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Measurement of serum cholesterol levels as a predictor of preterm delivery

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Abstract

Introduction: Pregnancy is considered as a unique and physiologically normal episode in a women's life. All pregnancies are at risk, while most pregnancies are uneventful. About 15% of pregnant women may develop a potentially life threatening complication in turn may require a major obstetrical intervention to survive.

Aim of the Study: To evaluate the association of elevated cholesterol levels at 14 to 24 weeks gestation in uncomplicated pregnancy and preterm delivery. To associate the elevated levels of cholesterol as predictor of preterm delivery.

Materials and Methods: The study group includes 300 healthy pregnant women, fasting cholesterol levels during 14 to 24 weeks gestation who have come to antenatal check-up at the Department of Obstetrics and Gynaecology, Madras Medical College, during the period August 2016 to July 2017.

Only those patients we could follow up to term and planning delivery at IOG were included in the study. The biochemical investigations were done at the Institute of Biochemistry, MMC. The hospital ethical committee approved the study.

Results: Out of 322 antenatal mothers selected on the basis of inclusion and exclusion criteria 22 were excluded during the study for various reasons. 4 developed PIH, 7 developed Gestational diabetes Mellitus, one case was a multiple pregnancy, 2 were abruption placenta, and 8 were lost to follow up.

Keywords: measurement, serum cholesterol, predictor, preterm delivery

Introduction

Pregnancy is considered as an unique and physiologically normal episode in a women's life. All pregnancies are at risk, while most pregnancies are uneventful. About 15% of pregnant women may develop a potentially life threatening complication in turn may require a major obstetrical intervention to survive.

Labour is a naturally occurring phenomenon which usually starts on its own. It is defined as the spontaneous onset of regular and painful uterine contraction associated with a progressive effacement with dilatation of cervix and descent of presenting part, with or without a show or ruptured membrane.

In the era of modern obstetrics, where there has been a rapid advancement in all specialities, preterm labour remains an enigma for the obstetricians today.

Preterm labour is defined by WHO as the onset of labour after the period of viability, that is after 28wks of gestation and before 37 completed weeks or 259 days of pregnancy.

It is estimated that 15million preterm births occur worldwide, of which more than 1million died as result of their prematurity. Preterm birth is associated with significant perinatal morbidity and mortality rates. Moreover, it is associated with an increased risk of adverse metabolic outcomes in later life such as type 2 Diabetes mellitus, Hypertension, CAD & Stroke. The mothers who delivered preterm infants also appeared to have increased risk of metabolic diseases later in life.

Preterm birth affect over 10% of all pregnancies and leads to significant neonatal morbidity and mortality [1]. Prevention of viable 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. If women can be identified to be at high risk of these adverse birth outcomes in early pregnancy, they can be targeted for more intensive antenatal surveillance and prophylactic interventions (Primary prevention).

Cholesterol in normal pregnancy

In normal pregnancy, the concentration of lipids, lipoproteins, apolipoproteins, are elevated. During early trimesters increased maternal fat accumulation is due to increased lipid synthesis,

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which subsequently leads to hypertriglyceridemia, occurring in late gestation.

Increased insulin resistance and oestrogen stimulation lead to maternal hyperlipidemia. This is primarily due to enhanced entry of triglyceride rich lipoprotein (VLDL), in to the circulation rather than removal. Also the placental lipoprotein lipase normally increases as term approaches.

The plasma TGL & Cholesterol levels increase during pregnancy & enhanced lipolytic activity play a key role in making free fatty acid available to the fetus. Hyperlipidemia is associated with endothelial dysfunction and also regarded as an instigator of inflammation and stress which is a significant factor in preterm birth. Hence, elevated levels of cholesterol & triglycerides are a marker for increased risk of preterm labour, we have evaluated the elevated cholesterol as a predictor and its association on risk of preterm delivery.

Aim of the Study

To evaluate the association of elevated cholesterol levels at 14 to 24 weeks gestation in uncomplicated pregnancy and preterm delivery. To associate the elevated levels of cholesterol as predictor of preterm delivery.

Primary objective

To determine the association between elevated Serum Cholesterol in Pregnancy & Pre-term Births.

Secondary objective

To determine the association between elevated Serum Cholesterol in Pregnancy & Pre-term Births.

Materials and Methods

The study group includes 300 healthy pregnant women, fasting cholesterol levels during 14 to 24 weeks gestation who have come to antenatal check-up at the Department of Obstetrics and Gynaecology, Madras Medical College, during the period August 2016 to July 2017.

Only those patients we could follow up to term and planning delivery at IOG were included in the study. The biochemical investigations were done at the Institute of Biochemistry, MMC. The hospital ethical committee approved the study.

Out of 322 antenatal mothers selected on the basis of inclusion and exclusion criteria 22 were excluded during the study for various reasons. 4 developed PIH, 7 developed Gestational diabetes Mellitus, one case was a multiple pregnancy, 2 were abruptio placenta, and 8 were lost to follow up.

Inclusion Criteria

Age = 17 – 35 years
Gestational age = from participants last menstrual period or modified by USG.

Exclusion Criteria

- GDM
- Pregnancy included Hypertension
- Previous H/O preterm delivery
- Multiple pregnancy
- Hydramnios
- Cervical Incompetence
- Pre-existing medical disease
- Cardiovascular disorder
- Renal disorder
- Congenital anomalies of fetus
- Smoking
- Unknown last menstrual period

Study Method

The design of the study prospective study. In all these antenatal mothers detailed history with special reference to diet and habits, followed by complete general and obstetric examination were done. The purpose of interrogation and investigation was explained to every patient and her informed consent obtained.

General Examination

Height, weight, pulse, blood pressure, edema, anemia, cardiovascular, respiratory and central nervous system disorder were examined.

Obstetric examination: Per Abdomen Examination

Procedure

From all the antenatal mothers who were included in the study, blood sample was taken after overnight fasting. Under strict aseptic precaution blood was obtained for other investigations by venepuncture. Cholesterol between 14 to 24 weeks gestation were obtained after overnight fast. The patients were followed till delivery.

Laboratory Tests

The blood samples for cholesterol were collected and analysed.

Results

Table 1: Serum cholesterol and Outcome of delivery

			Outcome		
			Term	Preterm	Total
SC Normal	<200	Count	104	6	110
		% Within Outcome	94.5%	5.5%	100%
200-300	200-300	Count	166	5	171
		% Within Outcome	97.1%	2.9%	100%
Above 300	Above 300	Count	7	12	19
		% Within Outcome	36.8%	63.2%	100%
Total	Total	Count	277	23	300
		% Within Outcome	92.3%	7.7%	100.0%

Pearson Chi-Square =88.84** P<0.0001

Mothers with normal cholesterol values had 96.1% term delivery and around 3.9% had pre-term delivery, whereas mothers with abnormal cholesterol had 63.1% pre-term delivery. The difference is statistically significant (p< 0.0001)

Serum cholesterol and outcome of delivery

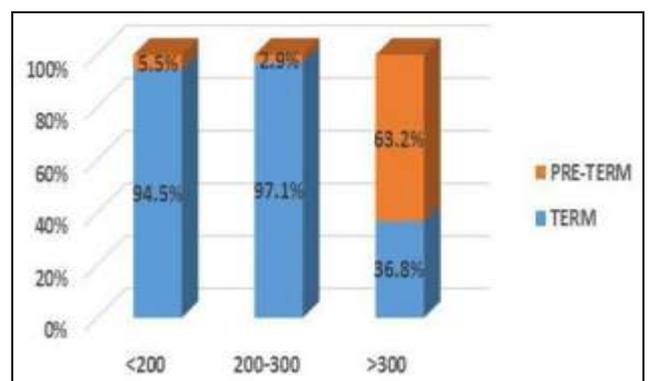


Fig 1: Comparison of SC normal with outcome

Table 2: Outcome of delivery vs Mode of delivery

Outcome of delivery	Mode of Delivery		
		Normal	LSCS
Count		168	109
Term	%age	60.6%	39.4%
Pre-Term	Count	19	4
	%age	82.6%	17.4%

Pearson Chi-Square =4.36, P<0.05

Table 3: Outcome of Fetal Weight (in Kgs)

Outcome of Delivery	#	Fetal Weight (in Kgs)	
		Mean	SD
Term	277	2.7812	0.2105
Preterm	23	1.9541	0.3869

The mean fetal weight of children delivered at term are significantly higher than that of pre-term children.

Table 4: Outcome of delivery and NICU Admissions

NICU_ Admission	NO	Count	Outcome1		
			Pre Term	Term	Total
			5	270	275
		% within	21.7%	97.5%	91.7%
		Outcome1			
	YES	Count	18	7	25
		% within	78.3%	2.5%	8.3%
		Outcome1			
Total		Count	23	277	300
		% within	100.0%	100.0%	100.0%
		Outcome1			

Person Chi-Square =159.45** P<0.0001

The outcome of deliveries had significant association with NICU admissions (p< 0.0001)

Discussion

Preterm delivery is defined as by WHO, birth occurring prior to 37 completed weeks gestation. The incidence in India is 10 – 12% and developed countries is 5% to 10%.

Serum cholesterol levels increase during pregnancy & is necessary uteroplacental vascularisation, placental transport functions. Hyperlipidaemia is also regarded as an instigator of inflammation and stress, which is a significant factor in preterm birth.

In this study, 300 antenatal mothers with singleton pregnancy between the gestational age of 14-24 weeks were enrolled. After detailed history taking and physical examination, fasting maternal serum cholesterol levels were estimated and the patients were followed till delivery (preterm / term).

The incidence of preterm delivery, mode of delivery, gestational age at delivery was noted; to study the linear trend and to estimate if there is a dose response relationship between increasing cholesterol values and gestational age at delivery.

American medical journal Obstetrics and Gynaecology 2007, December 197 (6) 610. Cator jim, Bodnar studied in early pregnancy lipid concentration and spontaneous preterm birth.

In that case control study of women with spontaneous preterm birth, cholesterol, high density lipoprotein, low density lipoprotein, triglycerides were evaluated. Lipid concentration and gestational changes as well as risk for preterm birth were

evaluated in women who delivered < 34 weeks (n=23)

> or = 34 (n=67) and > or = 37 weeks (n=199)

High cholesterol, triglycerides < or = 15 weeks were associated with a 2.8 fold and 2.0 fold (1.0 – 3.9) increased risk for preterm birth < 34 weeks and > or 34 < 37, respectively. Overweight female who delivered < 34 weeks had particularly elevated early pregnancy concentrations of cholesterol and low density lipoprotein. There was a reduced triglycerides response in the first half of pregnancy among female who delivered < 34 weeks. In our study Results indicate that the presence of maternal dyslipidemia in female results in spontaneous preterm birth and our result are statistically significant.

In current study out of 300 Antenatal mothers 190 are primi and 210 are second gravida. Blood collected at 14 – 24 weeks, respectively in 300 mothers.

Catov *et al.*, however, suggest that early sPTD (<34 weeks) is associated with both high and low pre-pregnancy TC [18]. This same finding is supported by Edison *et al.* during second trimester pregnancy and by Mudd *et al.* only for high TC level [13, 25].

Another study, Adegbesan-Omilabu Maymunah, Okunade Kehinde (2012) evaluated Hypercholesterolaemia in pregnancy as a predictor of adverse pregnancy outcome).

The incidences of the two adverse pregnancy outcomes examined in the study (preterm births and low birth weight (LBW) in term neonates) were 8.0% and 14.4% respectively. Preterm birth was 6.89-times more common in mothers with high cholesterol than in control mothers with normal total cholesterol level (38.5% versus 5.4%, P=0.029) while LBW was 7.99-times more common in mothers with high total maternal cholesterol than in mothers with normal cholesterol (87.5% versus 10.5%, P=0.019). Inflammation and dyslipidemia related to risk of spontaneous preterm birth.

All the mothers with normal cholesterol values had 92.6 % good outcome whereas of 63.2 % mothers with abnormal cholesterol values had preterm deliveries. This difference in statistically significant (p=0.0001).

A study by Catov JM [1], Bodnar LM, Ness RB, Barron SJ, Roberts JM. In the Department of Epidemiology, University of Pittsburgh, Pittsburgh, (PA 15261, USA. jmcst43@pitt.edu)

The authors considered that inflammation in women with spontaneous preterm birth (sPTB) might be related to their metabolic profile, such as lipids, and tested this in a nested case-control study from the Pregnancy Exposures and Preeclampsia Prevention Study (1997-2001). Cases were women with sPTB at 34-<37 weeks (n = 76) or < 34 weeks (n = 33). Controls were randomly selected women with term births (n = 228). Early pregnancy inflammation (C-reactive protein: > or = 8 microg/ml) and dyslipidemia (cholesterol: > 230 mg/dl or triglycerides: > 140 mg/dl) were evaluated in serum collected at < 21 weeks. Polycotomous logistic regression was used to estimate the effects of dyslipidemia on the risk of sPTB subtypes. After adjustment for race, body mass index, periconceptional vitamin use, and gestational age at sampling, early pregnancy inflammation (odds ratio = 2.9, 95% confidence interval (CI): 1.1, 7.2) and dyslipidemia (odds ratio = 2.0, 95% CI: 1.0, 4.2) were independently associated with sPTB at 34-<37 weeks. The presence of both conditions increased risk of sPTB at < 34 weeks 6.4-fold (95%)

These data may have important clinical significance because they provide a possible link between preterm delivery and high lipid level.

Finding by Catov and coworkers [26] 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 present cohort study where we reported an elevated risk for preterm birth among mothers with high maternal cholesterol.

There are several limitations to this study. Their demographic, socioeconomic or medical characteristics could be small. Our results from the specific ethnic groups may not be generalizable to other population. Socioeconomic factor such as dietary intake may affect triglycerides and cholesterol concentration and risk. Finally, elevated maternal cholesterol levels may play a role in the mechanism of under lying preterm delivery or may simply be a marker for risk of preterm delivery.

Summary

- This prospective study group included 300 uncomplicated pregnant women of 14 to 24 weeks of gestation during the period August 2016 to July 2017 at Department of obstetrics and Gynaecology, MMC
- From all the antenatal mothers included in the study the blood sample of serum cholesterol was taken after overnight fasting and were followed till delivery.
- 47% of this study population were in the age group of 22 – 24 years. (mean – 22.3)
- 46.7% were primis, 53.3% were second gravidas.
- In this study, we have not seen much influence of age and parity to the outcome of delivery.
- 93.7% mothers had normal cholesterol values, 6.3% had elevated cholesterol values.
- The study group with normal cholesterol values had good outcome were as 63.2% study group with elevated cholesterol values had preterm delivery is statistically significant ($p = 0.0001$)
- The mean fetal weight delivered at term are significantly higher than those of preterm
- Among the preterm deliveries, 78.3% babies were admitted in NICU, which is statistically significant ($p < 0.0001$)
- In the current study cholesterol levels was found to be simple marker for preterm delivery

Conclusion

Serum Cholesterol levels was evaluated in 300 antenatal mothers at 14 to 24 weeks of gestation with fasting cholesterol levels.

The findings of the present study showed that serum cholesterol levels were found to be elevated in patients who have gone in for preterm labour than those gone for term pregnancy.

Hence, Serum cholesterol levels has been found to be useful simple marker for preterm delivery.

This observation helps us to describe a generic framework for combining this screening information for designing a prophylactic intervention in future.

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