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Original Article

Maternal Serum Procalcitonin as a Predictor of Early-Onset Neonatal Sepsis in Preterm Premature Rupture of Membranes: A Study in a Tertiary Care Hospital in Bangladesh

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ABSTRACT

Background: Preterm premature rupture of membrane (PPROM) increases early-onset neonatal sepsis risk, but diagnosis is challenging due to nonspecific symptoms. Maternal procalcitonin (PCT) is a promising biomarker, yet limited data exist on its predictive role for EONS. Objective: To determine the association between maternal serum procalcitonin level and early-onset neonatal sepsis in patients with PPROM at a tertiary care hospital in Bangladesh. **Methods & Materials**: This prospective cohort study was conducted at Dhaka Medical College Hospital from January to December 2022. A total of 99 women with PPROM (24–34 weeks of gestation) were enrolled. Maternal venous blood was collected on admission, and serum PCT was measured by chemiluminescence. Neonates were evaluated for EONS within 3 days of delivery using clinical signs, C-reactive protein, absolute neutrophil count, and blood culture results. **Results**: Elevated maternal serum procalcitonin (>0.5 ng/ml) was found in 61.6% of patients. Early-onset neonatal sepsis was confirmed by blood culture in 8 (8.9%) neonates. All eight cases of EONS occurred in the elevated maternal PCT group. The association was statistically significant (p=0.016, relative risk 1.74 at 95% CI). Neonates in the elevated PCT group also had significantly higher mean CRP (4.0±1.6 vs. 2.9±1.2 mg/l, p=0.001) and more frequent clinical signs of sepsis. **Conclusion**: Elevated maternal serum procalcitonin in PPROM is significantly associated with early-onset neonatal sepsis. Maternal PCT is a clinically useful, non-invasive biomarker for predicting EONS risk.

Keywords: *Absolute neutrophil count, C-reactive protein, Early-onset neonatal sepsis, Maternal serum procalcitonin, Preterm premature rupture of membrane.*

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INTRODUCTION

Preterm premature rupture of membrane (PPROM), defined as the spontaneous rupture of fetal membranes before 37 weeks of gestation, before the onset of labor, complicates approximately 2-3% of all pregnancies and is responsible for nearly one-third of all preterm births [1]. This obstetric complication represents a major clinical challenge as it disrupts the protective barrier against ascending infection from the lower genital tract, predisposing both mother and fetus to serious infectious morbidities [2]. Early-onset neonatal sepsis (EONS) remains one of the most consequential complications of PPROM, occurring within the first 72 hours of life and resulting from vertical transmission of pathogens from mother to infant before or during delivery [3]. The incidence of culture-proven EONS in preterm infants ranges from 4% to 33% following PPROM, with significantly higher rates at lower gestational ages [4,5]. Neonates with EONS face substantial risks, including respiratory failure, hemodynamic instability, neurological injury, and mortality; the case fatality rate for culture-proven EONS in very low birth weight infants approaches 15-25% [3,6]. The clinical presentation of EONS is notoriously non-specific in preterm infants. Symptoms such as lethargy, temperature instability, respiratory distress, and feeding difficulties overlap considerably with manifestations of prematurity itself, making early clinical diagnosis exceptionally challenging [3,7]. Consequently, neonatologists often initiate empirical antibiotic therapy based on risk factors alone, leading to substantial overtreatment. In many neonatal intensive care units, 10-40 infants receive antibiotics for every one case of culture-proven EONS [3]. Given these diagnostic limitations, there has been growing interest in identifying reliable biomarkers that can accurately predict or exclude EONS. C-reactive protein (CRP) and absolute neutrophil count (ANC) are widely used but have well-recognized limitations, including delayed rise after infection onset (12-24 hours for CRP) and suboptimal specificity in the immediate neonatal period [3,8]. Procalcitonin (PCT), a 116-amino acid precursor of calcitonin, has emerged as a promising alternative biomarker. Unlike CRP, PCT rises rapidly (within 2-4 hours) in response to bacterial endotoxin and demonstrates better specificity for bacterial infection [9]. Several studies have investigated PCT in neonatal populations, demonstrating superior diagnostic accuracy compared to conventional markers [10,11]. A recent study reported that maternal serum PCT has a diagnostic accuracy of 99% for predicting EONS [12]. However, most existing literature has focused on neonatal or cord blood PCT levels. The utility of maternal serum PCT as a predictor of EONS in the context of PPROM remains comparatively underexplored [13]. Since EONS results from vertically transmitted pathogens, maternal inflammatory response may precede and predict neonatal infection. Establishing maternal PCT as an effective screening tool would offer a non-invasive, readily available method to identify pregnancies at highest risk, enabling targeted neonatal surveillance and potentially reducing unnecessary antibiotic

exposure. Therefore, this study aimed to determine the association between maternal serum procalcitonin level in PPROM patients and the development of early-onset neonatal sepsis.

METHODS & MATERIALS

This prospective cohort study was conducted at the Fetal-Maternal Medicine unit of the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Bangladesh, from January 2022 to December 2022. A total of 99 pregnant women with PPROM were enrolled using purposive sampling.

Inclusion criteria: Women aged 18–40 years with singleton pregnancy, gestational age between 24 and 34 weeks (confirmed by first-trimester ultrasonography), duration of membrane rupture to delivery less than 18 hours, and willingness to provide informed consent were included.

Exclusion criteria: Patients with pre-existing medical disorders (diabetes mellitus, hypertension, renal disease, chronic liver disease), COVID-19 positive status, fetal distress (heart rate <110 or >160 bpm), fetal anomalies, clinical chorioamnionitis, or neonatal death within 3 days of delivery were excluded.

Study procedure: On admission, 3 mL of maternal venous blood was collected aseptically. Serum procalcitonin was measured using a chemiluminescence sandwich technique on an immunochemistry autoanalyzer. Patients were followed until delivery. Neonates were examined for EONS within 72 hours of birth using clinical signs, complete blood count, C-reactive protein, absolute neutrophil count, and blood culture. EONS was confirmed by a neonatologist.

Data analysis: Data were analyzed using SPSS version 26.0. Continuous variables were compared using an unpaired t-test and categorical variables using a chi-square test. The relative risk with 95% confidence interval was calculated. A p-value <0.05 was considered statistically significant.

RESULT

A total of 99 women with preterm premature rupture of membranes were included in this study. The mean age of participants was 25.2±5.1 years, with the majority (53.5%) belonging to the 18-25 years age group. More than half (55.6%) had completed primary education, and most were housewives (92.9%) and Muslim (96.0%). Nearly half (48.5%) had a monthly family income below 10,000 Taka. The mean BMI was 23.6±3.5 kg/m², with 52.5% having a normal BMI (*Table I*).

Table I
Socio-demographic characteristics of the study population (*n*=99).

Characteristic	Category	n	%
Maternal age (years)	18-25	53	53.5
	26-34	40	40.4
	35-40	6	6.1
Educational status	Illiterate	1	1
	Primary	55	55.6
	SSC	25	25.3
	HSC	14	14.1
	Graduate	4	4
Religion	Islam	95	96
	Hindu	4	4
Occupation	Housewife	92	92.9
	Service	7	7.1
Monthly income (Taka)	<10,000	48	48.5
	10,000-25,000	37	37.4
	>25,000	14	14.1
BMI (kg/m²)	Undernutrition (<18.5)	4	4
	Normal (18.5-22.9)	52	52.5
	Overweight (23-24.9)	43	43.4

Mean BMI: 23.6±3.5 kg/m² (range: 18.1-29.7).

The two groups were comparable regarding age, education, religion, occupation, income, parity, pulse, blood pressure, and BMI (all p>0.05) *Table II*.

Table II
Comparison of baseline characteristics by maternal procalcitonin level.

Characteristic	Group A (>0.5 ng/ml) (n=61)	Group B (≤0.5 ng/ml) (n=38)	p-value
	Mean ±SD/n (%)		
Age (years)	25.1±5.2	25.2±5.0	0.977
BMI (kg/m²)	22.2±2.0	21.8±2.0	0.357
Primiparous	33 (54.1)	21 (55.3)	0.910
Pulse (bpm)	80.8±4.0	79.8±3.4	0.209
SBP (mmHg)	114.3±9.0	113.9±11.7	0.880
DBP (mmHg)	75.7±5.5	75.8±7.1	0.968

p-value from unpaired t-test for continuous variables and chi-square test for categorical variables.

Among the 90 live neonates, 15 (16.7%) had lethargy, poor cry, and refusal to suck; 9 (10.0%) had respiratory distress, apnea, and gasping; 24 (26.7%) had fever; 8 (8.9%) had hypotonia; and 4 (4.4%) had poor perfusion. All these clinical signs were significantly more frequent in Group A compared to Group B (*Table III*).

Table III
Clinical signs of neonates by maternal procalcitonin level.

Clinical sign	Group A (n=55)	Group B (n=35)	p-value
	n (%)		
Lethargy, poor cry, refusal to suck	15 (27.3)	1 (2.9)	0.003
Respiratory distress, apnea, gasping	9 (16.4)	0 (0.0)	0.010
Fever	21 (38.2)	3 (8.6)	0.002
Hypotonia, absent reflexes	8 (14.5)	0 (0.0)	0.017
Poor perfusion, prolonged CRT	4 (7.3)	0 (0.0)	0.139

NB: 9 babies died within 3 days; p-value from chi-square test.

Laboratory findings showed that the mean CRP was significantly higher in Group A (4.0±1.6 mg/L) compared to Group B (2.9±1.2 mg/L, p=0.001). Mean absolute neutrophil count was significantly lower in Group A (4794.5±1753.4 cells/µL) than in Group B (5489.9±1318.3 cells/µL, p=0.047). No significant differences were observed for hemoglobin, WBC, ESR, platelet count, or immature-to-total neutrophil ratio (*Table IV*).

Table IV
Neonatal laboratory parameters by maternal procalcitonin level.

Parameter	Group A	Group B	p-value
	Mean ±SD		
CRP (mg/L)	4.0±1.6	2.9±1.2	0.001
Absolute neutrophil count (cells/µL)	4794.5±1753.4	5489.9±1318.3	0.047
Hemoglobin (g/dL)	14.6±1.2	14.7±1.2	0.628
WBC ($10^3/m^3$)	9.2±2.6	10.2±1.9	0.060
ESR (mm/1st hour)	12.8±4.2	11.5±3.5	0.117
Platelet count ($10^3/m^3$)	228.8±88.3	250.1±62.9	0.218
IT ratio	0.16±0.06	0.14±0.05	0.355

NB: 9 babies died within 3 days; p-value from chi-square test.

Positive blood culture was found in 8 neonates (8.9% of total, 14.5% of Group A). All positive cultures occurred exclusively in Group A (p=0.016). Among isolates, Staphylococcus was most common (75.0%), followed by Pseudomonas (12.5%) and E. coli (12.5%) *Table V*.

Table V
Blood culture results and EONS association by maternal procalcitonin level.

Parameter	Group A	Group B	p-value
Positive blood culture, n (%)	8 (14.5)	0 (0.0)	0.016
Early-onset neonatal sepsis (EONS), n (%)	8 (14.5)	0 (0.0)	0.016
Organisms isolated (n=8)	n	%	
Staphylococcus	6	75	
Pseudomonas	1	12.5	
Escherichia coli	1	12.5	

Note: 9 babies died within 3 days of delivery and were excluded from analysis. Statistical test: Chi-square test; Relative risk (RR) for EONS: 1.74 (95% CI: 1.45–2.10).

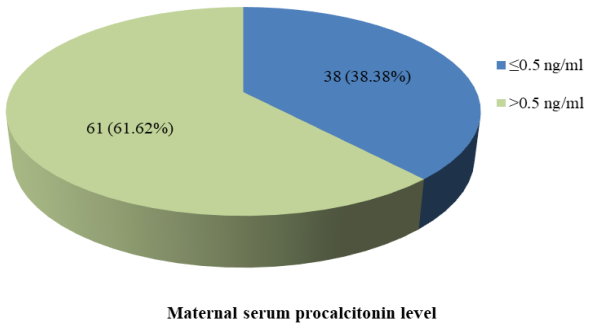

Figure 1 Distribution of maternal serum procalcitonin level.

Elevated maternal serum procalcitonin level (>0.5 ng/ml) was found in 61.6% of patients (Group A), while 38.4% had normal or decreased levels (Group B) *Figure 1*.

NICU admission was required for 24 babies (24.2%). All 8 cases of early-onset neonatal sepsis (100%) occurred in the elevated maternal procalcitonin group, with a relative risk of 1.74 (95% CI: 1.45-2.10, p=0.016). A positive correlation was observed between maternal procalcitonin and neonatal CRP (r=0.502, p=0.001), while a negative correlation was found with absolute neutrophil count (r=-0.362, p=0.001) *Table VI*.

Table VI
NICU admission requirements.

Outcome	n	%
NICU admission required	24	24.2
No NICU admission	75	75.8

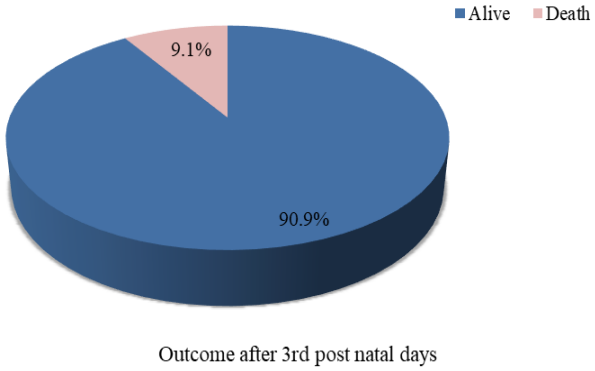

Figure 2 Neonatal outcome after 3rd postnatal day.

Regarding neonatal outcomes, 90 babies (90.9%) were alive after the 3rd postnatal day, while 9 (9.1%) died (*Figure 2*).

DISCUSSION

In this prospective cohort study of 99 women with preterm premature rupture of membranes, we observed that an elevated maternal serum procalcitonin level (>0.5 ng/ml) was significantly associated with the development of early-onset neonatal sepsis. All eight cases of culture-proven EONS occurred exclusively in the elevated maternal PCT group, with a relative risk of 1.74 (95% CI: 1.45-2.10, p=0.016). These findings suggest that maternal PCT is a clinically useful, non-invasive biomarker for identifying pregnancies at increased risk of EONS following PPROM. The prevalence of EONS in our study was 8.9%, which aligns with previously reported rates in PPROM populations. Ocviyanti and Wahono [5] reported EONS incidence ranging from 4% to 33% depending on gestational age and latency period. Similarly, in another study [4], it was found that the incidence of neonatal sepsis following PPROM before 34 weeks was 12.8%. The slightly lower rate in our study may be attributed to our exclusion of patients with membrane rupture exceeding 18 hours, which is an independent predictor of EONS [3]. Our finding that elevated maternal PCT was present in 61.6% of PPROM patients, with a significant association with EONS, is consistent with emerging literature. A study [13] demonstrated that maternal procalcitonin levels were significantly higher in women with subclinical intra-amniotic infection. In another study [11], it was reported that maternal PCT had good predictive value for chorioamnionitis in PPROM. The biological plausibility is strong: ascending bacterial infection triggers a maternal inflammatory response, with PCT production induced by bacterial endotoxins and inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha [9,14]. Neonates in the elevated maternal PCT group demonstrated significantly higher CRP levels (4.0±1.6 vs. 2.9±1.2 mg/L, p=0.001) and lower absolute neutrophil counts (4794.5±1753.4 vs. 5489.9±1318.3 cells/μL, p=0.047). The positive correlation between maternal PCT and neonatal CRP (r=0.502, p=0.001) suggests that maternal inflammatory status directly reflects or precedes neonatal systemic inflammation. This finding supports the work of Hahn et al. [10], who advocated for PCT as a superior early marker compared to CRP, which typically rises 12-24 hours after infection onset [3,8]. The negative correlation between maternal PCT and neonatal ANC (r=-0.362, p=0.001) requires careful interpretation. Neonatal neutropenia is a well-recognized finding in severe sepsis, often resulting from increased neutrophil consumption and depletion of the bone marrow storage pool [15,16]. In our study, the elevated PCT group had a mean ANC of 4794.5 cells/μL—still above the traditional cutoff for neutropenia (<1500 cells/μL) but significantly lower than the control group, indicating an early consumptive process. Clinical signs of EONS—including lethargy, respiratory distress, fever, and hypotonia—were all significantly more frequent in the elevated maternal PCT group. However, the absence of these signs in some culture-positive neonates underscores the well-documented limitation of clinical assessment alone [3,17]. In a previous study [3], it was emphasized that up to 50% of culture-proven EONS cases may be asymptomatic at birth, highlighting the critical need for reliable biomarkers. The predominance of Staphylococcus species (75%) among blood culture isolates differs from some published literature, where Group B Streptococcus and Escherichia coli are often reported as leading causes of EONS [17,18]. This variation may reflect regional differences in microbial epidemiology, antibiotic resistance patterns, or hospital-acquired colonization. Further studies with larger sample sizes are needed to confirm this finding. Mortality in our study was 9.1%, which is comparable to the 15-25% case fatality rate reported for culture-proven EONS in very low birth weight infants [3,6]. Notably, all deaths occurred in the elevated maternal PCT group, although our exclusion of neonatal deaths within 3 days from the EONS analysis may have underestimated the true association. The clinical implications of our findings are substantial. Maternal PCT measurement at PPROM admission is simple, rapid, and non-invasive. A negative result (PCT ≤0.5 ng/ml) in our study had 100% negative predictive value for culture-proven EONS, suggesting that neonates born to mothers with normal PCT may require less intensive surveillance. Conversely, a positive result should prompt heightened clinical vigilance and possibly earlier neonatal evaluation [19,20]. Limitations of this study include the single-center design, relatively modest sample size, exclusion of patients with prolonged rupture-to-delivery intervals, and lack of long-term neonatal follow-up. Additionally, we did not measure serial maternal PCT levels or amniotic fluid markers for comparison [21,22]. Future multicenter prospective studies with larger cohorts are needed to validate our findings and establish optimal cutoff values for different gestational age strata [23,24].

LIMITATIONS

This study has several limitations: single-center design, modest sample size, exclusion of patients with prolonged rupture-to-delivery intervals (>18 hours), lack of serial maternal PCT measurements, and absence of long-term neonatal follow-up data.

CONCLUSION

This study demonstrates that elevated maternal serum procalcitonin (>0.5 ng/ml) in PPROM is significantly associated with early-onset neonatal sepsis (p=0.016, RR 1.74). Maternal PCT is a clinically useful, non-invasive, and reliable biomarker for predicting EONS risk. Routine maternal PCT measurement at admission may guide targeted neonatal surveillance, potentially reduce unnecessary antibiotic exposure, and improve outcomes in resource-limited settings.

RECOMMENDATION

Routine maternal serum procalcitonin measurement should be incorporated into PPROM management protocols. Large multicenter studies are needed to validate optimal cutoff values across different gestational ages and to establish PCT-guided neonatal surveillance algorithms.

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