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Original Research Article

Prediction of the maternal and perinatal outcomes in premature rupture of membranes at and after 37 weeks of gestation using maternal serum C reactive protein levels

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ABSTRACT

Background: Premature rupture of membranes (PROM) complicates 5-10% of pregnancies, mostly at term, and increases the risk of maternal and neonatal morbidity due to intrauterine infection. Early prediction is crucial, and C-reactive protein (CRP), an acute-phase reactant, is frequently studied, though its diagnostic accuracy in PROM remains uncertain. This study was conducted to evaluate the role of maternal serum CRP in predicting chorioamnionitis and associated complications in term PROM.

Methods: This prospective observational study included 90 women with term PROM admitted to Swami Dayanand Hospital, New Delhi, between August 2022 and February 2024. Maternal serum CRP was measured at admission, and patients were followed for development of chorioamnionitis, mode of delivery, and maternal and neonatal outcomes. Diagnostic accuracy was calculated.

Results: Of 90 women, 72% were aged 21-30 years and 65.6% were primigravida; mean gestational age was 38.4 weeks. Adverse outcomes were significantly higher with leaking >24 hours ($p=0.008$). CRP ≥ 5 mg/l was associated with caesarean delivery (35.1% vs. 11.3%, $p=0.02$), postpartum febrile morbidity (32.4% vs. 7.5%, $p=0.004$), and neonatal antibiotic requirement (35.1% vs. 11.3%, $p=0.006$). No significant association was observed with chorioamnionitis, postpartum haemorrhage, low Apgar scores, neonatal intensive care unit (NICU) admission, or perinatal death. CRP predicted adverse outcomes with 64.7% sensitivity, 73.2% specificity, and 70% diagnostic accuracy.

Conclusions: Maternal CRP ≥ 5 mg/L is a useful predictor of adverse outcomes in term PROM, particularly postpartum infection and neonatal sepsis risk. Its high negative predictive value supports its role as a simple, cost-effective screening tool.

Keywords: C-reactive protein, Chorioamnionitis, Neonatal sepsis, Premature rupture of membranes

INTRODUCTION

Premature rupture of membranes (PROM) is defined as rupture of the fetal membranes with leakage of amniotic fluid before the onset of labour. It may occur at term (≥ 37 weeks) or preterm (< 37 weeks), and complicates 5-10% of pregnancies, of which nearly 80% occur at term. The reported incidence of term PROM is around 8%.¹

The fetal membranes consist of the amnion and chorion, whose collagen-rich structure provides tensile strength. Disruption of this integrity due to infection, inflammation, or intrinsic weakness predisposes to rupture.² Genital tract infections, particularly Group B Streptococcus (GBS), and altered vaginal microbiota are recognized contributors, while other risk factors include smoking, polyhydramnios, multiple pregnancies, and a history of preterm labour.³

The most important maternal complication of term PROM is intrauterine infection (chorioamnionitis), with risk increasing as the rupture delivery interval lengthens. Chorioamnionitis is associated with higher rates of caesarean section, postpartum haemorrhage, wound infection, and endometritis. Perinatal consequences include early-onset neonatal sepsis, asphyxia, intraventricular haemorrhage, cerebral palsy, and perinatal death.⁴ Early recognition of women at risk is therefore critical to improve outcomes.

Several laboratory parameters, including total leukocyte count, erythrocyte sedimentation rate, and amniotic fluid cultures, have been evaluated for predicting infection in PROM. Among them, maternal serum C-reactive protein (CRP), an acute-phase reactant synthesized by the liver, is widely used due to its affordability and availability. However, its diagnostic accuracy remains variable. Recent studies also indicate that even modest elevations of CRP may be associated with adverse maternal and neonatal outcomes, though consensus is lacking.⁵

Given these uncertainties, further evaluation of maternal serum CRP in term PROM is warranted. The present study was undertaken to assess the association between maternal CRP levels on admission and maternal as well as perinatal outcomes, and to determine its predictive accuracy in this clinical setting.

METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Swami Dayanand Hospital, New Delhi, from August 2022 to February 2024. Ethical approval was obtained from the Institutional Ethics Committee, and informed written consent was taken from all participants.

A total of 90 women with singleton pregnancies at ≥ 37 weeks of gestation presenting with leaking per vaginam of < 12 hours duration was included. PROM was confirmed on sterile speculum examination. Women with preterm PROM, intrauterine fetal death, congenital anomalies, multiple gestation, previous caesarean section, malpresentation, indication for emergency caesarean section at admission (e.g., fetal distress, meconium-stained liquor in early labour, cephalopelvic disproportion), chronic medical disorders (diabetes, hypertension), or clinical evidence of intrauterine infection at admission were excluded.

At admission, demographic and obstetric details were recorded. 2 mL of blood sample was drawn. Maternal serum CRP levels were measured using a quantitative turbidimetric test (CRP-Turbilatex). Patients were stratified into two groups: CRP < 5 mg/L and CRP ≥ 5 mg/L.

All women were managed as per standard obstetric protocols. Empirical antibiotic prophylaxis with third-

generation cephalosporins was administered. If spontaneous labour did not occur within 6 hours of membrane rupture, induction was initiated with 25 μ g sublingual misoprostol.

Maternal outcomes assessed included mode of delivery, chorioamnionitis, febrile morbidity, antepartum and postpartum haemorrhage. Perinatal outcomes studied were Apgar score at 1 minute, need for intravenous antibiotics, NICU admission, neonatal sepsis, and perinatal death.

Sample size was calculated using specificity of CRP (80%) and prevalence of chorioamnionitis (25%) from previous literature, with 10% margin of error, yielding a minimum of 82; hence 90 patients were enrolled.

Data were analysed using SPSS version 25.0. Continuous variables were expressed as mean \pm SD or median (IQR), and categorical variables as frequency (%). The independent t-test was applied for quantitative variables, while Chi-square test or Fisher's exact test was used for categorical data. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of CRP were calculated. Logistic regression was used to identify independent predictors. A p-value < 0.05 was considered statistically significant.

RESULTS

The mean age of participants was 26.9 ± 4 years (range 19-35 years), with most women (72.2%) between 21-30 years. Nearly two-thirds (65.6%) were primigravida. The mean gestational age was 38.4 ± 1 weeks; 60% were between 37-38.6 weeks and 40% between 39-40.6 weeks (Table 1).

Table 1: Demographic and obstetric characteristics of study subjects (n=90).

Variable	Category	N (%)	Mean \pm SD
Age (years)	19-20	7 (7.8)	26.9 \pm 4.0
	21-25	30 (33.3)	
	26-30	35 (38.9)	
	31-35	18 (20.0)	
Gravida	Primigravida	59 (65.6)	-
	Multigravida	31 (34.4)	
Gestational age (weeks)	37-38.6	54 (60.0)	38.4 \pm 1.0
	39-40.6	36 (40.0)	

Overall, 68.9% delivered vaginally, 10% by instrumental delivery, and 21.1% by caesarean section. Chorioamnionitis occurred in 12.2%, postpartum haemorrhage (PPH) in 6.7%, and febrile morbidity in 17.8%. The majority of women (76.7%) had a leak-delivery interval of 12-24 hours, while 22.2% had > 24 hours and only 1.1% had < 12 hours. Adverse maternal and perinatal outcomes increased significantly with longer leak-delivery interval, being highest when > 24 hours (65%) compared to 30.4% with 12-24 hours and none with < 12 hours ($p=0.008$). Women with CRP ≥ 5 mg/l had

significantly higher caesarean section rates (35.1% vs. 11.3%, $p = 0.02$) and febrile morbidity (32.4% vs. 7.6%, $p = 0.004$). While chorioamnionitis and PPH were more frequent in this group, the differences were not statistically

significant. Adverse maternal outcomes overall were significantly more common with elevated CRP (48.7% vs. 18.9%, $p = 0.003$) (Table 2).

Table 2: Association of maternal and perinatal outcomes with CRP on admission.

Outcome	CRP <5 mg/l (n=53)	CRP ≥5 mg/l (n=37)	Total (n=90)	p value
Mode of delivery				
Normal vaginal	42 (79.3)	20 (54.1)	62 (68.9)	0.02*
Instrumental	5 (9.4)	4 (10.8)	9 (10.0)	
Caesarean section	6 (11.3)	13 (35.1)	19 (21.1)	
Chorioamnionitis	4 (7.6)	7 (18.9)	11 (12.2)	0.189
Postpartum haemorrhage	2 (3.8)	4 (10.8)	6 (6.7)	0.224
Febrile morbidity	4 (7.6)	12 (32.4)	16 (17.8)	0.004*
Adverse maternal outcomes	10 (18.8)	18 (48.6)	28	0.003*
Apgar <7 at 1 min	8 (15.1)	7 (18.9)	15 (16.7)	0.632
Requirement of IV antibiotics	6 (11.3)	13 (35.1)	19 (21.1)	0.006*
NICU admission	3 (5.7)	3 (8.1)	6 (6.7)	0.687
Perinatal death	0 (0)	2 (5.4)	2 (2.2)	0.166
Adverse perinatal outcomes	9 (16.9)	17 (45.9)	26 (28.8)	0.003*

*Significant at $p < 0.05$; NICU = neonatal intensive care unit; IV = intravenous

Apgar <7 at 1 minute was noted in 16.7% of neonates, without significant difference between CRP groups. However, neonates of mothers with CRP ≥5 mg/l more often required intravenous antibiotics (35.1% vs. 11.3%, $p = 0.006$). NICU admissions (8.1% vs. 5.7%) and perinatal deaths (5.4% vs. 0%) were higher with elevated CRP, though not statistically significant. Adverse perinatal outcomes overall were significantly more frequent in the high CRP group (45.9% vs. 16.9%, $p = 0.003$) (Table 2).

perinatal outcomes. CRP ≥5 mg/l showed the highest area under the curve (AUC) for perinatal death (0.80; 95% CI: 0.70-0.88), followed by febrile morbidity (0.71; 95% CI: 0.60-0.80). The sensitivity ranged from 46.7% to 100%, and specificity from 60.0% to 73.2%. The negative predictive value (NPV) was consistently high across outcomes (84.9-100%), indicating that a low CRP effectively excluded adverse events. Overall diagnostic accuracy for composite adverse outcomes was 70% (Table 3).

C-reactive protein (CRP) demonstrated moderate diagnostic accuracy for predicting adverse maternal and

Table 3: Diagnostic performance of CRP in predicting adverse outcomes.

Outcome	Sensitivity (%)	Specificity (%)	AUC (95% CI)	PPV (%)	NPV (%)	Accuracy (%)
Chorioamnionitis	63.6	62.0	0.63 (0.52-0.73)	18.9	92.5	62.2
Caesarean section	68.4	66.2	0.67 (0.57-0.77)	35.1	88.7	66.7
Postpartum haemorrhage	66.7	60.7	0.64 (0.53-0.74)	10.8	96.2	61.1
Febrile morbidity	75.0	66.2	0.71 (0.60-0.80)	32.4	92.5	67.8
Apgar <7 at 1 min	46.7	60.0	0.53 (0.43-0.64)	18.9	84.9	57.8
IV antibiotics needed	68.4	66.2	0.67 (0.57-0.77)	35.1	88.7	66.7
NICU admission	50.0	59.5	0.55 (0.44-0.65)	8.1	94.3	58.9
Perinatal death	100.0	60.2	0.80 (0.70-0.88)	5.4	100.0	61.1
Adverse maternal and perinatal outcomes	64.7	73.2	0.69 (0.58-0.78)	59.5	77.4	70.0

PPV = positive predictive value; NPV = negative predictive value; AUC = area under the curve

Table 4: Multivariate logistic regression to identify significant risk factors of adverse maternal and perinatal outcome.

Variables	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio lower bound (95%)	Odds ratio upper bound (95%)
Gravida						
Primi				1.000		
Multi	-1.237	0.587	0.035	0.290	0.092	0.916

Continued.

Variables	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio lower bound (95%)	Odds ratio upper bound (95%)
Duration of LPV (hours)						
<12 hours				1.000		
12 to 24 hours	-1.194	2.388	0.617	0.303	0.003	32.651
>24 hours	-0.218	2.449	0.929	0.805	0.007	97.755
CRP on admission(mg/L)						
<5 mg/l				1.000		
≥5 mg/l	1.632	0.512	0.001	5.113	1.875	13.947

Multivariate logistic regression was performed to identify independent predictors of adverse maternal and perinatal outcomes. CRP ≥ 5 mg/l on admission was found to be a significant independent predictor of adverse maternal and perinatal outcomes ($p = 0.001$). Women with elevated CRP had 5.1 times higher odds of adverse outcomes (adjusted odds ratio = 5.11; 95% CI: 1.88-13.95) compared to those with CRP < 5 mg/l. Multigravida women had a significantly lower risk (adjusted odds ratio = 0.29; 95% CI: 0.09-0.92; $p = 0.035$) compared to primigravida. The duration of leaking per vaginam did not show a significant association with adverse outcomes ($p > 0.05$) (Table 4).

DISCUSSION

Premature rupture of membranes (PROM) remains a major obstetric challenge due to its strong association with maternal and neonatal morbidity. In this prospective study of 90 term PROM cases, we evaluated maternal serum CRP as a predictor of adverse outcomes. Nearly 38% of women experienced complications, with significantly higher rates in the high-CRP group (≥ 5 mg/l), underscoring its clinical utility as an adjunct marker.

The mean maternal age was 26.9 years, comparable with Blossia et al and Yasmina et al, confirming PROM is commonest in women in their twenties.^{6,7} Primigravidae predominated and showed higher adverse outcomes, likely reflecting prolonged labour and greater interventions, consistent with Pradeep et al.⁸ Most women presented at 37-38.6 weeks, similar to Gupta et al and Popowski et al.^{9,10} Importantly, adverse outcomes were significantly higher when the leak-delivery interval exceeded 24 hours, reinforcing prior evidence that prolonged latency increases infection risk. However, on multivariate analysis, this association was attenuated, and maternal CRP ≥ 5 mg/L emerged as the independent predictor of adverse outcomes. These findings highlight that while the leak-delivery interval is clinically important, biochemical markers such as CRP may provide a more objective and immediate assessment of infection risk. Multigravida status was protective, possibly reflecting shorter labour durations and greater cervical readiness compared to primigravidas.

Mode of delivery was strongly influenced by CRP: LSCS rates were higher with elevated CRP (35% vs. 11%),

largely due to fetal distress. Studies suggest cord compression after membrane rupture contributes to non-reassuring cardiotocography. Our findings agree with Gupta et al and Marchocki et al, who reported more operative interventions with raised inflammatory markers.¹¹ Clinical chorioamnionitis occurred in 12%, more frequent in the high CRP group but not statistically significant. Reliance on clinical rather than histological diagnosis likely underestimated subclinical infection, as noted by Popowski et al. Previous studies report mixed results, highlighting the need for combining CRP with other markers. Among other maternal outcomes, febrile morbidity (18%) was significantly associated with CRP ≥ 5 mg/l (32% vs. 7.6%, $p = 0.004$). This association is supported by Starrach et al and Blossia et al, who found raised CRP and prolonged rupture correlated with higher postpartum infection.¹² Postpartum haemorrhage (6.7%) was more frequent in the high-CRP group, though not statistically significant. The increased risk of PPH may be explained by inflammation-induced uterine dysfunction, which compromises effective myometrial contractions after delivery.

Neonatal outcomes varied: 2 early neonatal deaths (2.2%), both due to sepsis, occurred exclusively in the high-CRP group. While Apgar < 7 and NICU admissions did not differ significantly, neonates of CRP-positive mothers required antibiotics more often (35% vs. 11%). Similar findings were reported by Suryavanshi et al and Ibrahim et al, confirming maternal CRP as a useful guide for neonatal infection surveillance.^{13,14}

Overall, CRP ≥ 5 mg/L demonstrated moderate sensitivity (65%), good specificity (73%), and acceptable diagnostic accuracy (70%) for predicting adverse outcomes. These results mirror Nasker et al and Shaaban et al, supporting CRP as a practical, inexpensive predictor of maternal and perinatal morbidity in PROM.^{15,16}

The strengths of this study include its prospective design, standardized diagnostic criteria, and comprehensive assessment of both maternal and neonatal outcomes. Limitations include relatively small sample size, reliance on clinical rather than histological diagnosis of chorioamnionitis, and the lack of serial CRP measurements to assess dynamic trends.

CONCLUSION

We conclude that maternal serum CRP estimation at admission in term PROM demonstrated limited predictive value for chorioamnionitis and postpartum haemorrhage but showed a significant association with postpartum febrile morbidity and neonatal need for intravenous antibiotics. A negative CRP reliably excluded infectious morbidity, highlighting its role as a useful screening tool rather than a confirmatory marker. Routine CRP testing in women with term PROM may therefore aid in risk stratification and guide timely maternal and neonatal management, though larger multicentric studies are warranted to validate these findings.

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