

## RESEARCH ARTICLE

# Role of CRP (C- Reactive Protein) in clinical outcome in patient of PPROM

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## ABSTRACT

**Objective:** To evaluate the role of CRP in clinical outcome in patient of PPROM. **Methodology:** A prospective study was done on 90 cases with PPROM and raised CRP (>9mg/l) and 90 cases of control group with PPROM and normal CRP (<9mg/l). All mothers and babies were observed from the time of admission to the time of discharge. **Results:** The incidence of chorioamnionitis was seen to be higher in the cases with raised CRP. The socioeconomic status, parity were found to have an important role in patients developing chorioamnionitis. The sensitivity of the test (raised CRP) in causing clinical chorioamnionitis is more than 90% and specificity in 50%. Odds ratio is 12.5 i.e cases (raised CRP) have 12.5 times more chances of having clinical chorioamnionitis than those of controls (normal CRP). **Conclusion:** In cases of PPROM, raised CRP is a predictor of clinical chorioamnionitis.

**Keywords:** CRP, PPROM, chorioamnionitis, socioeconomic status.

The normal development, structural integrity and function of the fetal membranes are essential for the normal progress of pregnancy, process of labour and outcome of pregnancy. One of the most important functions of the membrane is to remain intact until the onset of labour at term. Without intervention, their spontaneous rupture usually occurs near the end of first stage of labour. However in about 10% of pregnancies, fetal membranes fails to maintain their structural integrity and ruptures either before term or at term, but before onset of labour and of these cases, about 98% lands up in labour within 48 hours. If the rupture of the membranes occurs after 28 weeks but before 37 weeks

of gestation it is termed as PPROM (Preterm Premature Rupture of Membrane) and when it ruptures after onset of labour it is called PROM (Premature Rupture of Membrane) <sup>1</sup>. The incidence of PPROM is variable between 2- 4.5% of all deliveries <sup>2</sup>. It is responsible for 30% of preterm deliveries and contributes around 10% of perinatal mortality.

Maternal complications of PPROM are chorioamnionitis, unfavourable cervix, cord prolapse, cord compression, dysfunctional labour, increased incidence of caesarean section, PPH, subinvolution, puerperal sepsis, post partum haemorrhage, endometritis. Fetal complications include increased

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incidence of prematurity, growth retardation, intrauterine infection, fetal infection, fetal distress, IUFD, hyaline membrane disease, intraventricular haemorrhage, postural deformity, neonatal sepsis - all of which leads to increased morbidity and mortality of the newborn<sup>3-7</sup>.

Early detection of infection would allow preterm birth to be expedited. The use of laboratory marker would help to distinguish women at risk from those whose pregnancy can be safely prolonged to facilitate timely management to avoid mortality and morbidity. Those that might be earlier used in routine care are CRP levels, WBC count, ESR and bacterial analysis of vaginal samples.

CRP is an acute phase protein synthesized in the liver during infection. It is a sensitive marker of inflammation that remains stable in serum. Production of CRP is stimulated by release of pro inflammatory cytokines including interleukin1, IL-6, INF-alpha. Although sometimes referred to as acute phase reactant, CRP accompanies both acute and chronic inflammatory disorder. Elevated concentration of CRP is seen both in the peripheral circulation and in the amniotic fluid in patients with intrauterine infection<sup>8,9</sup>. CRP is being used in different parts of the world as early predictor of chorioamnionitis. The aim of the study was to evaluate the role of CRP in clinical outcome in patient of PPRM.

**Methodology**

The study on the role of raised CRP (>9mg/l) in clinical outcome in patient of PPRM in 90 cases between 28-36 weeks of gestation with equal number of control groups (90 cases of PPRM with normal CRP levels, <9mg/l) was conducted at Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital within the period of May 2012 to April 2013. Pregnant women with singleton pregnancy, cephalic presentation, between 28-36 weeks with PPRM were included in this study. A patient is clinically diagnosed to be having chorioamnionitis if temperature >100 degree F, Tachycardia>100/min (1<sup>st</sup> inclusion criteria) with or without uterine tenderness and foul smelling discharge per vaginum (2<sup>nd</sup> inclusion

criteria, subjective). Exclusion criterias were multiple pregnancies, uterine anomalies, myoma uterus, antepartum haemorrhage, chronic renal failure, class 2 and class 4 cardiac diseases, gestational diabetes, fetal weight<1kg and>2.5kg, post caesarean pregnancy and pregnancy with fetal anomalies.

The data were collected in structured proforma. After admission, detailed workup including history, general physical examination, abdomen and pelvic examination and relevant /specific investigations were noted. Data were analyzed through relevant statistical tools. This study was initiated after taking permission from institutional ethic committee.

**Results**

The total number of deliveries during the study period was 15111 (May 2012- April 2013) of which 800 (5%) cases were PPRM. In our study with 90 cases of positive CRP status (CRP level > 9mg/l), 20

**Table 1: Analysis of PPRM cases with CRP status with clinical course according to the socio-economic status**

Socio-economic status	Study group		Control group	
	Cases with raised CRP>9 mg/dl	Chorioamn ionitis cases, No(%)	Cases with raised CRP<9 mg/dl	Chorioamn ionitis cases, No (%)
Upper class	3	0	3	0
Middle class	7	1(14.2%)	7	0
Lower class	80	19(23.7%)	80	2(2.5%)

cases shows sign and symptoms of chorioamnionitis (22%). Out of 90 control group (CRP < 9mg/l), two shows sign and symptoms of chorioamnionitis (2%). This findings is statistically significant (p=0.001).

In our study lower class represents maximum cases with PPRM with raised CRP, 80 cases, out of which 23.7% shows sign and symptoms of chorioamnionitis. Control group shows 2.5% chorioamnionitis in lower socio-economic group. Most of the cases coming

GMCH were from lower socio-economic group and multipara category. In this study 20 cases of PPROM

**Table 2: Analysis of PPROM cases with CRP status with clinical course according to booked or unbooked cases, parity, duration of PPROM, gestational age, baby weight.**

Categories	Study group		Control group		P value	
	CRP>9 mg/l	Chorioamnionitis cases, No (%)	CRP<9mg/l	Chorioamnionitis cases, No (%)		
Booked / Unbooked	Booked	5	0	5	0	0.05
Parity	Unbooked	85	20 (23.5%)	85	2 (2.3%)	
Duration of PPROM (in hours)	Primi	20	1(5%)	20	0	0.1
	Multi	70	19(27%)	70	2 (2.8%)	
Gestational age	<12 hrs	10	0	10	0	0.015
	13-24 hrs	20	0	20	0	
	>24 hrs	60	20 (33%)	60	2 (3%)	
Baby weight in Kg	28-30 wks	20	5 (25%)	20	0	
	31-34 wks	40	10 (25%)	40	2 (5%)	
	35-36 wks	30	5 (16.6%)	30	0	
Baby weight in Kg	1-1.5 Kg	20	5 (25%)	20	0	
	1.6-2 Kg	40	10 (25%)	40	2 (5%)	
	2.1-2.5 Kg	30	5 (16.6%)	30	0	

(>24 hour draining) with raised CRP shows sign and symptoms of chorioamnionitis (33%) and this is statistically significant (p=0.015). PPROM cases with raised CRP were 22% in 28-30 weeks(1-1.5kg), out of which 25% shows sign and symptoms of chorioamnionitis, 44% in 31-34 weeks (1.5-2kg) out of 25% shows sign and symptoms of chorioamnionitis, 33% in 35-36 weeks(2-2.5kg) out of which 16.6% shows sign and symptoms of chorioamnionitis. Control

low literacy rate.

In this study, 95% of PPROM cases with raised CRP were unbooked, out of which 23.5% shows sign and symptoms of chorioamnionitis. Multipara represent 77% of the PPROM cases with raised CRP, out of which 27 % shows sign and symptom of chorioamnionitis. In primipara it is 22 % out of which

group shows 2% chorioamnionitis in 31-34 weeks category. The incidence of chorioamnionitis was high when baby weight was less than 2kg (1-2kg).

The mode of delivery in accordance to parity and fetal weight did not show any statistical significance. Most of the patients give consent for vaginal delivery, so were put in expectant management and were delivered in meantime.

**Table 3: Analysis of PPROM cases with CRP status with clinical course and perinatal morbidity**

Causes	Study group		Control group	
	CRP>9mg/l cases in Number	Chorioamnionitis cases in Number	CRP<9mg/l cases in Number	
Hyperbilirubinaemia	65	20	15	
Sepsis	60	20	5	
RDS	5	5	10	
Birth asphyxia	1	1	-	

In CRP raised mother (study group) which were without chorioamnionitis, following delivery the neonate shows early onset sepsis in 86% of babies in comparison to CRP negative mother (control group). In control group perinatal morbidity is 16%. In the study group more neonates had hyperbilirubinaemia (65 cases) as compared to control group (16 cases). In our study perinatal

5% shows sign and symptom of chorioamnionitis. In control group shows 2.8% cases of chorioamnionitis in

mortality is 22%. The mortality is more in 28-32 weeks gestation with EFW < 2 kg. More than 50% perinatal

mortality is due to RDS.

In control groups perinatal mortality is 4%. Sepsis also accounted for 10% perinatal mortality.

In our study the sensitivity and specificity in predicting chorioamnionitis in cases of PPROM by

symptoms of chorioamnionitis, 33% in 35-36 weeks (2-2.5kg), out of which 16.6% showed signs and symptoms of chorioamnionitis.

It has been seen that raised CRP concentration in PPROM cases is the most accurate infectious marker

for prediction of early onset sepsis in routine use with a sensitivity >90% (Thomas Poposaki et al)<sup>13</sup>. Our study support this, as CRP cases without chorioamnionitis shows early onset sepsis in 86% of babies delivered.

In our study, perinatal mortality is 22%, of which 45% is due to RDS, of which mortality is more in 28-32

weeks with weight <2kg. This is comparable to study by Cox and colleague 52% due to RDS<sup>14</sup>. The high incidence of maternal and neonatal infection may be a consequence of decreased anti-bacterial activity in the amniotic fluid which is low in early pregnancy and increases with gestational age. Another factor is the limited ability of the preterm infant to fight infection. Perinatal morbidity and mortality decreases as the birth weight increases.

Post partum complications were seen to be less, which could be because of the higher standard antibiotic coverage. No maternal mortality was recorded. The proportion of clinical chorioamnionitis cases in raised CRP cases was 22%, which was significantly higher than those of controls. In our study, Odds ratio is 12.5 i.e cases (raised CRP) have 12.5 times more chances of having clinical chorioamnionitis than those of controls (normal CRP). In this study, the sensitivity of the test (raised CRP) in causing clinical chorioamnionitis is more than 90% and specificity in 50%. Our study is comparable to Hawry llyshyn et al<sup>15</sup>, 1983 study which shown sensitivity of 100% & specificity of 62%.

**Conclusion**

From this study we can conclude that detection of maternal CRP in cases of PPROM at admission is the

**Table 4: Contingency table of counts based on the diagnostic test and gold standard**

Diagnostic test	Non-chorioamnionitis Cases	Chorioamnionitis Cases	Total
CRP<9mg/l	88	2	90
CRP>9mg/l	70	20	90
	Estimated value	Lower limit(95% confidence level)	Upper limit(95% confidence level)
Prevalence	0.122	0.07	0.16
Sensitivity	0.9	0.69	0.98
Specificity	0.5	0.42	0.57
Odds ratio			12.5

CRP was found to be 90% (high prediction for positive cases) and 50% respectively.

**Discussion**

The incidence of PPROM in one year was found to be 5% from May 2012-April 2013 and it was comparable to other hospitals of India, Swati et al (2000) showed 7.7%<sup>10</sup>, Anjana Devi et al (1980) showed 5% incidence. Out of 90 CRP positive cases, 22% had chorioamnionitis in study group. Ramsey et al. 2005 shows prevalence of 13% for clinical chorioamnionitis<sup>11</sup>. In the study group, lower socio economic class represents maximum cases with PPROM with raised CRP (88%), out of which 23.7% showed signs and symptoms of chorioamnionitis.

In study group, multipara represented 77% of the PPROM cases with raised CRP, out of which 27% showed signs and symptoms of chorioamnionitis. Multiparity is a risk factor for PPROM due to long standing infection, previous trauma to cervix, patulous os. Distribution pattern is comparable to study by Sanyal rural medical college WB<sup>12</sup>. In this study, PPROM cases with raised CRP were 22% in 28-30 weeks(1-1.5kg),out of which 25% shows signs and symptoms of chorioamnionitis, 45% in 31-34 weeks (1.5-2kg), out of which 25% showed signs and

most sensitive marker (with sensitivity more than 90%) for early prediction of clinical chorioamnionitis. It is also a sensitive marker for prediction of preterm delivery in PPRM and is also a sensitive marker for prediction of early onset neonatal infection. In cases of PPRM, raised CRP is a predictor of clinical chorioamnionitis.

**Conflict of interest:** None. **Disclaimer:** Nil.

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