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Hypercholesteremia As Predictor Of Pre Term Labor.

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ABSTRACT

INTRODUCTION: Hypercholesterolemia is primarily due to enhanced entry of cholesterol rich lipoproteins into the circulation. Elevated serum total cholesterol results in placental insufficiency which leads to preterm labor and low birth weight

Objective of study: To determine the association between elevated maternal serum total cholesterol during second trimester between 14-20 weeks of gestation, as a predictor of preterm delivery

MATERIAL AND METHODS Fasting blood samples are obtained to measure total serum cholesterol concentrations at 14-20 weeks of gestation.

Study design : Prospective observational study

Period of study : 2016-2018

Place of study : Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai, Tamilnadu

Sample size : 304

RESULTS: Among 304 patients, 32 patients with high serum total cholesterol, out of which 56.25% had preterm delivery. Among 304 patients in the study population, 272 patients with normal serum total cholesterol only 6.6% of them had preterm delivery.

CONCLUSION: To conclude from our study that measurement of serum total cholesterol level can potentially be used for predicting preterm labour which suggests that high maternal serum cholesterol is associated with preterm delivery

Keywords: Hypercholesterolema, prediction, preturm labour

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INTRODUCTION

Preterm labor is defined as the onset of regular, painful, frequent, uterine contractions causing progressive effacement and dilatation of the cervix occurring before 37 completed weeks of gestation from the day of last menstrual period. Any infant born before 37 completed weeks should be called as preterm.

Prevention of spontaneous preterm birth and low birth weight through screening is one of the key aims of antenatal care as these have implications for the child, mother and society.

Maternal cholesterol is essential for both the hormonal and physical changes of early pregnancy.¹

Hypercholesterolemia is primarily due to enhanced entry of cholesterol rich lipoproteins into the circulation. Estrogen may play a major role in the lipoprotein patterns seen in human pregnancy, where LDL cholesterol is more influenced by both estrogen and progesterone.

Placental lipoproteins lipase normally increases as term approaches.

Enhance the lipolytic activity in making free fatty acids available to the fetus.

As the elevated serum total cholesterol is the marker for increased risk of preterm labor, the mechanism as follows.

Elevated cholesterol deposition in the fetal aorta causes atherosclerosis of uteroplacental spiral arteries, hypercoagulation and thrombosis which leads to placental infarction and thereby results in placental insufficiency, low birth weight and preterm labor. Preterm birth is known to be initiated by multiple mechanisms and various reports have suggested a possibly increased risk for prematurity with very high maternal cholesterol.^{2,3} Finding by Catov and coworkers.⁴ showed that an elevation in maternal cholesterol level early in gestation was associated with an increased risk of preterm delivery. This was corroborated by the finding from this cohort study where we reported an elevated risk for preterm birth among mothers with high maternal cholesterol.

MATERIAL AND METHODS

Fasting blood samples are obtained to measure total serum cholesterol concentrations at 14-20 weeks of gestation and the sera were then analyzed enzymatically by the cholesterol oxidase: p-aminophenazone (chod pap) method.

Normal Value: FIRST TRIMESTER : 141-210 mg/dl. SECOND TRIMESTER : 176-299mg/dl. (Williams obstetrics) THIRD TRIMESTER : 219-349mg/dl.

Study design : Prospective observational study, Period of study : 2016-2018 Place of study - tertiary care center, Sample size : 304, INCLUSION CRITERIA: low risk Singleton Pregnant women between 18yrs to 35 year age group were taken for study.

Multiple Gestation, Gestational Diabetes mellitus/ Overt Diabetes Mellitus, Gestational Hypertension, Rheumatic Heart Disease, Recurrent pregnancy loss, History of Cervical Incompetency, Previous History Of Preterm delivery were excluded from study.

RESULTS

Among 304 members in my study population, majority of patients were in the age group of 25-28 years (TABLE-1) Among 304 patients, 185 Primigravidas and Multigravida -119 were involved with study group. Among 304 members in my study population, majority of patients were in the age group of 25-28 years. Among 304 patients involved in the study group, out of which 32 patients had raised serum Total cholesterol >299mg/dl. (TABLE 2)

Among 304 patients in my study, majority of them that is 41.1% were overweight., and among 32 patients with hypercholesterolemia 27 patients were obese and 5 patients were overweight(.TABLE -3). Among 304 women the cholesterol level and gestational age at delivery was observed . out of 304 women in study ,125 had less than 176 mg/dl and 6.4%of them delivered preterm and 93.6%had term delivery. 147 of 304 women the cholesterol level was between176-299mg/dl and 6.8% delvedat preterm 93.1% delvered at term. Out of 304 women, 32 patients who had raised serum total cholesterol of >299mg/dl, out of which 18 patients(56.2%) had preterm delivery,14 patients (43.7%) had term delivery(TABLE -4) Patients with >299mg/dl serum total cholesterol, 29 patients delivered by SVD with episiotomy and 3 patients delivered by lscs. (severe oligo, fetal distress, previous lscs) association of cholesterol level and preterm delivery (n=304).

Among 304 patients, 32 patients with high serum total cholesterol, out of which 56.25% had preterm delivery. Among 304 patients in the study population, 272 patients with normal serum total cholesterol only 6.6% of them had preterm delivery. (TABLE -5)

BASED ON STUDY POPULATION- (n=304)

TABLE.1 AGE DISTRUBUTION:

Variables	No. of cases (n=304)	Percentage (%)
Age group n=304		
< 20 years	8	2.6 %
21-24 years	60	19.7%
25-28 years	120	39.5%
29-32 years	88	28.9%
>32 years	28	9.2%
Total	304	100%

Among 304 members in my study population, majority of patients were in the age group of 25-28years.

TABLE. 2 CHOLESTROL LEVELS:

Total cholesterol mg/dl	Number of cases (n=304)	Percentage(%)
<176	125	41.1%
176-299	147	48.4%
>299	32	10.5%
Total	304	100%

Among 304 patients involved in the study group, out of which 32 patients had raised serum Total cholesterol >299mg/dl.

TABLE.3 BMI AND CHOLESTEROL LEVELS (n=304)

BMI AND CHOLESTEROL LEVELS (n=304)				
TC values	Normal (18.5 -24.9)	Overweight (25-29.9)	Obese (>/- 30)	Total
<176	58 (46.4%)	54 (43.2%)	13 (10.4%)	125
176-299	58 (39.4%)	66 (44.8%)	23 (15.6%)	147
>299	0	5 (15.65)	27 (84.3%)	32
Total	116 (38.1%)	125(41.1%)	63 (20.7%)	304

Among 304 patients in my study, majority of them that is 41.1% were overweight.

TABLE. 4 CHOLESTEROL AND OUTCOME OF DELIVERY n=304

CHOLESTEROL AND OUTCOME OF DELIVERY n=304			
TC values	Pre term	Term	Total
<176	8 (6.4%)	117 (93.6 %)	125 (41.1%)
176-299	10 (6.8%)	137 (93.1%)	147 (48.3%)
>299	18 (56.2%)	14 (43.7%)	32 (10.5%)
Total	36 (11.8%)	268 (88.1%)	304 (100%)

Among 32 patients who had raised serum total cholesterol of >299mg/dl, out of which 18 patients(56.2%) had preterm delivery, 14 patients (43.7%) had term delivery.

TABLE.5 STUDY POPULATION RESULTS BASED ON HYPERCHOLESTEROLEMIA

Variable	Normal TC (<299mg/dl) n=272/304	High TC (>299mg/dl) n=32/304	Total (n=304) n=36/304	P.value
Gestational age at delivery				
Pre term	18 (6.6%)	18 (56.25%)	36 (11.8%)	0.037
Term	254 (93.5%)	14 (43.7%)	268 (88.1%)	
Total	272 (89.4%)	32 (10.5%)	304 (100%)	

Among 304 patients, 32 patients with high serum total cholesterol, out of which 56.25% had preterm delivery. Among 304 patients in the study population, 272 patients with normal serum total cholesterol only 6.6% of them had preterm delivery.

DISCUSSION

This prospective observational study carried out among pregnant women at a tertiary hospital in Sri Ramachandra institute of higher education and research, Porur-Chennai, Tamilnadu, India examined how a substantially high value of maternal serum cholesterol levels in second trimester pregnancy would affect and be used as predictor for later events, such as preterm delivery and fetal outcome.

High cholesterol plays a major role in the lipoproteins patterns seen in the pregnancy, although cholesterol is more influenced by the combined effect of increased estrogen and progesterone. In addition, placental lipoprotein lipase normally increases as term approaches. It is known that plasma cholesterol levels, increases during pregnancy and that enhanced lipolytic activity play a key role in making free fatty acids available to fetus.

Various studies showed numerous risk factors for the preterm delivery, such as lifestyle, smoking, malnutrition, and no or less weight gain in pregnancy. Other risk factors in previous studies include addiction to narcotics, use of alcohol, ambient poisons, prolonged standing, intensive work, activity, stress, young mother, poor education and poor socioeconomic support, first pregnancy, multiparity, hydramnios, surgery in pregnancy, anomalies of the uterus, febrile illness, during pregnancy, early trimester bleeding, asymptomatic bacteriuria, pyelonephritis.⁵ According to the World Health Organization (WHO) Preterm delivery is defined as the delivery of an infant before the completion of 37 weeks' (259 days') of gestation. The most important outcome of preterm delivery is a premature infant, which is the most common cause of infant mortality after the congenital abnormalities. There are 3.6 million/year neonatal deaths around the world, of which 99 percent deaths are contributed by the developing countries.

Study conducted by Kramer et al.⁶ which was a case control study in a large number consisting of 5337 case, had concluded that high plasma homocysteine and HDL cholesterol were significantly and independently associated with the risk of spontaneous preterm birth.

Similar study conducted by Alleman⁷ et al.¹² among cohort of 2699 pregnant women, showed the best predictive model for preterm delivery were maternal serum total cholesterol, alpha fetoprotein and inhibin A. The model showed better discriminatory ability than preterm delivery history alone.

Study conducted by Sowmiya et al.²⁰¹⁵⁸, 374 patients who had normal cholesterol delivered at term, however 15 patients out of 26 (57.7%) patients who showed abnormal cholesterol had preterm delivery and 22 patients out of 35 (62.8%) patients with abnormal triglycerides level delivered prematurely. Out of 400 mothers included in the study, only 37 (9.25%) had preterm delivery. Even though the incidence of preterm delivery was acceptable to the other standard studies, we noticed that those patients who had combined elevation of both cholesterol and triglycerides had higher incidence. This indicates that both elevated serum cholesterol and triglycerides level would better predict the preterm delivery.

After comparing my study with other standard studies done in the various part of the world, where we need to understand the physiology behind the relationship between the abnormal cholesterol and preterm birth risk, Maternal hyperlipidemia is common and consistent metabolic alteration in pregnancy. Plasma cholesterol and triglycerides may increase by 25% to 50% and 150% to 300% respectively.^{9,10}

Atherosclerosis of the utero placental spiral arteries may be induced by the Hyperlipidemia in pregnancy. Atherosclerosis of the vital placental arteries combined with hyper coagulation may result in thrombosis and placental infarctions, leading to placental insufficiency and thereby fetal compromise.¹¹ This fetal compromise is in the form of preterm delivery (birth <gestation week 37) and/or low birth weight (<2500 g).

Wang et al. (2017)¹² found associations between elevations in first trimester TG, TC, LDL, and HDL levels and risk of preterm labor.

Maymunah et al.¹³ (2014) studied hypercholesterolemia as one of the predictors of undesirable pregnancy outcomes and reported that both high maternal age and body mass index (BMI) increased maternal cholesterol levels and, thus, the risk of preterm delivery. Harville et al. (2011)¹⁴ demonstrated that high LDL, TG and TC levels before pregnancy could increase the risk of cardiovascular diseases and premature labor [35](#)

In our study Out of 304 patients ,32 patients (10.5%) had hypercholesterolemia. among these,56.2% had preterm delivery .272 patients (89.4%) with normal cholesterol levels , among these, 6.6% had preterm delivery. Even though the incidence of preterm delivery was acceptable to the other standard studies, 18 we noticed that those patients who had elevation of cholesterol had higher incidence, This indicates that elevated serum cholesterol level would better predict the preterm delivery.

SUMMARY

The elevated levels of cholesterol in pregnancy is a marker for increased risk of preterm labor in pregnant women. It has been described in many studies that association of elevated maternal serum total cholesterol in pregnancy causes increased morbidity and adverse pregnancy outcome such as preterm labor and low birth weight and its complications. In our study we have evaluated the relationship between the raised serum total cholesterol and preterm birth risk.

In our study 304 pregnant women were enrolled, majority women belongs to the age group of 25-28years (table-1). We included 185 primigravidas, and 119 multigravid women.

In all patients fasting blood was collected for lipid analysis during second trimester that is 14-20 weeks of gestation and the sere were analysed enzymatically by chod-pap method in our laboratory. None were subjected for lipid analysis beyond 32weeks of gestation or before 14weeks of geststion.

We considered the normal range in the second trimester -176-299mg/dl. With these study population of 304 patients, majority of them were grouped into overweight category that is 41.1% which is shown in .

Sensitivity And Specificity Based On Study Population.

	PRETERM	TERM	Total
Hypercholesterolemia >299mg/dl	18 (A)	14(B)	32
Normal <299mg/dl	18(C)	254(D)	272
	36	268	304

SENSITIVITY OF THE TEST- $A/A+C *100$ = 50%
 SPECIFICITY OF THE TEST- $D/B+D *100$ = 94.77%
 POSITIVE PREDICTIVE VALUE- $A/A+B *100$ = 56.2%
 NEGATIVE PREDICTIVE VALUE- $D/C+D *100$ = 93.38%

To summaries the conducted study based on 304 study population, where 18 patients (56.25%) out of 32 patients who showed abnormal serum total cholesterol value had preterm delivery., 14 patients (43.7%) had term delivery. And among (89.4%)272 patients with normal serum total cholesterol only (6.6%) 18 patients had preterm delivery.

Therefore to conclude 6.6% of mothers with normal serum total cholesterol values and 56.25% of mothers with abnormal serum total cholesterol values had preterm delivery these differences are statistically significant (Pvalue 0.037) Which shows sensitivity of 50.0% and specificity of 94.77% based on our study.

Thus this study shows the positive predictive value of preterm birth risk, (ie) only 56.2% risk of going into preterm labor if the patient has raised serum total cholesterol. The negative predictive value of the study explains that there is 93.38% of chance of not going into preterm labor if the patient has normal cholesterol value.

Therefore this is also one of the test that can be done during the course of pregnancy in second trimester to predict the preterm birth and fetal outcome.

CONCLUSION

To conclude from our study that measurement of serum total cholesterol level can potentially be used for predicting preterm labour which suggests that high maternal serum cholesterol is associated with preterm delivery

We can infer from this study that increase maternal age and high maternal BMI are associated with high maternal serum cholesterol (hypercholesterolaemia) which in turn is associated with preterm birth and low birth weight in neonates.

We therefore recommend that further validation of these findings with more robust prospective and longitudinal characterization of maternal serum cholesterol profiles in pregnancy, with elimination of major confounding variables such as maternal age and BMI, be carried out in subsequent investigations to determine the optimal cholesterol range in pregnancy, and until such more studies are performed. The Pregnant women should be encouraged to follow a healthy, balanced diet and regular antenatal visit to their healthcare provider.

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