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Research Article

Association of hyperlipidemia in preterm delivery

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ABSTRACT

Background: There are 3.6 million/year neonatal deaths around the world, of which 99 percent deaths are contributed by the developing countries. An infant born before 37 completed weeks is called as preterm. Normal human pregnancy results in a pronounced physiological hypertriglyceridemia involving a gestational rise in blood triglycerides (TGL) and cholesterol. As elevated circulating levels of triglycerides and cholesterol are markers for increased risk of preterm labor in pregnant women. Atherosis of the Utero placental spiral arteries may be induced by the Hyperlipidemia in pregnancy to cause preterm delivery.
Methods: The study group included 444 healthy pregnant women in the age group of 17-35 years and whose gestational age was confirmed either by their last menstrual period or by dating ultrasound. This study was conducted to evaluate the association of elevated serum triglycerides and cholesterol levels, in an uncomplicated pregnancy and preterm delivery. In all these antenatal mothers (study group) a detailed history with special reference to diet and habits, followed by a complete obstetric and general examination were done. All antenatal mothers who were included in the study were subjected for serum triglycerides and cholesterol estimation from the overnight fasting blood samples, at 24, 28, & 32 weeks of gestation.
Results: In this study 374 patients who had normal cholesterol delivered at term, however 15 patients out of 26 (42.5%) patients who showed abnormal cholesterol had preterm delivery and 22 patients out of 35 (62.8%) patients with abnormal triglycerides level delivered prematurely.
Conclusions: The measurement of serum total cholesterol and triglycerides along with other measures like clinical and serum screening of Alpha fetoprotein and inhibin A can potentially be used for predicting the preterm labor

Keywords: Preterm, Labor, Cholesterol, Hyperlipidemia, Predictor, Marker

INTRODUCTION

Obstetrics is a fine art built on the facts gathered by the scientific research. In the era of modern obstetrics where there has been a rapid advancement in all specialties, preterm labor remains an enigma for the obstetricians today.

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.[1]

Normal human pregnancy results in a pronounced physiological hypertriglyceridemia involving a gestational rise in blood triglycerides (TGL) and cholesterol.[2] During the first half of the normal pregnancy, increased maternal fat accumulation is presumed to be important for the subsequent hypertriglyceridemia normally occurring in later gestation. Circulatory concentrations of VLDL & LDL normally increase with gestational age as reflected by the

marked increase in serum TGL &Cholesterol. The hypertriglyceridemia is primarily due to enhanced entry of triglyceride rich lipoproteins in to the circulation rather than to diminished removal. Estrogen may play a major role in the lipoprotein patterns seen in human pregnancy, although LDL cholesterol is more influenced by the combined effect of increased estrogen and progesterone[1]. Additionally placental lipoprotein lipase normally increases as term approaches.

It is known that plasma triglycerides and cholesterol levels, increase during pregnancy and that enhanced lipolytic activity play a key role in making free fatty acids available to the fetus. The influence of elevated maternal triglycerides and cholesterol has not been extensively studied. As elevated circulating levels of triglycerides and cholesterol are markers for increased risk of preterm labor in pregnant women. So we evaluated the relationship of elevated triglycerides and cholesterol on the risk of preterm labor.

Aim of the study

To evaluate the association of elevated serum triglycerides and cholesterol levels 24, 28 & at 32 weeks of gestation in an uncomplicated pregnancy and preterm delivery. To associate the elevated levels of serum triglycerides and cholesterol levels as a predictor of preterm delivery.

METHODS

The study group included 444 healthy pregnant women in the age group of 17-35years and whose gestational age was confirmed either by their last menstrual period or by dating ultrasound. Patients having pregnancy induced hypertension (PIH), previous preterm delivery, multiple pregnancy, hydromnios, cervical incompetence and medical disorders were excluded from the study. This study was conducted at the institute of obstetrics Kasturba Gandhi Hospital for Women and Children, Triplicane, Chennai.

In all these antenatal mothers (study group) a detailed history with special reference to diet and habits, followed by a complete obstetric and general examination were done. The purpose of interrogation and investigation was explained to every patient and their informed consent was taken.

All antenatal mothers who were included in the study were subjected for serum triglycerides and cholesterol estimation from the overnight fasting blood samples, at 24, 28, & 32 weeks of gestation. Total serum cholesterol was determined by automated enzymatic method using Burstein, Lopes-Vivella CHOD-PAP method. Triglycerides were estimated by Enzymatic Colorimetric test GPO-PAP method using reagent supplied by centronic Gm6H-Germany.

RESULTS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi-square and 'P' kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'P' value less than 0.05 is taken to denote significant relationship. In our study 400 pregnant women were enrolled, majority women included were belongs to the age group of 20-24 years and the mean age was 22.04 years (Table 1). We included 190 (47.5%) primigravids, 210 (52.5%) multigravid women. In all patients fasting blood was collected for lipid analysis after 24 weeks of gestation. None of the patients were subjected for lipid analysis beyond 32 weeks of gestation. Lipid analysis was done in 192 (48%) at 24 weeks, 154 (38.5%) at 28 weeks, and 54 (13.5%) at 32 weeks of gestation (Table 2). We considered the normal range for the cholesterol is 141 mg/dl-210 mg/dl in the first trimester 176 mg/dl-299 mg/dl in the second trimester, and 219 mg/dl-349 mg/dl in the third trimester of the pregnancy.

Table 1: Age distribution.

Age group	Cases	
	Number	**%**
Less than 20 years	31	7.8
20-24 years	321	80.3
25-29 years	48	12.0
Total	400	100
Range	19-27 years	
Mean ± SD	22.04 ± 1.94 years	

Majority of the women included in this study were 20-24 years old. The study group had a mean age of 22.04 years and a standard deviation of 1.94 years.

Table 2: Gestational age at which blood was collected for lipid analysis.

	Cases	
	Number	**%**
Trimester at the time of blood cases		
2ndTrimester	356	86.5
3rdTrimester	44	13.5
Total	400	100
Gestational age		
24 weeks	197	49.25
28 weeks	159	39.75
32 weeks	44	11
Total	400	100

Lipid levels were assessed for 356 mothers in second trimester and for 44 mothers in the second trimester

In this study 26 (6.9%) mothers had an abnormal cholesterol level from the second trimester and was maintained above the normal range even in third trimester, however ten patients in whom serum cholesterol was estimated in third trimester out of 44 (22.7%) patients showed abnormal cholesterol level (Table 3). We considered the normal range for the Triglycerides is 40 mg/dl-159 mg/dl in the first trimester, 73 mg/dl-382 mg/dl in the second trimester, and 131 mg/dl-453 mg/dl in the third trimester of the pregnancy. 25 patients out of 321 (7.5%) in whom serum triglycerides (Table 4) was estimated in the second trimester showed abnormal values, however only 10 patients out of 44 (122.7%) showed abnormal value in whom triglycerides was estimated in third trimester.

Table 3: Total cholesterol level estimation.

Trimester	Total cholesterol level			
	Normal		Abnormal (mg/dl)	
	No.	%	No.	%
2nd trimester (346)	330	95.4	16	4.8
3nd trimester (54)	44	81.5	10	18.9
Total (400)	374	93.5	26	6.7
Range	145-397			
Mean ± SD	247.3 ± 41.3			

26 mothers (6.7%) had abnormal cholesterol levels in the second trimester and 10 mothers (18.9%) in the third trimester. The study had a serum cholesterol level of 247.3 ± 41.3 mg/dl.

Table 4: Serum triglycerides level estimation.

Trimester	Serum triglycerides (TGL) (mg/dl)			
	Normal		Abnormal	
	No.	%	No.	%
2nd trimester (346)	321	90.2	25	7.5
3nd trimester (54)	44	81	10	18.9
Total (400)	365	91.2	35	8.8
Range	86-472 mg/dl			
Mean ± SD	278.9 ± 79.6			

7.5% of mothers in the second trimester and 18.9% of mothers in the third trimester had abnormal triglycerides values. The mothers had an average TGL of 278.9 mg/dl

In this study, 374 patients who had normal cholesterol delivered at term, however 15 patients out of 26 (42.5%) patients who showed abnormal cholesterol had preterm delivery (Table 5) and 22 patients out of 35 (62.8%) patients with abnormal triglycerides level delivered prematurely (Table 6). The percentage of preterm deliveries among primigravid mothers and Multi gravid mothers did not show any statistically significant difference (P=0.5611), (Table 7). The mean fetal weight of children delivered at term was significantly higher than that of the pre-term children (P=0.0001) (Table 8).

Table 5: Serum cholesterol and pregnancy outcome.

Serum cholesterol	No. of cases	Outcome of delivery			
		Good		Preterm	
		No.	%	No.	%
Normal	374	374	100	-	-
Abnormal	26	11	42.3	15	42.3
Sr. cholesterol (Mean ± SD)	245.2 ± 329.3				
	39.5 ± 25.3				
'P'	0.0001 Significant				

All the mothers with normal cholesterol values had good outcomes, whereas 42.3% of mothers with abnormal cholesterol values had preterm deliveries. This difference is statistically significant (P=0.0001)

Table 6: Serum triglycerides and pregnancy outcome.

Serum triglycerides	No. of cases	Outcome of delivery			
		Term delivery		Preterm	
		No.	%	No.	%
Normal	365	364	99.7	1	0.3
Abnormal	35	13	37.5	22	62.8
Sr. TGL (Mean ± SD)	275.2 ± 411.3				
	77.3 ± 50.4				
'P'	0.0001 Significant				

0.3% of mothers with normal triglyceride values and 62.8% of mothers with abnormal values had pre term delivery. The mean TGL values of these two types of outcome were275.5 and 411.3. These differences are statistically significant (P<0.05)

Table 7: Obstetric index and outcome of delivery.

Obstetrics index	No. of cases	Outcome of delivery			
		Term		Preterm	
		No.	%	No.	%
Primigravida	190	172	90.5	18	9.47
Multigravida	210	191	90.95	19	9.04
'P'	0.5611 Not Significant				

The percentage of preterm deliveries among primi gravid mothers and multi gravid mothers did not statistically significant difference (P=0.5611).

Table 8: Outcome of delivery and fetal weight.

Outcome of delivery	Fetal weight (kg)
	Mean ± SD
Term delivery	2.87 ± 1.23
Preterm delivery	1.93 ± 0.16
'P'	0.0001, Significant

The mean fetal weight of children delivered at term was significant higher than of the pre-term children (P=0.0001).

DISCUSSION

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.[3] The most important outcome of preterm delivery is a premature infant, which is the most common cause of infant mortality after the congenital abnormalities.[4] There are 3.6 million/year neonatal deaths around the world, of which 99 percent deaths are contributed by the developing countries.[5]

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.[6-8] Atherosis of the utero placental spiral arteries may be induced by the Hyperlipidemia in pregnancy. Atherosis of the vital placental arteries combined with hyper coagulation may result in thrombosis and placental infarctions, leading to placental insufficiency and thereby fetal compromise.[9] This fetal compromise is in the form of preterm delivery (birth <gestation week 37) and/or low birth weight (<2500 g).[10]

Study conducted by Kramer et al.[11] 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 Alleman 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.

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.[13,14] It would be difficult for us to say that elevated serum cholesterol and triglycerides level can be used as significant serum markers to predict preterm delivery, as in our present study many of the above variables were missed in the questionnaire design.

In this study, 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,[15] 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.

CONCLUSION

The measurement of serum total cholesterol and triglycerides along with other measures like clinical and serum screening of Alpha fetoprotein and inhibin A can potentially be used for predicting the preterm labor.

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