely to influence the observed association. These finding suggests that elevated cholesterol alone, rather than the gestational window of

testing, may be the primary factor linked to risk of preterm. Similar findings have been reported in earlier cohort studies where mid-pregnancy lipid levels were predictive of adverse outcomes irrespective of the exact timing of measurement within the second trimester [6,7]. The lack of association between maternal age, parity, and mode of delivery with preterm outcome in the current study further highlights the independent role of metabolic factors in determining the duration of pregnancy.

The biological plausibility of these findings is evidenced by the maternal cholesterol which plays a key role in placental development and immune modulation. The excess cholesterol may accumulate within the placental macrophages, triggering pro-inflammatory signalling pathways and increase the production of cytokines such as IL-6 and TNF- α , which are the known mediators of early parturition [4,5]. Also, oxidative modification of low-density lipoproteins may increase the prostaglandin synthesis and matrix metalloproteinase activation, leading to premature rupture of membranes and early labor onset [4]. These mechanisms provide a pathophysiological basis for the strong relationship between the increased maternal cholesterol and preterm birth in the present study.

The statistically significant associations demonstrated through continuous and categorical variable analyses provide solid evidence supporting the role of maternal cholesterol as an essential predictor of preterm delivery. The results of this research are consistent with the prior research proving the importance of metabolic risk factors in pregnancy and underscore the potential value of estimating lipid profile as part of antenatal risk assessment [3,6,7].

Conclusion

The current research adds to the growing literature suggesting that maternal lipid metabolism may influence both the gestational duration, fetal growth, and neonatal outcomes. Identification of increased cholesterol levels during the early antenatal care may allow the obstetricians to identify the pregnant mothers at higher risk for preterm birth and implement closer surveillance strategies. Further large-scale studies are needed to establish threshold values and explore whether targeted interventions aimed at reducing the maternal lipid profiles could decrease the burden of preterm delivery.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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