COMPARISON OF C REACTIVE PROTEIN IN VARIOUS HIGH RISK GROUP DURING PREGNANCY

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BACKGROUND: Common disorders of pregnancy are Hypertensive Disorders, Premature Rupture of Membrane and premature birth. Maternal health is especially affected when preeclampsia or more severe complications such as eclampsia or HELLP syndrome develops. C-reactive protein (CRP) is an abnormal serum glycoprotein produced by the liver during acute inflammation. Its production regulates by Interleukins 1b and 6 and tumour necrosis factor. Also, it had been a measure of acute phase reactions to inflammation for the last 15 years. Therefore, the aim of this study to determine diagnostic value of C-reactive protein (CRP) during pregnancy complicated by premature rupture of the membranes (PROM). Preterm labour and its subsequent complications makes it common, costly and catastrophic complications. **OBJECTIVE:** Comparison of CRP in Case and Controls. **MATERIALS AND METHODS:** A comparative case control study was conducted on randomly selected 200 patients with clinically diagnosed preeclampsia prelabour rupture of membrane and preterm labour in their third trimester attending outpatient department or admitted in Department of Obstetrics and Gynaecology Padmashree Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune. **RESULTS:** Out of 40 cases of Preeclampsia 34 were showed positive C reactive protein, and out of total 30 cases of both preterm labor and pre rupture of membranes both showed 18 cases positive for C reactive protein individually whereas out of 100 controls only 2 came out positive for C reactive protein

KEYWORDS: C reactive protein, Premature rupture of membranes(PROM), Preeclampsia, Preterm.

INTRODUCTION: Preterm delivery, defined as delivery prior to the completion of 37 weeks gestation and which is an important determinant of neonatal and infant morbidity and mortality, complicated some 11.9% of pregnancies in the United States in 2001 and has been steadily increasing for the past two decades.¹ Although the pathophysiology of preterm delivery remains unknown, accumulating evidence suggests that subclinical infections and chronic inflammation may account for a majority of preterm deliveries. Importantly, some investigators have indicated that infections are major causes of preterm deliveries (PTD), responsible for somewhere between 30% and 50% of all cases.^{2,3} Available evidence suggest that bacterial infection of the chorioamnion, or extraplacental membrane, may lead to chorioamnionitis, a condition strongly associated with premature rupture of membranes and preterm delivery.^{4,5} Intrauterine infections are also known to play an important etiologic role in preterm birth. Preeclampsia is a complication of pregnancy constituting a major cause of maternal and fetal morbidity and mortality.^{6,7} Moreover there is increasing evidence which suggests that other infectious processes occurring elsewhere in the body may contribute to preterm delivery.⁸⁻¹⁰

Preeclampsia is a complication of pregnancy constituting a major cause of maternal and fetal morbidity and mortality.

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It is a pregnancy specific syndrome that usually occurs after 20 weeks of gestation its clinical features include hypertension proteinuria and varying degree of ischemic end organ damage. That also may be associated with other signs and symptoms such as edema, visual disturbances, headache, and epigastric pain. Endothelial cell dysfunction and inflammation are considered to have a crucial role in the pathophysiological mechanism of preeclampsia.¹¹ Although the etiology of endothelial dysfunction in preeclampsia is unknown it has been postulated to be a part of an exaggerated maternal inflammatory response to pregnancy.¹² This inflammatory response involves also both the immune system, the clotting and fibrinolytic system.

Endothelial dysfunction is accompanied by elevated level of inflammatory markers, such as C-reactive protein (CRP).¹³ Which is a positive acute phase protein, increase in presence of infection or inflammation.¹⁴ Inflammatory response which increases during pregnancy may be explained by different stimuli occurring at different phases of pregnancy such as implantation, and the monocytes/macrophage production.

Premature rupture of the membranes (PROM) defined as rupture of membranes before onset of labor¹⁵, which is one of the most common complications of pregnancy. It occurs in approximately 10% of all pregnancies, and it is implicated in more than one third of preterm deliveries. Approximately 80% of all cases of PROM occur in term of gestations more than or equal 37 weeks; the other 20% occur in preterm gestations less than 37 weeks. Therefore, the clinical significance of PROM depends on the gestational age at which it occurs¹⁶. The etiology of PROM is multifactorial.¹⁷

C-reactive protein (CRP) is a sensitive marker of inflammation that remains stable in serum.¹⁸ Elevated concentrations of CRP in peripheral circulation have been associated with the presence of intrauterine infection.^{19,20} Additionally, investigators have noted elevated amniotic fluid CRP concentrations among women with intrauterine infections as compared with controls.^{16,17} Elevated concentrations of CRP in maternal serum during early pregnancy were associated with a 2-fold increased risk of preterm delivery.¹⁶ This early Maternal concentrations of CRP have been studied as an aid to diagnosing subclinical infection in pregnant women who experience preterm labor and premature rupture of membranes.^{6,7} Recently, elevated levels of CRP measured during gestation have been linked to adverse pregnancy outcomes such as preeclampsia^{8,9} and intrauterine growth restriction.⁹ To our knowledge, there are only two studies of the relation between CRP levels in maternal circulation during the second trimester of pregnancy and risk of preterm delivery. These studies showed contradictory results.

MATERIALS AND METHODS: A comparative case control study was conducted on randomly selected 200 patients with clinically diagnosed preeclampsia prelabour rupture of membrane and preterm labor in their third trimester attending outpatient department or admitted in Department of Obstetrics and Gynecology Padmashree Dr. D. Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune. Age gestational age matched 100 apparently healthy pregnant subjects in their third trimester were chosen as controls from the general population.

This study will commence from July 2011 and end in September 2013.

This study will include (100) cases diagnosed as having preeclampsia with different groups (group A) (20) diagnosed as mild preeclampsia and 20 diagnosed as severe preeclampsia. (30) diagnosis of preterm delivery was made using American College of Obstetricians and Gynecologists (ACOG) guidelines. 30 cases as premature rupture of membrane.

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After a thorough history taking and clinical examination, the procedure was explained to the subjects and an informed consent was obtained. Blood pressure and proteinuria in the cases were noted. 3ml of venous blood sample (fasting) was collected from antecubital vein under all aseptic precautions in a plain bulb. It was allowed to clot and then centrifuged for serum separation. Serum was used for the analysis of serum CRP. The tests were done on the same day after serum separation within 6 hours after admission.

Estimation of CRP was done by PARTICLE ENHANCED IMMUNOTURBIDIMETRIC method (Autospan Turbigold Kit).

STATISTICAL ANALYSIS: Data were entered in MS-EXCEL sheet, compiled and analyzed by Epi Info 6 version and SPSS 17 version by proper statistical tests. P-value of < 0.05 was considered statistically significant.

P value > 0.05 was taken as non-significant.

P value < 0.05 was taken as significant.

P value < 0.01 was taken as highly significant.

P value < 0.001 was taken as very highly significant.

ETHICAL CLEARANCE: Institutional ethical committee clearance was obtained prior to conduct the study.

RESULTS:

PROM:

Age (years)	Number of cases N=30	Percentage
18-20	4	13.33
20-25	16	53.33
25-30	10	33.33

Table 1: Comparison of age in study groups

PRE-TERM:

Age(years)	Number of cases N=30	Percentage
18-20	7	23.33
20-25	20	66.66
25-30	3	10

PREECLAMPSIA:

Age(years)	Number of cases N=40	Percentage
18-20	5	16.66
20-25	18	60
25-30	17	56.67

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Parameter	PROM		Preeclampsia		Preterm		F Value	P Value
	Mean	SD	Mean	SD	Mean	SD		
Age (Yrs)	23.47	3.21	25.08	3.94	22.50	2.35	5.43	<0.01

In our study PROM cases were 30 with age group 18-30 and mean age calculated to be 23.47+3.21.

In Preeclampsia 40 cases with age group 18-30 and mean age calculated to be 25.08+ 3.94.

In our study Preterm cases were 30 with age group 18-30 and mean age calculated to be 22.50+ 2.35 and the association between three different groups come out to be statistically significant ($p<0.05$) using ANOVA.

CRP	Preeclampsia	Preterm	PROM	Control
Positive	34(85%)	18(60%)	18(60%)	2
Negative	6(15%)	12(40%)	12(40%)	98
Total	40(100%)	30(100%)	30(100%)	100
Mean	34	18	18	2
Standard deviation (SD)	2.26	2.68	2.68	1.4
Variance	5.1	7.2	7.2	1.96

Table 2: Comparison of CRP in Cases and Control

Bar Diagram showing CRP in Case and Control groups

Table 2: Shows comparison of cases of preeclampsia, preterm, PROM with control, using ANOVA, a highly statistical difference ($p<0.00$) was noted, implying significance of C reactive protein implying all above condition.

DISCUSSION: In our study done on 100 cases at Obstetrics and Gynecology department of Dr. D.Y. Patil Medical college showed positive levels of C reactive proteins in 85% in Pre eclampsia and 60% positive both in PROM and Preterm.

In study Ustun et al showed that level of CRP to be significantly higher in women with mild and severe preeclampsia than in normal pregnant women with similar chronological age, gestational age, and body mass index.¹¹

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Hwang HS et al showed that CRP level was positively correlated with pregnancy duration in healthy women and could be used as a severity marker in women with severe preeclampsia.²¹

In these studies, it has been shown that CRP levels were positively related to the degree of blood pressure elevation. In our study, we found significantly higher levels of CRP in severe preeclampsia than mild preeclampsia.

Research of Ghezzi et al (2002) showed that the value of CRP in amniotic fluid is higher in those women who had delivered prematurely (before 37 weeks gestation) compared to pregnant women who delivered at term.²⁰

Loukovaara MJ agreed to our results studied serum CRP in preterm premature rupture of membranes and concluded that the increase in the highly sensitive CRP in PROM patients may reflect the presence of a subclinical inflammation.²¹

CONCLUSION:

1. The maternal morbidity and perinatal morbidity increases with duration of rupture of membrane. So strict aseptic precautions, regular antenatal care and prophylactic measures can prevent adverse perinatal and maternal outcome. Therefore, tests like CRP can help to prevent morbidity and mortality.
2. This study reveals that elevated serum CRP could help to predict adverse maternal and fetal outcomes and if timely preventive prophylactic therapies are tried, would help to prevent morbidity and mortality in pregnancy disorders.

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