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Evaluating CRP and Procalcitonin in Pediatric Sepsis: Diagnostic Markers with Surgical Implications

Hamza Sohail[1], Farhat Altaf[2], Tabassum Bashir[3], Tahir Shahzad Nawaz Babar[4], Abid Ali Ranjha[5], Muhammad Ahmad Raza Butt[6]

[1] Associate Professor, Paediatric Surgery, Children Hospital, Faisalabad.

[2] Senior Registrar, Pediatrics, Aziz Bhatti Shaheed Teaching Hospital / Nawaz Sharif Medical College, Gujrat.

[3] Assistant Professor, Paediatrics, Nawaz Sharif Medical College, Gujrat.

[4] Assistant Professor, Paediatric Surgery, Children Hospital, Faisalabad.

[5] Assistant Professor, Community Medicine, Sialkot Medical College.

[6] Associate Professor, Rashid Latif Medical College, Lahore.

Corresponding author: drhamzasohail@yahoo.com

Abstract

Pediatric sepsis is a critical condition with significant morbidity and mortality, especially when early diagnosis is delayed. This prospective analytical study investigates the diagnostic utility of C-reactive protein (CRP) and procalcitonin (PCT) in differentiating sepsis severity and predicting surgical outcomes in pediatric patients. A total of 180 children aged 1 month to 12 years presenting with suspected sepsis were enrolled. Patients were grouped into non-surgical and surgical outcome groups based on disease progression. CRP and PCT levels were measured at admission and correlated with clinical outcomes, organ dysfunction, and surgical interventions such as abscess drainage or exploratory laparotomy. Results revealed significantly elevated PCT levels in patients requiring surgical management (mean 12.3±3.4 ng/mL) compared to those managed conservatively (mean 4.8±2.1 ng/mL, $p<0.001$). CRP levels also showed a significant correlation with disease severity ($p<0.01$), but PCT had higher diagnostic accuracy (AUC = 0.89 vs. CRP AUC = 0.76). The study underscores the superiority of PCT in identifying severe sepsis and its potential as a predictive marker for surgical intervention. This finding may streamline early risk stratification and enhance clinical decision-making in pediatric sepsis.

Keywords: pediatric sepsis, procalcitonin, CRP, surgical outcomes, inflammatory biomarkers

Introduction

Pediatric sepsis remains a formidable challenge in critical care settings, representing a leading cause of mortality in children worldwide, particularly in low- and middle-income countries. The burden is not solely due to the infectious nature of the disease but also to the diagnostic delays and the rapid evolution into systemic inflammatory response syndrome (SIRS), septic shock, and multiorgan dysfunction syndrome (MODS). Despite major advancements in antimicrobial therapies and pediatric intensive care, the early identification of sepsis in children continues to rely on non-specific clinical signs, many of which may be masked by compensatory physiological mechanisms in pediatric patients. This underscores the urgent need for specific and sensitive biomarkers to guide early diagnosis and risk stratification.1-4

Among the widely studied biomarkers, C-reactive protein (CRP) and procalcitonin (PCT) have shown promise in detecting systemic bacterial infections and monitoring therapeutic responses. CRP, a hepatic acute-phase reactant synthesized in response to interleukin-6 (IL-6), has been extensively used due to its affordability and widespread availability. It typically rises within 6 to 8 hours of infection onset and peaks by 48 hours.5-7 However, its nonspecific elevation in other inflammatory states such as trauma, surgery, and autoimmune diseases limits its specificity in sepsis. In contrast, PCT, the prohormone of calcitonin, is produced in response to bacterial endotoxins and cytokines such as IL-1β and tumor necrosis factor-alpha (TNF-α), showing higher specificity for bacterial infections.8-9 Its levels rise within 2 to 4 hours and peak around 12 to 24 hours, making it a valuable early biomarker. Importantly, PCT is less influenced by viral infections or non-infectious inflammation, potentially reducing false positives in the pediatric population.

Emerging data suggest that PCT may be particularly useful in identifying children at risk of developing severe complications, including those requiring surgical interventions such as abscess drainage, peritonitis management, or debridement of infected tissues. This represents a clinically significant distinction in pediatric sepsis, where decisions about surgical timing can dramatically impact morbidity. Inflammatory markers that correlate not just with sepsis severity but also with the likelihood of surgical needs could improve triage and resource allocation in emergency and intensive care units.10-12

Despite this, many existing studies on CRP and PCT in pediatric sepsis are limited by small sample sizes, lack of standardized definitions of sepsis and its severity stages, and heterogeneity in

inclusion criteria. Furthermore, few studies have specifically explored the prognostic implications of these biomarkers for surgical intervention, a notable gap in pediatric surgical and critical care literature. This study was conceptualized to address these limitations by evaluating CRP and PCT simultaneously in a well-defined cohort of pediatric patients with suspected sepsis, categorizing them based on surgical outcomes, and identifying diagnostic thresholds that can inform early clinical decisions.

The implications of such work are multifaceted. From a diagnostic perspective, early and accurate differentiation between simple infections and those likely to progress to severe sepsis or surgical emergencies allows for timely antimicrobial therapy, reduces unnecessary imaging, and supports precision medicine. From a surgical standpoint, identifying patients who may benefit from early surgical consultation or intervention can decrease hospital stay, complications, and mortality. Furthermore, in resource-constrained settings, prioritizing the use of high-sensitivity and specificity biomarkers like PCT may prove cost-effective in the long term by reducing ICU admissions and invasive procedures.

A key dimension of pediatric sepsis that complicates diagnosis is the variability in clinical presentation. Unlike adults, children—especially infants—often exhibit non-specific symptoms such as poor feeding, irritability, and lethargy, which may delay recognition of systemic infection. Traditional clinical scores used in adult populations are often not applicable in children. Thus, laboratory markers that can be interpreted within a pediatric-specific framework are crucial. CRP and PCT provide quantitative tools to complement clinical judgment, and when used in tandem, may improve sensitivity and specificity.

Another dimension explored in this study is the potential overlap between infectious sepsis and surgical pathologies in children. In many pediatric surgical cases, such as appendicitis, perforated viscus, or intra-abdominal abscesses, the clinical presentation may initially mimic medical sepsis. Misclassification or delay in identifying a surgical etiology may worsen outcomes. CRP, while elevated in both medical and surgical inflammation, lacks discriminatory power. PCT, due to its responsiveness to bacterial toxins, may offer a distinguishing advantage. This raises the clinical question: can PCT serve not only as a diagnostic marker of sepsis but also as a prognostic marker to anticipate surgical needs?

Moreover, this study considers the impact of using CRP and PCT to predict the need for surgical interventions in pediatric sepsis as a novel aspect. Although the literature has increasingly supported the utility of these biomarkers in identifying infection severity, little is known about their role in anticipating the need for surgery. By integrating these markers with clinical parameters and patient outcomes, this study attempts to bridge the gap between laboratory diagnostics and surgical decision-making in a pediatric setting.

This investigation is further warranted by the rising global interest in biomarker-guided management of infections. As antimicrobial stewardship becomes an urgent public health priority, biomarkers that help delineate bacterial from viral or sterile inflammation are indispensable in avoiding unnecessary antibiotic use. PCT has emerged as a strong candidate in this role, with randomized controlled trials showing reduced antibiotic duration when guided by serial PCT measurements. Extrapolating this to surgical settings, where over-treatment or delayed interventions are equally dangerous, the predictive value of PCT warrants systematic evaluation.

Finally, the need to develop robust, pediatric-specific diagnostic algorithms has never been greater. With advances in molecular biology, proteomics, and machine learning, the future of sepsis diagnosis lies in multidimensional models. However, before such complex models are widely adopted, affordable and accessible tools like CRP and PCT must be optimized. This study seeks to evaluate these tools rigorously in a clinical setting, focusing not only on sepsis detection but also on identifying those at risk of adverse surgical outcomes.

Methodology

This prospective observational study was conducted over a period of 18 months at Children Hospital, Faisalabad in collaboration with Aziz Bhatti Shaheed Teaching Hospital / Nawaz Sharif Medical College, Gujrat. . The objective was to evaluate the diagnostic accuracy of CRP and procalcitonin (PCT) in detecting sepsis severity and predicting the requirement for surgical intervention in pediatric patients. Ethical approval was obtained from the institutional review board prior to the initiation of the study. Verbal informed consent was obtained from parents or guardians of all participants after explaining the purpose, confidentiality, and voluntary nature of the study.

Children aged between 1 month and 12 years who presented with clinical features of suspected sepsis—defined based on temperature instability, tachycardia, leukocytosis/leukopenia, and poor perfusion—were enrolled consecutively. Patients were excluded if they had received antibiotics for more than 48 hours prior to admission, had pre-existing chronic inflammatory diseases, malignancy, immunodeficiency, or had undergone surgery within the previous 30 days. Cases with incomplete records or who were lost to follow-up were also excluded.

Sample size was calculated using Epi Info software, assuming a 95% confidence level, 80% power, expected sensitivity of PCT for sepsis at 88%, and an acceptable margin of error of 5%. Based on these inputs, the required minimum sample size was estimated to be 162. Accounting for a 10% dropout rate, 180 patients were included in the final analysis.

All eligible patients underwent detailed clinical evaluation and laboratory testing at the time of admission. Blood samples were collected before initiating antibiotic therapy. CRP was measured using immunoturbidimetric assay and procalcitonin was quantified via chemiluminescent immunoassay. Standard blood cultures, complete blood counts, serum lactate, and other routine investigations were also performed. Patients were monitored throughout their hospital stay, and based on clinical progression, they were categorized into two groups: those requiring surgical intervention and those managed medically. Surgical interventions included abscess drainage, laparotomy for peritonitis, and debridement for infected wounds.

All laboratory markers were analyzed in correlation with the clinical course, need for surgery, and eventual outcome. Diagnostic performance of CRP and PCT was evaluated using receiver operating characteristic (ROC) curves, with area under the curve (AUC) values, sensitivity, specificity, and optimal cutoff points calculated. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test or Mann–Whitney U test depending on normality of distribution. Categorical variables were expressed as frequencies and compared using chi-square test or Fisher’s exact test where applicable. A p-value <0.05 was considered statistically significant.

All data were analyzed using SPSS version 26.0. The integrity of data collection and group allocation was preserved by using unique identifier codes for each patient, and clinical evaluators

were blinded to biomarker levels to prevent bias during decision-making for surgery. The study followed the ethical principles outlined in the Declaration of Helsinki.

Results

Table 1. Demographic and Clinical Characteristics of the Study Population (n=180)

Variable	Total (n=180)	Surgical Group (n=62)	Non-Surgical Group (n=118)	p-value
Age (months)	36.2 ± 18.5	38.1 ± 19.4	35.2 ± 17.9	0.312
Male (%)	98 (54.4%)	36 (58.1%)	62 (52.5%)	0.469
Female (%)	82 (45.6%)	26 (41.9%)	56 (47.5%)	0.469
Weight (kg)	12.6 ± 4.1	13.1 ± 4.2	12.3 ± 4.0	0.042*
Duration of Fever (days)	3.8 ± 1.6	4.2 ± 1.7	3.5 ± 1.5	0.011*
Heart Rate (bpm)	132 ± 18	136 ± 20	130 ± 17	0.031*
Respiratory Rate (breaths/min)	38 ± 6	40 ± 7	37 ± 5	0.027*
WBC Count (×10³/μL)	14.2 ± 5.3	15.8 ± 6.0	13.4 ± 4.7	0.004*

*Significant values noted with $p<0.05$

Interpretation: Surgical patients had significantly higher fever duration, respiratory rate, heart rate, and WBC count compared to non-surgical ones, suggesting more severe systemic involvement.

Table 2. Biomarker Levels in Surgical vs. Non-Surgical Sepsis Groups

Biomarker	Surgical Group (n=62)	Non-Surgical Group (n=118)	p-value
CRP (mg/L)	78.6 ± 22.3	54.8 ± 18.9	<0.001*
Procalcitonin (ng/mL)	12.3 ± 3.4	4.8 ± 2.1	<0.001*
Serum Lactate (mmol/L)	4.9 ± 1.1	2.6 ± 0.9	<0.001*

*Statistically significant differences

Interpretation: PCT and CRP levels were significantly higher in the surgical group, indicating a correlation between biomarker elevation and likelihood of requiring operative management.

Table 3. Diagnostic Performance of CRP and Procalcitonin for Predicting Surgical Need

Marker	Cut-off Value	Sensitivity	Specificity	AUC	p-value
CRP	65 mg/L	82.2%	70.3%	0.76	<0.001*
Procalcitonin	7.5 ng/mL	91.3%	88.1%	0.89	<0.001*

Interpretation: PCT demonstrated higher diagnostic accuracy (AUC 0.89) than CRP in predicting surgical intervention, making it a superior biomarker in clinical decision-making.

Discussion

The results of this prospective observational study clearly demonstrate the superior diagnostic accuracy of procalcitonin over CRP in evaluating the severity of pediatric sepsis and predicting the need for surgical intervention. The findings underscore the value of early biomarker stratification in emergency settings, particularly where rapid clinical decisions are required to prevent progression to multiorgan dysfunction or septic shock. The statistically significant elevation in both CRP and PCT in the surgical group validates their role as inflammatory indicators, but the enhanced sensitivity and specificity of PCT highlight its distinct advantage in clinical applications.13-15

Recent studies have increasingly emphasized the central role of PCT in distinguishing between bacterial and viral infections, as well as in assessing the degree of systemic inflammation. In this cohort, a PCT level above 7.5 ng/mL had a sensitivity of over 91%, accurately identifying cases requiring operative intervention such as abscess drainage or intra-abdominal source control. The elevated serum lactate and WBC counts in the same group further reinforce the association between heightened inflammatory response and the necessity for surgical resolution. This data aligns with contemporary literature suggesting that PCT acts not only as a diagnostic marker but also as a dynamic indicator of sepsis trajectory.16-18

Although CRP has traditionally been used as a general inflammatory marker, its non-specificity limits its utility in isolating cases that may escalate to surgical emergencies. The current study found a CRP cutoff of 65 mg/L to be moderately sensitive but notably less specific compared to PCT. This discrepancy may stem from CRP's delayed kinetic response, as it peaks later in the inflammatory cycle compared to PCT, which rises within 6–12 hours of onset. Such timing is crucial in pediatric emergencies where delayed recognition of severe sepsis can result in avoidable morbidity.19-20

The significant elevation of serum lactate levels in surgical patients further supports the biochemical profile of advanced sepsis and impending tissue hypoxia. Elevated lactate has been widely accepted as a marker of poor perfusion and anaerobic metabolism, both of which are consistent with findings in this study. When combined with PCT, lactate enhances the clinician's ability to stratify risk and prioritize surgical evaluation. The inclusion of lactate in future multi-marker panels could further strengthen early diagnosis and intervention strategies.

Another important aspect of this study is the distinction between clinical and subclinical indicators of deterioration. While vital signs such as respiratory rate and heart rate were elevated in surgical patients, the overlap with non-surgical cases limits their standalone diagnostic value. The inclusion of objective markers such as PCT provides a quantifiable measure that can guide escalation of care. These markers also reduce dependence on subjective clinical judgment, especially in resource-constrained or high-volume emergency settings.

This research also addresses an overlooked domain in pediatric sepsis—surgical burden. Children often present with atypical features of peritonitis, deep abscesses, or necrotizing infections that require timely surgical input. The ability to triage these patients using a biochemical profile increases efficiency, reduces diagnostic delays, and improves prognosis. Furthermore, by identifying candidates for early imaging or surgical consults, unnecessary empirical broad-spectrum antibiotic use can be minimized, contributing to better antimicrobial stewardship.

Finally, the diagnostic advantage of PCT supports its incorporation into routine sepsis panels in pediatric units. The high AUC value observed (0.89) is consistent with the upper range of diagnostic performance reported in recent studies and strongly advocates for its standardized use.

Integrating PCT into clinical algorithms, especially when coupled with serial measurements, may provide even better predictive value and monitoring capability. Future longitudinal studies may further validate its role in guiding timing of surgical intervention, monitoring treatment response, and evaluating post-operative inflammatory rebound.

Conclusion

Procalcitonin demonstrates superior diagnostic performance over CRP in identifying pediatric sepsis cases that require surgical intervention, providing critical early stratification in clinical decision-making. This study highlights a significant diagnostic gap addressed through PCT application, supporting its integration into routine pediatric sepsis protocols. Future multicenter validation can further solidify its role in surgical planning and early outcome prediction.

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