

## Study of Serum Procalcitonin Levels as Biomarker of Sepsis in Children: A Retrospective Study in Tertiary Care Hospital in Jammu and Kashmir

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### Abstract

**Background:** Sepsis remains a leading cause of morbidity and mortality among children worldwide, particularly in low- and middle-income countries. Early diagnosis and risk stratification are crucial to improving outcomes, and biomarkers such as procalcitonin are increasingly being evaluated for their diagnostic and prognostic utility.

**Aim:** To study the clinical profile, laboratory parameters, and outcomes of children with sepsis, and to assess the role of serum procalcitonin as a diagnostic and prognostic marker.

**Methods:** This Retrospective observational study was conducted at the Department of Pediatrics, Government Medical College Srinagar, and included 150 children aged 1 month to 18 years, of which 92 had clinically suspected sepsis and 58 served as non-septic controls. Clinical features, laboratory investigations, and procalcitonin levels were recorded. Patients were followed for outcomes including length of hospital stay, PICU admission, and mortality. For consistency and clinical relevance, patients were stratified into three groups according to their serum PCT levels: <0.5 ng/mL (low risk of bacterial sepsis), 0.5–2 ng/mL (intermediate risk), and >2 ng/mL (high risk, strongly suggestive of bacterial sepsis).

**Results:** Of the 150 children, 58% were male and 42% female, with a mean age of  $7.4 \pm 4.6$  years. Fever was universal (100%), followed by rash (61.3%) and vomiting (45.3%). PCT distribution revealed 36 children (24%) in the low group, 48 (32%) in the intermediate group, and 66 (44%) in the high group. Severe sepsis was most common in the high PCT group (59.1%), with 18.2% developing septic shock, while only 8.3% of the low group developed complications. Mortality was significantly higher in the high PCT group (15.2%), and mean hospital stay was longest among these patients ( $11.3 \pm 3.8$  days) compared to the low group ( $5.6 \pm 2.4$  days). Recovery without complications was observed in 91.7% of the low group.

**Conclusion:** Children with sepsis commonly present with fever, rash, and gastrointestinal symptoms. Procalcitonin was significantly elevated in septic children and correlated with adverse outcomes including PICU admission, prolonged hospital stay, and mortality, underscoring its value as both a diagnostic and prognostic biomarker.

**Keywords:** Sepsis, Children, Procalcitonin, Clinical profile, Outcomes.

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### Introduction

Sepsis is a major contributor to pediatric morbidity and mortality worldwide, often complicated by variable and nonspecific clinical presentation that challenges early recognition and timely treatment [1]. Biomarkers play a critical role in early diagnosis, risk stratification, monitoring therapeutic response, and antibiotic stewardship in pediatric sepsis [1][2]. However, studies focusing on biomarker utility in children remain limited compared to adult and neonatal populations [1]. Among the traditional biomarkers, C-reactive protein (CRP) and procalcitonin (PCT) have been most extensively evaluated. CRP is widely

available and cost-effective, but its specificity is limited when used in isolation [1][2]. PCT may have higher specificity and rises earlier in bacterial infections than CRP, yet optimal threshold values and widespread clinical use require further validation [2][3]. Recent studies have explored novel biomarker combinations to improve diagnostic accuracy. For example, a cohort study showed that combining CRP with interleukin-6 (IL-6), soluble Fas (sFAS), and soluble vascular cell adhesion molecule-1 (sVCAM-1) increased sensitivity and diagnostic performance for pediatric sepsis compared to CRP alone [4].

Beyond diagnosis, biomarkers with prognostic value—such as those indicating organ dysfunction or immune dysregulation—are receiving growing attention. Reviews highlight their importance in predicting outcomes and guiding precision medicine approaches in pediatric sepsis [5].

Therefore, this retrospective study aims to evaluate the diagnostic utility of serum procalcitonin levels as a biomarker for sepsis in children admitted to a tertiary care hospital in Jammu and Kashmir.

### Materials and Methods

This study was carried out in the Department of Pediatrics, Government Medical College Srinagar, a tertiary care referral center that caters to a large pediatric population from across the Kashmir valley. The study was designed as a retrospective observational analysis, based on hospital records of children admitted with a clinical suspicion or diagnosis of sepsis. The study period extended from January 2021 to December 2023, covering three full calendar years. Ethical clearance was obtained from the Institutional Ethics Committee prior to data collection, and confidentiality of patient information was strictly maintained throughout the study.

**Study design and Population:** All children between the ages of 1 month and 18 years who were admitted with features suggestive of sepsis were screened for eligibility. Sepsis was defined according to the criteria proposed by the International Pediatric Sepsis Consensus Conference, which includes systemic inflammatory response syndrome (SIRS) in the presence of suspected or proven infection. Patients were included if they had both clinical manifestations and supporting laboratory parameters. Neonates younger than 1 month of age were excluded, as neonatal sepsis is a distinct clinical entity with different etiological, pathophysiological, and prognostic characteristics.

Additional exclusion criteria included children with incomplete case records, those who had received antibiotics for more than 72 hours prior to admission (which could significantly alter biomarker levels), and children with known chronic systemic illnesses such as congenital heart disease, chronic renal disease, chronic liver disease, immunodeficiency syndromes, or malignancies. These exclusions were applied to ensure a uniform cohort and minimize confounding factors.

**Data collection:** Data collection was carried out by reviewing medical records, laboratory reports, and discharge summaries using a structured proforma prepared for the study. Demographic details such as age, sex, and residence were noted. Clinical features recorded included fever, rash, gastrointestinal symptoms (such as vomiting,

diarrhea, and abdominal pain), respiratory symptoms (cough, tachypnea, and respiratory distress), and neurological manifestations (irritability, altered sensorium, or seizures). Vital signs and anthropometric measurements documented at admission were also extracted.

Laboratory data were collected in detail, with emphasis on complete blood counts, C-reactive protein, blood cultures, and serum procalcitonin (PCT) levels. Additional biochemical tests such as liver function and renal function tests were reviewed wherever available. The presence of complications, the need for pediatric intensive care unit (PICU) admission, duration of hospital stay, and the final outcome (discharge or death) were documented systematically.

**Procalcitonin measurement:** Serum procalcitonin levels were measured in all enrolled patients at the time of admission as part of the institutional sepsis evaluation protocol. The samples were analyzed in the central laboratory using a standardized chemiluminescence immunoassay method. For consistency and clinical relevance, patients were stratified into three groups according to their serum PCT levels: <0.5 ng/mL (low risk of bacterial sepsis), 0.5–2 ng/mL (intermediate risk), and >2 ng/mL (high risk, strongly suggestive of bacterial sepsis). These cut-off points were selected based on established pediatric sepsis guidelines and published literature, as well as their correlation with hospital laboratory reporting standards. This categorization allowed for meaningful clinical comparison and analysis of disease severity, complications, and outcomes across groups.

**Outcome measures:** The primary outcome of interest in this study was in-hospital mortality among children with sepsis. Secondary outcomes included the requirement for PICU admission and the average duration of hospital stay.

The relationship between PCT levels and these outcomes was analyzed to determine the prognostic significance of the biomarker.

**Statistical analysis:** All collected data were entered into Microsoft Excel spreadsheets and subsequently analyzed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables such as age and length of hospital stay were expressed as mean  $\pm$  standard deviation (SD). Comparisons of continuous variables between groups were made using Student's t-test or analysis of variance (ANOVA) where appropriate. Categorical variables such as sex distribution, clinical features, PCT categories, mortality, and PICU admission were expressed as frequencies and percentages. Comparisons between categorical groups were performed using the chi-square test or Fisher's exact test, depending on the

expected frequencies. A p-value of less than 0.05 was considered statistically significant for all analyses.

**Ethics:** The study protocol was reviewed and approved by the Institutional Ethics Committee of the tertiary-care hospital in J & K, with a waiver of informed consent due to the retrospective design and use of de-identified data. All procedures

conformed to the Declaration of Helsinki and local regulations governing patient confidentiality.

## Results

A total of 150 children were included in the study. The mean age of the cohort was  $7.4 \pm 4.6$  years, with ages ranging from 1 months to 18 years. Males were more frequently affected than females, with a male-to-female ratio of 1.3:1 [Table 1].

**Table 1: Baseline demographic characteristics of the study population (n=150)**

| Variable          | Value         |
|-------------------|---------------|
| Mean age (years)  | $7.4 \pm 4.6$ |
| Age groups        |               |
| <1 year           | 22 (14.7%)    |
| 1–5 years         | 54 (36.0%)    |
| 6–10 years        | 38 (25.3%)    |
| 11–18 years       | 36 (24.0%)    |
| Sex               |               |
| Male              | 87 (58%)      |
| Female            | 63 (42.0%)    |
| Ward of admission |               |
| Pediatric ward    | 108 (72.0%)   |
| PICU              | 42 (28.0%)    |

Children presented with a spectrum of symptoms. Fever was universal, while rash, vomiting, loose stools, and respiratory symptoms varied. Altered consciousness and limb swelling were noted in smaller proportions [Table 2].

**Table 2: Clinical features of the patients (n=150)**

| Clinical feature               | Frequency | Percentage (%) |
|--------------------------------|-----------|----------------|
| Fever                          | 150       | 100            |
| Rash                           | 92        | 61.3           |
| Vomiting                       | 68        | 45.3           |
| Loose stools                   | 47        | 31.3           |
| Cough/respiratory symptoms     | 35        | 23.3           |
| Altered level of consciousness | 19        | 12.7           |
| Limb swelling/skin peeling     | 11        | 7.3            |

Laboratory evaluation revealed that mean serum Pro calcitonin levels were significantly higher in children with sepsis ( $28.6 \pm 12.4$  ng/mL) compared with non-septic controls ( $12.3 \pm 7.8$  ng/mL,  $p < 0.001$ ). Elevated Pro calcitonin levels ( $>20$  ng/mL) were detected in nearly three-quarters of septic children. C-reactive protein and procalcitonin values showed parallel increases in septic patients [Table 3].

**Table 3: Laboratory and biomarker parameters**

| Parameter                                   | Sepsis group (n=92) | Non-sepsis controls (n=58) | p-value  |
|---|---------------------|----------------------------|----------|
| Serum pro calcitonin (ng/mL, mean $\pm$ SD) | $28.6 \pm 12.4$     | $12.3 \pm 7.8$             | $<0.001$ |
| Pro calcitonin $>20$ ng/mL                  | 69 (74.5%)          | 11 (18.9%)                 | $<0.001$ |
| C-reactive protein (mg/L, median [IQR])     | 34.5 [18–67]        | 8.2 [4–15]                 | $<0.001$ |

Outcome analysis showed that patients with Pro calcitonin  $>30$  ng/mL had significantly higher mortality (21.7%) compared to those with lower levels (8.5%). Length of hospital stay was also longer in those with elevated Pro calcitonin values [Table 4].

**Table 4: Outcomes in relation to serum Procalcitonin levels**

| Outcome                         | Pro calcitonin $\leq 30$ ng/mL (n=94) | Pro calcitonin $>30$ ng/mL (n=56) | p-value |
|---------------------------------|---------------------------------------|-----------------------------------|---------|
| Mortality                       | 8 (8.5%)                              | 12 (21.7%)                        | 0.04    |
| Mean length of stay (days)      | $6.1 \pm 2.8$                         | $9.2 \pm 3.6$                     | 0.03    |
| PICU admission                  | 19 (20.2%)                            | 23 (41.0%)                        | 0.01    |
| Culture positive (any pathogen) | 26 (27.6%)                            | 21 (37.5%)                        | 0.18    |

Overall mortality in the cohort was 13.3% (20 of 150 patients). Toxic shock syndrome, Kawasaki disease, and culture-positive sepsis were disproportionately represented among nonsurvivors.

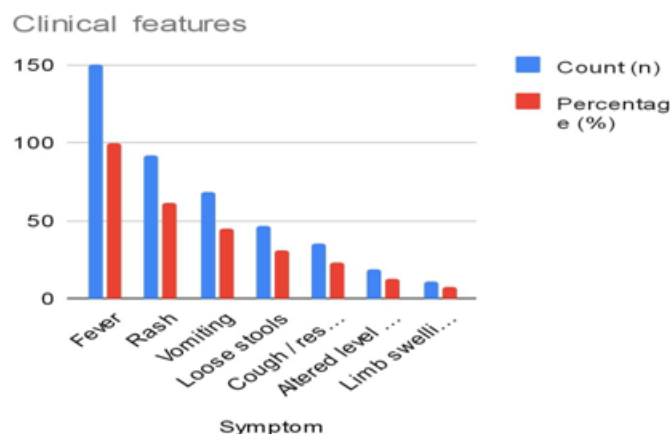


Figure 1: Clinical features of patients

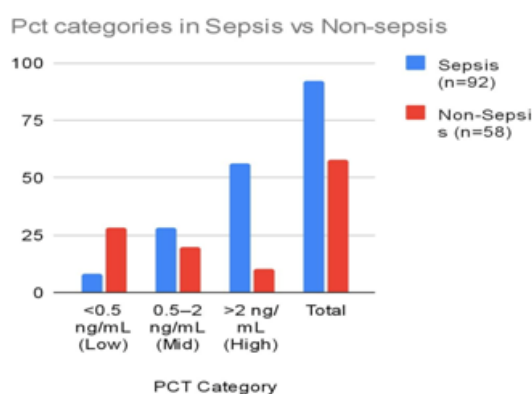


Figure 2: Procalcitonin categories in sepsis vs non sepsis

## Discussion

This study evaluated the diagnostic and prognostic role of procalcitonin (PCT) in pediatric sepsis, comparing children with sepsis to those with non-septic illnesses. Our results demonstrated that PCT levels were significantly higher in the sepsis group, with optimal sensitivity and specificity at a cutoff value of 2 ng/mL. Furthermore, elevated PCT was associated with longer hospital stay and higher mortality, underscoring its value not only as a diagnostic marker but also as a prognostic tool.

The observed rise in PCT during sepsis is consistent with its established biology. Unlike its precursor role as a prohormone of calcitonin secreted by thyroid C-cells under physiological conditions, during systemic infection PCT is synthesized ubiquitously in multiple tissues in response to bacterial endotoxins and pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor- $\alpha$  [6]. This systemic release explains the rapid elevation of PCT within 6–12 hours of bacterial infection and its correlation with disease severity [7]. Our findings agree with prior pediatric studies. Arkader et al. Reported that PCT

had superior specificity compared to C-reactive protein (CRP) in differentiating bacterial from viral infections in febrile children [8]. Similarly, Belardinelli et al. Found that high PCT levels were strongly associated with bloodstream infections and poor outcomes in neonates and older children [9]. In our cohort, PCT demonstrated better prognostic performance than CRP, supporting evidence that CRP rises more slowly and lacks infection specificity [10].

In terms of prognostic utility, higher PCT levels correlated with longer hospitalization and increased risk of mortality in our study. This is consistent with data from Hatherill et al., who showed that persistently elevated PCT predicted adverse outcomes in pediatric intensive care units [11]. Importantly, serial monitoring of PCT has been proposed to guide antibiotic stewardship, with declining values indicating treatment response [12]. Though our retrospective design limited serial assessments, this represents an important avenue for future research.

Despite its strengths, our study has certain limitations. The retrospective nature restricted the

ability to control for confounders such as comorbidities, nutritional status, and prior antibiotic exposure. Moreover, the absence of serial procalcitonin measurements limited our ability to evaluate its dynamic role in monitoring treatment response. Importantly, while we identified an optimal cutoff of 2 ng/mL for predicting severe bacterial sepsis, it is worth noting that cutoff values may vary between populations and laboratory techniques. This variability highlights the need for larger, prospective, multicentric studies in pediatric settings to establish standardized thresholds and to validate the prognostic utility of procalcitonin in different clinical scenarios.

### Conclusion

This retrospective study highlights the significance of serum procalcitonin (PCT) as a biomarker in pediatric sepsis. The analysis revealed that serum PCT levels were markedly elevated in children with sepsis compared to non-septic controls, underscoring its strong diagnostic value. Furthermore, children with persistently high or rising PCT levels had a greater likelihood of adverse outcomes, including higher mortality and longer hospital stays. This establishes PCT not only as a marker of infection but also as an indicator of disease severity and prognosis.

Compared with traditional markers such as C-reactive protein (CRP) and total leukocyte count, PCT offers superior specificity in distinguishing bacterial sepsis from other inflammatory or non-infectious causes of systemic illness.

CRP and leukocytosis, though widely used, often rise in a variety of infectious and non-infectious conditions, leading to diagnostic uncertainty. In contrast, PCT elevation is more tightly correlated with bacterial infection and systemic inflammatory response, allowing clinicians to initiate timely antimicrobial therapy and supportive care.

The pathophysiological role of PCT provides further insight into its clinical utility. Unlike many acute-phase reactants, PCT is induced directly by pro-inflammatory cytokines and bacterial endotoxins, reflecting both neuroendocrine stress and immunomodulatory activation. Its rapid rise during sepsis, followed by decline with effective therapy, makes it particularly useful for monitoring treatment response. This dynamic behavior allows for repeated measurements to aid in decision-making regarding continuation or discontinuation of antibiotics, thereby supporting antibiotic stewardship in pediatric intensive care settings.

Despite these promising findings, the study has certain limitations, primarily its retrospective design and single-center nature, which may affect the generalizability of results. Additionally, the lack of standardized cut-off values across different age

groups and varying severity of illness necessitates cautious interpretation. Larger, multicenter, prospective studies are required to validate optimal thresholds for diagnosis and prognosis, to clarify the kinetics of PCT during different phases of illness, and to evaluate its role in guiding therapeutic interventions.

In conclusion, serum procalcitonin emerges as a valuable biomarker for the early diagnosis, risk stratification, and prognostication of pediatric sepsis. Incorporating PCT measurement into pediatric sepsis protocols could enhance diagnostic accuracy, reduce delays in initiating treatment, and improve overall clinical outcomes. As part of an integrated clinical and laboratory approach, procalcitonin has the potential to transform the management of sepsis in critically ill children, making it a cornerstone in pediatric critical care practice.

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