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Levels of hs-CRP and Lipid Profile in Preeclampsia

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ABSTRACT

Preeclampsia is a potentially serious disorder in pregnancy. The present study compared the changes in serum lipid profile and serum hs CRP in normal pregnancy and in women with preeclampsia during antenatal period and 48hrs of postnatal period. hs CRP levels were seen to be significantly higher in preeclamptic women when measured in the last trimester compared to normal pregnant women. Lipid levels were deranged in most of the women belonging to the preeclampsia group and there were significant changes in the lipid levels in postnatal period. hs CRP and lipid profile estimation might help in diagnosis of preeclampsia.

Keywords: Preeclampsia, hs CRP, lipid profile

INTRODUCTION

Preeclampsia is a pregnancy specific disorder characterized by host of abnormalities resulting in vascular endothelial damage and vasospasm leading to development of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive and non-proteinuric women[1]. In developing countries, the incidence of disease is reported to be 4-18%[2]. For every woman who dies, it is estimated that around 20 other women suffer from severe morbidity and disability[3]. In India the incidence of preeclampsia is reported to be 8-10% of the pregnancies[4]. The incidence in primigravida is about 10% and in multigravida about 5%[5]. Without intervention the mother is at substantial risk for seizures (eclampsia), renal and liver failure, pulmonary oedema, stroke, and death. For the foetus, preeclampsia results in an increased risk for intrauterine growth restriction, prematurity, and death. Preeclampsia is also recognized as a major risk factor for cardiovascular disease later in life for both the woman and her child. Unfortunately, there is no effective therapy for the management of severe preeclampsia, and the only "cure" is to deliver the baby [6]. Adverse perinatal outcome including, but not limited to, foetal intracranial haemorrhage and death can occur from untreated hypertension in pregnancy. Appropriate maintenance of blood pressure in pregnancy is therefore of paramount importance.

Preeclampsia is diagnosed by de novo development of hypertension i.e. systolic blood pressure ≥140 mm hg and/or diastolic blood pressure ≥ 90 mm hg and proteinuria after 20 weeks of gestation. Proteinuria is defined as a 24hour urinary protein excretion exceeding 300mg, a urine protein: creatinine ratio of >0.3, or persistent 30 mg/dl (≥1+ on dipstick) protein in random urine samples.[1]

The occurrence of this potentially devastating disorder called preeclampsia needs to be reduced or prevented. This requires better understanding of the etiology and pathophysiology of preeclampsia. Also, there is a need for useful screening tests to identify those who are at risk. Despite considerable research, the cause or causes of preeclampsia remain unclear and currently, there are no clinically useful screening tests to identify women in whom it will develop[7]. Acute onset of severe systolic hypertension, severe diastolic hypertension or both can occur during pre-natal, intra natal or

postnatal periods and require standardized, evidence based clinical diagnostic factors for appropriate and expeditious management. In the mother, pre-eclampsia may cause premature cardiovascular disease, such as chronic hypertension, ischemic heart disease and stroke later in life, while children born after preeclamptic pregnancies and who are relatively small at birth with increased risk of stroke, coronary heart disease and metabolic syndrome in adult life[8].

High sensitivity C - reactive protein (hs CRP) is an objective and sensitive index of overall inflammatory activity in the body[9]. The hs CRP concentration in peripheral circulation is also known to be associated with Body Mass Index (BMI) and other markers of adiposity[10,11]. It has been suggested that hs CRP, in accordance with its proposed function, may play a role in eliciting the inflammatory response characteristics of preeclampsia[12]. Elevated hs CRP level are correlated with obesity. It is to be known that hs CRP and obesity are associated factors which predisposes to preeclampsia. Systemic maternal inflammatory response to pregnancy is responsible for the endothelial dysfunction which gives the clinical and pathological picture of preeclampsia .The association between hs CRP levels and subsequent preeclampsia supports the hypothesis that systemic inflammation is involved in the pathogenesis of preeclampsia which starts from the first trimester of pregnancy. Abnormal lipid profiles may have role in development of oxidative stress and maternal endothelial dysfunction which is a classical hallmark of preeclampsia.

Until date, endothelial dysfunction in the placental vasculature is considered as a widely accepted theory for the etiology and the pathogenesis of the disease[13]. Several studies have shown that endothelial dysfunction is related to hyperlipidaemia [14,15]. Studies in the field of cardiovascular research have shown that serum lipids have a direct effect on endothelial function and in this way abnormal serum lipid profiles are associated with endothelial dysfunction[16].

According to the current knowledge, rise in hs CRP and lipid levels are major contributing factor in pathogenesis of preeclampsia. The association of altered lipid profile in essential hypertension is well documented. In early pregnancy there is increased body fat accumulation due to increased lipogenesis and early pregnancy dyslipidaemia is associated with an increased risk of preeclampsia[17].

Various studies have shown that lipid levels are elevated during pregnancy. Alteration in hormones during pregnancy results in changes of serum lipids and usually levels of lipids revert to normal shortly after delivery. Compared to normal pregnancies, in preeclampsia endocrinological alterations are more, hence there will be a change in serum lipids in preeclampsia also[18]. The alteration of lipid metabolism may play a key role in the development of symptoms of preeclampsia.

The present study had been undertaken to compare the changes in serum lipid profile and serum hs CRP in normal pregnancy and in women with preeclampsia during antenatal period and at 48hours of postnatal period.

MATERIALS AND METHODS

This was a prospective observational study conducted in the Department of Obstetrics & Gynaecology in collaboration with Department of Biochemistry of a tertiary care medical college and hospital of West Bengal, conducted over one year and two months. The study was conducted after obtaining prior ethical clearance from the ethics committee. Antenatal mothers attending the department of obstetrics and gynaecology at 29-40 weeks of gestation were enrolled according to inclusion and exclusion criteria into the following groups:

Group A – Pregnant women with gestational age at 29 to 40 weeks with preeclampsia were considered as case.

Group B – Age and gestational age matched normotensive pregnant women were taken as controls.

Inclusion criteria:

- Women aged between 18-35yrs
- Women diagnosed as Preeclampsia
- Women in third trimester of pregnancy
- Age and gestational period matched normotensive mothers without preeclampsia

Exclusion criteria:

- Gestational diabetes mellitus
- Chronic systemic disorders like essential hypertension, diabetes, severe anemia, over-weight based on BMI, renal disease, thyroid disorders, collagen vascular disease.
- Recent history of fever
- Any known chronic inflammatory diseases
- History of smoking
- Ultrasound proven congenital anomalies
- PROM
- Patient taking any drug which may alter lipid profile
- Patient in labour

All subjects included in our study were subjected to detailed history regarding age, parity, gravida according to the predesigned and pretested questionnaire, after taking proper informed consent. General physical examination, along with obstetrical examination with special reference to BMI, oedema, blood pressure and gestational period in weeks was evaluated.

High sensitivity CRP, total cholesterol, HDL- cholesterol, LDL-cholesterol, VLDL- cholesterol, triglycerides of all the pregnant women in the study group was assayed. Special investigations were repeated 48 hours after delivery in both case and control group to measure the changes in these parameters in women with preeclampsia as compared to normal pregnant women.

All the relevant data was analysed by appropriate statistical tests using Statistical Package for Social Sciences (SPSS) version 20.0.Continuous variables were expressed as mean, median, standard deviation (SD) and compared across the groups using Mann-Whitney U test . Categorical variables were expressed as number and percentage of patients and compared across the groups using Fishers exact test. An alpha level of 5% had been taken, if any p value was less than 0.05, it was considered as significant.

RESULTS

For each of the tables 1, 2, 3, 4, 5 and 6:

Table 1: Comparison of the Two Groups in Terms of change in hs-CRP (mg/L) over time

hs-CRP (mg/L)	Subgroups included				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Case (n=62)		Control(n=64)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
At enrolment	15.45 (3.27)	18.95 (4.15)	4.06 (1.54)	4.40 (2.35)	<0.001
48-Hours Postpartum	38.07 (3.89)	41.65 (5.67)	13.48 (2.07)	13.30 (2.50)	<0.001
Absolute Change	-20.62 (3.16)	-22.35 (2.73)	-9.42 (2.61)	-9.20 (3.70)	<0.001
Percent Change	-128.2% (35.9)	-117.5% (43.5)	-312.2% (240.1)	-239.3% (234.7)	<0.001
P Value for change in hs-CRP (mg/L) over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in hs-CRP (mg/L) over time between the two groups (Generalized Estimating Equations Method)	<0.001				

Non-parametric tests were used to make statistical inference as data were not normally distributed. Wilcoxon rank-sum test (Mann Whitney U test) was used to compare the two groups at each of the timepoints (right-most column in each of the tables). Wilcoxon signed-rank test was used to explore the difference in the respective

parameter between the two time points within each group (second-last row in each of the tables). Generalized Estimating Equations method was used to explore the difference in change in the respective parameter between the two groups over time (last row in each of the tables).

In Pre-eclamptic women, the mean hs-CRP (mg/L) increased from a minimum of 15.45 at the Enrolment timepoint to a maximum of 38.07 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 0.0, p = <0.001).

In normal pregnant women, the mean hs-CRP (mg/L) increased from a minimum of 4.06 at the Enrolment timepoint to a maximum of 13.48 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 0.0, p = <0.001). The overall change in hs-CRP (mg/L) over time was compared in the two groups using the Generalized Estimating Equations method. There was a significant difference in the trend of hs-CRP (mg/L) over time in both the groups (p = <0.001).

Table 2: Comparison of the Two Groups in Terms of change in Total Cholesterol over time (n = 126)

Total Cholesterol	The study groups				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Case (n=62)		Control (n=64)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Enrolment	201.11 (9.86)	200.00 (13.75)	171.48 (22.43)	167.00 (40.00)	<0.001
48-Hours Postpartum	173.56 (10.97)	172.00 (13.75)	152.98 (22.24)	150.00 (41.25)	<0.001
Absolute Change	27.55 (3.89)	27.00 (4.00)	18.50 (2.65)	19.00 (3.00)	<0.001
Percent Change	13.7% (2.2)	13.4% (2.8)	10.9% (2.0)	10.9% (3.2)	<0.001
P Value for change in Total Cholesterol over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in Total Cholesterol over time between the two groups (Generalized Estimating Equations Method)	<0.001				

The two groups did not differ in terms of Total Cholesterol at any of the timepoints. The mean Total Cholesterol decreased from a maximum of 201.11 at the Enrolment timepoint to a minimum of 173.56 at the 48-Hours Postpartum timepoint in the case group of women. This change was statistically significant (Wilcoxon Test: V = 1953.0, p = <0.001).

In control group, the mean Total Cholesterol decreased from a maximum of 171.48 at the Enrolment timepoint to a minimum of 152.98 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 2080.0, p = <0.001).

The overall change in Total Cholesterol over time was compared in the two groups using the Generalized Estimating Equations method. There was a significant difference in the trend of Total Cholesterol over time in both the groups (p = <0.001).

In Pre-eclamptic women, the mean Triglyceride decreased from a maximum of 197.37 at the Enrolment timepoint to a minimum of 171.29 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 1953.0, p = <0.001).

The mean Triglyceride decreased from a maximum of 143.72 at the Enrolment timepoint to a minimum of 127.48 at the 48-Hours Postpartum timepoint in control group. This change was statistically significant (Wilcoxon Test: V = 2080.0, p = <0.001).

The overall change in Triglyceride over time was compared in the two groups using the Generalized Estimating Equations method. There was a significant difference in the trend of Triglyceride over time in both the groups (p = <0.001).

Table 3: Comparison of the Two Groups in Terms of change in Triglyceride over time

Triglyceride	Study population				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Case (n=62)		Control (n=64)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Enrolment	197.37 (24.96)	196.00 (39.75)	143.72 (7.28)	146.00 (12.00)	<0.001
48-Hours Postpartum	171.29 (24.21)	168.50 (39.75)	127.48 (6.34)	128.00 (12.25)	<0.001
Absolute Change	26.08 (3.64)	27.00 (6.75)	16.23 (3.04)	17.00 (6.00)	<0.001
Percent Change	13.4% (2.2)	13.2% (2.8)	11.3% (1.9)	11.9% (2.9)	<0.001
P Value for change in Triglyceride over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in Triglyceride over time between the two groups (Generalized Estimating Equations Method)	<0.001				

Table 4: Comparison of the Two Groups in Terms of change in LDL- Cholesterol over time (n = 126)

LDL- Cholesterol	Study groups				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Case group		Control group		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Enrolment	105.97 (13.65)	105.00 (20.25)	97.25 (11.33)	99.50 (19.50)	<0.001
48-Hours Postpartum	93.42 (13.73)	92.00 (17.75)	79.59 (11.47)	82.00 (21.00)	<0.001
Absolute Change	12.55 (1.83)	13.00 (3.00)	17.66 (1.64)	18.00 (3.00)	<0.001
Percent Change	12.0% (2.3)	12.1% (2.7)	18.4% (2.9)	18.2% (3.7)	<0.001
P Value for change in LDL- Cholesterol over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in LDL-Cholesterol over time between the two groups (Generalized Estimating Equations Method)	<0.001				
Overall P Value for comparison of change in LDL-Cholesterol over time between the two groups (Generalized Estimating Equations Method)	<0.001				

The two groups did not differ in terms of LDL- Cholesterol at any of the timepoints.

In women belonging to case group, the mean LDL- Cholesterol decreased from a maximum of 105.97 at the Enrolment timepoint to a minimum of 93.42 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 1953.0, p = <0.001).

In normal pregnant women, the mean LDL- Cholesterol decreased from a maximum of 97.25 at the Enrolment timepoint to a minimum of 79.59 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 2080.0, p = <0.001).

The overall change in LDL-Cholesterol over time was compared in the two groups using the Generalized Estimating Equations method. There was a significant difference in the trend of LDL-Cholesterol over time in both the groups (p = <0.001).

The two groups did not differ in terms of HDL- Cholesterol at any of the timepoints.

In women with preeclampsia, the mean HDL- Cholesterol increased from a minimum of 46.60 at the Enrolment timepoint to a maximum of 51.81 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 0.0, p = <0.001).

Normal pregnant women, the mean HDL- Cholesterol increased from a minimum of 48.91 at the Enrolment timepoint to a maximum of 56.55 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 0.0, p = <0.001).

The overall change in HDL- Cholesterol over time was compared in the two groups using the Generalized Estimating Equations

method. There was a significant difference in the trend of HDL- Cholesterol over time in both the groups (p = <0.001).

Table 5: Comparison of the Two Groups in Terms of change in HDL- Cholesterol over time (n = 126)

HDL- Cholesterol	Groups included in our study				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Case (n=62)		Control (n=64)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Enrolment	46.60 (8.10)	45.50 (13.00)	48.91 (6.72)	48.00 (11.25)	0.087
48-Hours Postpartum	51.81 (8.15)	50.50 (14.75)	56.55 (6.71)	56.00 (10.50)	0.001
Absolute Change	-5.21 (0.79)	-5.00 (1.00)	-7.64 (0.68)	-8.00 (1.00)	<0.001
Percent Change	-11.5% (2.6)	-11.2% (4.3)	-15.9% (2.8)	-15.3% (3.6)	<0.001
P Value for change in HDL- Cholesterol over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in HDL-Cholesterol over time between the two groups (Generalized Estimating Equations Method)	<0.001				

Table 6: Comparison of the Two Groups in Terms of change in VLDL- Cholesterol over time (n = 126)

VLDL- Cholesterol	GROUPS				P value for comparison of the two groups at each of the timepoints (Wilcoxon-Mann-Whitney U Test)
	Cases (n=62)		Control (n=64)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Enrolment	54.97 (5.54)	54.50 (8.75)	33.78 (2.99)	33.50 (4.25)	<0.001
48-Hours Postpartum	38.35 (5.27)	37.50 (8.50)	23.05 (2.78)	23.00 (4.00)	<0.001
Absolute Change	16.61 (1.12)	17.00 (2.00)	10.73 (0.72)	11.00 (1.00)	<0.001
Percent Change	30.5% (3.0)	30.6% (3.2)	31.9% (2.7)	32.3% (3.0)	<0.001
P Value for change in VLDL- Cholesterol over time within each group (Wilcoxon Test)	<0.001		<0.001		
Overall P Value for comparison of change in VLDL-Cholesterol over time between the two groups (Generalized Estimating Equations Method)	<0.001				

The two groups did not differ in terms of VLDL- Cholesterol at any of the timepoints.

In the cases: Present, the mean VLDL- Cholesterol decreased from a maximum of 54.97 at the Enrolment timepoint to a minimum of 38.35 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 1953.0, p = <0.001).

In the controls, the mean VLDL-Cholesterol decreased from a maximum of 33.78 at the Enrolment timepoint to a minimum of 23.05 at the 48-Hours Postpartum timepoint. This change was statistically significant (Wilcoxon Test: V = 2080.0, p = <0.001).

The overall change in VLDL-Cholesterol over time was compared in the two groups using the Generalized Estimating Equations method. There was a significant difference in the trend of VLDL-Cholesterol over time in both the groups (p = <0.001).

Table 7: Performance of Study Parameters for Predicting Pre-eclampsia
Description of Variables

Variable	Category(s) Suggesting Outcome Present	Category(s) Suggesting Outcome Absent	Total Positives	True Positives	True Negatives	False Positives	False Negatives
Pre-eclampsia	Present	Absent	62 (49.2%)	-	-	-	-
hs-CRP (mg/L) (Enrolment) (Cut off :10 by ROC)	>=10	<10	55(43.6%)	55 (43.6%)	65 (51%)	0 (0%)	0 (0%)
Total Cholesterol (Enrolment) (Cut off:190 by ROC)	>=190	<190	76 (60.3%)	60 (48%)	48 (38%)	16 (13%)	2 (2%)
Triglyceride (Enrolment) (Cut off: 165 by ROC)	>=165	<165	62 (49.2%)	62 (49%)	64 (51%)	0 (0%)	0 (0%)

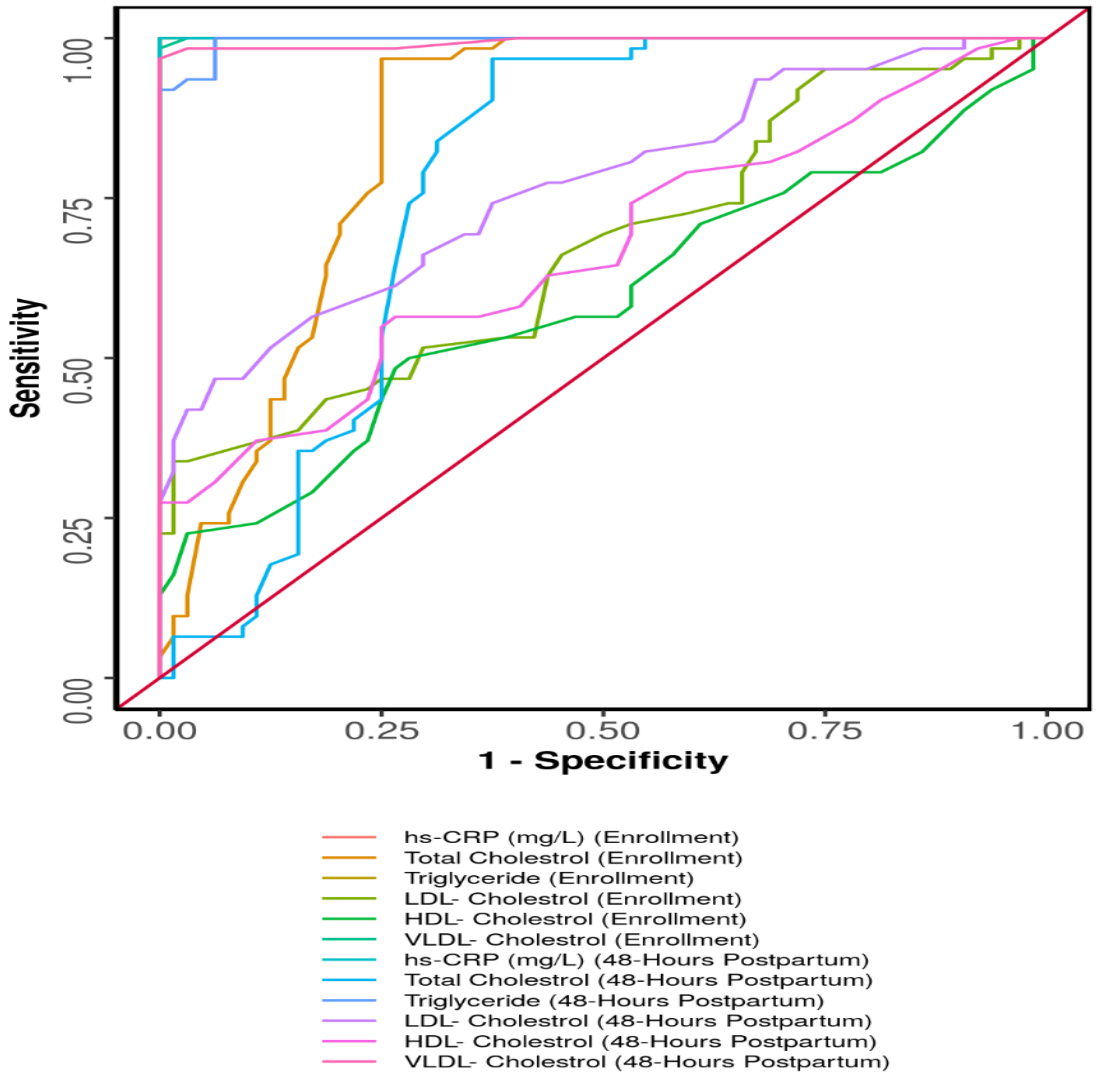
LDL- Cholesterol (Enrolment) (Cut off: 112 by ROC)	>=112	<112	22 (17.5%)	21 (17%)	63 (50%)	1 (1%)	41 (33%)
HDL- Cholesterol (Enrolment) (Cut off: 45 by ROC)	<=45	>45	49 (38.9%)	31 (25%)	46 (37%)	18 (14%)	31 (25%)
VLDL- Cholesterol (Enrolment) (Cut off: 48 by ROC)	>=48	<48	61 (48.4%)	61 (48%)	64 (51%)	0 (0%)	1 (1%)
hs-CRP (mg/L) (48-Hours Postpartum) (Cut off: 28.6 ROC)	by>=28.6	<28.6	54 (42.8%)	54 (42.8%)	65 (51%)	0 (0%)	0 (0%)
Total Cholesterol (48-Hours Postpartum) (Cut off: 160 ROC)	by>=160	<160	84 (66.7%)	60 (48%)	40 (32%)	24 (19%)	2 (2%)
Triglyceride (48-Hours Postpartum) (Cut off: 138 ROC)	by>=138	<138	66 (52.4%)	62 (49%)	60 (48%)	4 (3%)	0 (0%)
LDL- Cholesterol (48-Hours Postpartum) (Cut off: 94 ROC)	by>=94	<94	33 (26.2%)	29 (23%)	60 (48%)	4 (3%)	33 (26%)
HDL- Cholesterol (48-Hours Postpartum) (Cut off: 52 ROC)	by<=52	>52	52 (41.3%)	35 (28%)	47 (37%)	17 (13%)	27 (21%)
VLDL- Cholesterol (48-Hours Postpartum) (Cut off: 32 ROC)	by>=32	<32	60 (47.6%)	60 (48%)	64 (51%)	0 (0%)	2 (2%)

Primary Diagnostic Parameters

Table 8. ROC CURVE COMPARING THE VARIABLES ASSAYED IN THE STUDY

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
hs-CRP (mg/L) (Enrolment) (Cut off: 10 by ROC)	98.8% (94-100)	91.5% (94-100)	90.16%% (94-100%%	100)	98.10% (97-100)
Total Cholesterol (Enrolment) (Cut off: 190 by ROC)	96.8% (89-100)	75.0% (63-85)	78.9% (68-87)	96.0% (86-100)	85.7% (78-91)
Triglyceride (Enrolment) (Cut off: 165 by ROC)	97.4% (94-100)	96.2% (94-100)	98.0% (94-100)	80.0% (94-100)	99.3% (97-100)
LDL- Cholesterol (Enrolment) (Cut off: 112 by ROC)	33.9% (22-47)	98.4% (92-100)	95.5% (77-100)	60.6% (51-70)	66.7% (58-75)
HDL- Cholesterol (Enrolment) (Cut off: 45 by ROC)	50.0% (37-63)	71.9% (59-82)	63.3% (48-77)	59.7% (48-71)	61.1% (52-70)
VLDL- Cholesterol (Enrolment) (Cut off: 48 by ROC)	98.4% (91-100.0% (94-100)		100.0% (94-100)	98.5% (92-100)	99.2% (96-100)
hs-CRP (mg/L) (48-Hours Postpartum) (Cut off: 28.6 by ROC)	97.9% (94-100)	90.27% (94-100)	94.7% (94-100)	82% (94-100)	96.8% (97-100)
Total Cholesterol (48-Hours Postpartum) (Cut off: 160 by ROC)	96.8% (89-100)	62.5% (50-74)	71.4% (61-81)	95.2% (84-99)	79.4% (71-86)
Triglyceride (48-Hours Postpartum) (Cut off: 138 by ROC)	95.2% (94-100)	93.8% (85-98)	93.9% (85-98)	90.0% (94-100)	96.8% (92-99)
LDL- Cholesterol (48-Hours Postpartum) (Cut off: 94 by ROC)	46.8% (34-60)	93.8% (85-98)	87.9% (72-97)	64.5% (54-74)	70.6% (62-78)
HDL- Cholesterol (48-Hours Postpartum) (Cut off: 52 by ROC)	56.5% (43-69)	64.4% (61-84)	67.3% (53-80)	63.5% (52-74)	65.1% (56-73)
VLDL- Cholesterol (48-Hours Postpartum) (Cut off: 32 by ROC)	96.8% (89-100.0% (94-100)		100.0% (94-100)	97.0% (89-100)	98.4% (94-100)

hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), VLDL- Cholesterol (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum), Triglyceride (48-Hours Postpartum), VLDL-Cholesterol (48-Hours Postpartum), Total Cholesterol (Enrolment), Total Cholesterol (48-Hours Postpartum), LDL- Cholesterol (48-Hours Postpartum), LDL- Cholesterol (Enrolment), HDL- Cholesterol (48-Hours Postpartum) significantly predicted preeclampsia.



Trends (table 9):

Best parameter in terms of AUROC: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), VLDL (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum).

Best parameter in terms of sensitivity: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum), Triglyceride (48-Hours Postpartum).

Best parameter in terms of specificity: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), VLDL- Cholesterol (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum), VLDL- Cholesterol (48-Hours Postpartum).

Best parameter in terms of positive predictive value: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), VLDL- Cholesterol (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum), VLDL-Cholesterol (48-Hours Postpartum).

Best parameter in terms of negative predictive value: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), hs CRP (mg/L) (48-Hours Postpartum), Triglyceride (48-Hours Postpartum).

Best parameter in terms of diagnostic accuracy: hs-CRP (mg/L) (Enrolment), Triglyceride (Enrolment), hs-CRP (mg/L) (48-Hours Postpartum).

Table 9. Pairwise comparison of parameters for predicting Pre-eclampsia (Parameters have been arranged in descending order of AUROC):

Parameter	1	2	3	4	5	6	7	8	9	10	11	12
1. hs-CRP (mg/L) (Enrolment)	-											
2. Triglyceride (Enrolment)		-										
3. VLDL- Cholesterol (Enrolment)			-									
4. hs-CRP (mg/L) (48-Hours Postpartum)				-								
5. Triglyceride (48-Hours Postpartum)					-							
6. VLDL- Cholesterol (48-Hours Postpartum)						-						
7. Total Cholesterol (Enrolment)							-					
8. Total Cholesterol (48-Hours Postpartum)								-				
9. LDL- Cholesterol (48-Hours Postpartum)									-			
10. LDL- Cholesterol (Enrolment)										-		
11. HDL- Cholesterol (48-Hours Postpartum)											-	
12. HDL- Cholesterol (Enrolment)												-

Green Block: AUROC of the row parameter is significantly greater than AUROC of column parameter (by DeLong's Test); Yellow Block: No statistically significant difference in the diagnostic performance of the corresponding row and column variables.

DISCUSSION

Preeclampsia is a major cause of maternal and perinatal morbidity and mortality in all developed as well as developing countries especially in India. Management of preeclampsia aims to minimize complications, avoiding unnecessary prematurity and maximize maternal and perinatal/neonatal survival. However, Preeclampsia is a disease of theories whose pathogenesis is not clearly understood. Studies among Caucasian women have suggested that maternal predisposition to preeclampsia may be explained by abnormal lipid metabolism.[19]

The serum hs CRP levels in the preeclamptic women had a median value of 18.95 mg/L as compared to the median value in normal pregnant women being 4.40 mg/L at the time of enrolment in our study. These values rose in both the groups when measured 48hrs in postpartum period to a significant value. In the preeclamptic women it increased from a minimum of 18.45mg/L at the time of enrolment to a maximum of 41.07mg/L at 48 hours postpartum timepoint and in the women with normal pregnancy it increased from a minimum of 4.06mg/L at the enrolment timepoint to a maximum of 13.48mg/L at 48 hours postpartum (table 1). The changes as seen in study conducted by Onuegbu A et al[20] showed significantally higher serum hs CRP levels in preeclamptic women group i.e 8.57+/-0 2.68mg/l and control showing 6.46+/- 2.46 mg/l (p value=0.001). The rise in hs CRP levels in both the groups is seen 48hrs postpartum may be explained by the inflammatory reactions taking place in the postpartum phase in all the women, owing to changes like lochial discharge, retraction of uterus, breast changes during feeding etc.

In our study serum levels of total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and VLDL cholesterol of preeclamptic women and normotensive women were assessed in the antepartum and at 48hrs postpartum period. In the antepartum period mean serum total cholesterol was decreased from a maximum of 201.11mg/dl at the time of enrolment to a minimum of 173.56mg/dl at 48 hours postpartum. The change was statistically significant (p <0.001). The mean total Cholesterol decreased from a maximum of 171.48mg/dl at the enrolment timepoint to a minimum of 152.98mg/dl at 48 hours postpartum period in normal pregnant women. This change was statistically significant (p<0.001)(table 2). There was significant increase in the values in preeclamptic group of women but the fall in values in postpartum period was comparable in each of them. Vijayalakshmi P et al [21] in their study, also suggest that the levels of total cholesterol rose significantly in women with preeclampsia as compared to that of normal pregnant women signifying its role in determining preeclampsia at an earlier gestational age in high risk women.

The serum triglyceride level in preeclamptic women had a mean value of

197.37mg/dl in antenatal period which decreased in postnatal period showing mean value of 171.29mg/dl. As compared to normal antenatal mothers having mean value of 143.73mg/dl and in postpartum phase shows a mean value of 128mg/dl. Values in both the groups are statistically significant ($p<0.001$)(table 3). The principle modulator of this hypertriglyceridemia is oestrogen as pregnancy is associated with hyper-estrogenemia. Estrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL[22].This process may be modulated by hyperinsulinemia found in pregnancy[23] .Increased TG, found in pregnancy induced hypertension is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL[24] .Moreover, this hypertriglyceridemia may be associated with hypercoagulability. Although it is still unclear whether hypertriglyceridemia becomes a risk factor for preeclampsia or whether there is any causal association between these. High triglyceride levels seem to increase the risk of placental vascular disorders, which trigger endothelial dysfunction, atherosclerosis and thrombosis [6,25]. The development of atherosclerosis in the placental spiral arteries of preeclamptic women indicates that elevated levels of triglycerides are involved in this disorder[26.] Ray et al reported that women with elevated triglycerides had twice the risk of preeclampsia, studies was adjusted for confounders (age, BMI and parity) indicated that the risk was four times higher when compared with women with normal triglyceride level[27.] Several other investigators have reported that hypertriglyceridemia could be involved in the pathogenesis of hypertensive disorders during pregnancy.[28,29,25]

In the present study, the mean value of following lipid parameters like LDL-cholesterol, HDL cholesterol, VLDL cholesterol in the preeclamptic women during antenatal period at the time of enrolment were 105.97mg/dl, 46.60mg/dl and 54.97mg/dl respectively. The normal counterparts of the same variables were seen to have a mean value of 97.25mg/dl, 48.91mg/dl and 33.78mg/dl respectively. The postpartum period of our study showed mean value of LDL,HDL,VLDL was 93.42mg/dl, 51.81mg/dl, 38.35mg/dl respectively and the normal control group had the mean values of 79.59mg/dl, 56.55mg/dl, 23.05mg/dl respectively (tables 4,5,6).

Diareme M. et al[30] in his study on lipid profile of healthy women during normal pregnancy found that after delivery the values of total cholesterol, TG, VLDL and HDL decreased, except LDL which remained steady for some weeks before starting to fall. In our study in the normotensive subjects mean serum total cholesterol, TG, LDL and VLDL levels fall significantly ($P<0.001$) and HDL level rises significantly in postpartum period ($P<0.01$), which does not correspond with the findings of Diareme M et al. Similar changes were noted in the study carried out by Parchwani D. et al[31] , whereas study by Q. Lei et al[32] showed significant decrease in serum total cholesterol, triglyceride, LDL levels but no significant change in HDL level after delivery.

In the subjects with preeclampsia mean serum total cholesterol, TG, VLDL level fell significantly ($P<0.001$) in the postpartum period in the present study. Study conducted by Gohil J.T. et al[33] showed significant decrease in postpartum mean serum total cholesterol, TG, LDL, VLDL and rise in postpartum HDL in women with preeclampsia. So, our study corresponds with the findings of Gohil J.T.et al[33].

Q. Lei et al[32] showed a decreasing trend in the mean serum total cholesterol, triglyceride, LDL and an increasing trend in mean serum HDL level in the postpartum period but the changes were not statistically significant.

The sensitivity and specificity of the total cholesterol in our study used to predict the development of preeclampsia are 96.6% and 75%,whereas sensitivity and specificity of TG , LDL,HDL,VLDL are 97.4% and 96.2%; 33.9% and 88.4% ; 50% and 71.9% ; 98.4% and 100% respectively(tables 7,8).

The differences in all these variables as compared to other studies may be due to the difference in geographical parameters, nutrition, race and most importantly the methodology of these studies[31,32,33].

The mean value of serum hs CRP levels was on the higher side in preeclamptic group at both times of sampling (15.45 vs 38.07) compared to normal pregnant women (4.06 vs 13.48). Similarly, the mean values of all the lipid profile variables were high except serum HDL levels in preeclamptic women in comparison to normal pregnancy. The HDL values were lower in the preeclamptic women whereas this value is higher to some extent in normal pregnant women.

CONCLUSION

- In the present study hs CRP levels were seen to be significantly higher in preeclamptic women when measured in the last trimester compared to normal pregnant women. The sensitivity and predictive value of hs CRP was high in these patients.
- hs CRP increased postnatally in both the study groups to a significant extent.
- This study found out that the lipid levels were deranged in most of the women belonging to the preeclampsia group and there were significant changes in the lipid levels in postnatal period.
- Diagnosis of preeclampsia by the use of the lipid parameters (especially triglyceride) might help in detection of such patients.
- We observed by this study that pregnant women with deranged lipid levels had high risk of developing preeclampsia, because dyslipidaemia in the form of high total cholesterol, TG, LDL, VLDL and low levels of HDL lasted from antepartum period to postpartum period in these women.

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