Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/yw3eex20

EVALUATION OF SERUM BIOMARKERS IN SEPSIS PROGNOSIS: A PROSPECTIVE OBSERVATIONAL STUDY

Zeeshan Khan[1*], Arvind Kumar[2], Shilpa Rani[3], Sameer Khan[4], Shoaib Khan[5]

[1*]Assistant Professor, Department of Medicine, Kanti Devi Medical College and Research Centre, Mathura, Uttar Pradesh, India, khanzeeshan486@gmail.com
[2]Assistant Professor, Department of Medicine, Hamdard Institute of Medical Sciences and Research (HIMSR), New Delhi, India, arvindchaudhary59@gmail.com
[3] DNB Resident, Department of Surgery, Max Superspeciality Hospital, Vaishali, Ghaziabad, Uttar Pradesh, India, shilpa1995rani@gmail.com
[4] MD Student (Final Year), Department of Medicine, All American Institute of Medical Sciences, 66 High Street, Black River, St. Elizabeth Jamaica, West Indies, Sameer_khan@aaims.edu.jm
[5] MD Student (Final Year), Department of Medicine, All American Institute of Medical Sciences, 66 High Street, Black River, St. Elizabeth Jamaica, West Indies, shoaib_khan@aaims.edu.jm

***Corresponding Author-** Zeeshan Khan
***Email-** khanzeeshan486@gmail.com

Received- July 10, 2025; **Revised-**July 25, 2025; **Accepted-**Aug. 5, 2025; **Published-**Aug. 22, 2025

Abstract

Background: Sepsis is a life-threatening condition characterized by dysregulated host response to infection, leading to organ dysfunction and high mortality. Early identification of prognostic biomarkers is essential for guiding therapeutic decisions. Procalcitonin (PCT) and Interleukin-6 (IL-6) have emerged as potential biomarkers for predicting sepsis severity and outcomes.

Objectives: To evaluate the prognostic utility of serum Procalcitonin and IL-6 levels in patients with sepsis admitted to the Department of Medicine at Kanti Devi Medical College and Research Centre, Mathura, Uttar Pradesh, India, between February 2024 and January 2025.

Methods: This prospective observational study included 120 adult patients diagnosed with sepsis based on Sepsis-3 criteria. Serum PCT and IL-6 levels were measured within 24 hours of admission. Patients were followed for 28 days, and survival outcomes were analyzed using Kaplan–Meier survival curves. Data on common sources of sepsis were also recorded.

Results: Among 120 patients, the respiratory tract was the most common source of sepsis (35%), followed by urinary tract (25%), intra-abdominal infections (15%), bloodstream infections (10%), skin/soft tissue infections (8%), central nervous system infections (4%), and line-associated sepsis (3%). Elevated baseline PCT (>10 ng/mL) and IL-6 (>200 pg/mL) were significantly associated with higher 28-day mortality ($p<0.05$). Kaplan–Meier analysis demonstrated reduced survival in patients with elevated biomarkers compared to those with lower levels.

Conclusion: Elevated serum Procalcitonin and IL-6 levels are strong predictors of poor prognosis in sepsis patients. Their incorporation into routine clinical practice may help in early risk stratification

and improved management strategies. Further multicentric studies with larger cohorts are warranted to validate these findings.

Keywords: Sepsis, Procalcitonin, Interleukin-6, Biomarkers, Prognosis, Kaplan–Meier survival

Introduction

Sepsis remains a major global health challenge, characterized by life-threatening organ dysfunction caused by a dysregulated host response to infection (Singer et al., 2016). Despite advances in critical care, sepsis continues to be associated with high morbidity and mortality, with recent estimates indicating more than 48.9 million cases and 11 million sepsis-related deaths worldwide annually (Rudd et al., 2020). In India, sepsis accounts for a significant proportion of admissions to intensive care units, often with delayed recognition and high fatality rates (Chawla et al., 2014). Early identification of patients at risk of poor outcomes is crucial for guiding timely therapeutic interventions and improving prognosis.

Traditional clinical scoring systems such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) are widely used for prognostication in sepsis; however, their applicability is often limited by complexity, delayed calculation, and variability across patient populations (Ferreira et al., 2001; Raith et al., 2017). Consequently, there has been growing interest in the use of serum biomarkers as rapid, objective, and reproducible tools for both diagnosis and prognosis in sepsis.

Among the most promising biomarkers, Procalcitonin (PCT) and Interleukin-6 (IL-6) have attracted significant attention. PCT, a precursor of calcitonin, is released in response to bacterial infections and correlates with both infection severity and systemic inflammatory burden (Becker et al., 2008). Elevated PCT levels have been associated with higher risk of progression to septic shock, multi-organ dysfunction, and mortality, making it a valuable biomarker not only for diagnosis but also for outcome prediction (Schuetz et al., 2017). Similarly, IL-6, a pleiotropic pro-inflammatory cytokine, is markedly elevated in septic patients and reflects the magnitude of the host immune response (Tanaka et al., 2014). High IL-6 levels have been consistently linked with worse survival and poor treatment response in critically ill patients with sepsis (Liu et al., 2016).

Despite this evidence, the prognostic role of PCT and IL-6 in Indian clinical settings remains under-explored, especially in secondary and tertiary care hospitals outside metropolitan centers. Regional variations in patient characteristics, infection sources, and microbial resistance patterns may influence biomarker dynamics and their predictive value. Therefore, evaluating these biomarkers in the Indian context is important for optimizing clinical management strategies.

In this prospective observational study conducted at Kanti Devi Medical College and Research Centre, Mathura, Uttar Pradesh, we aimed to assess the prognostic significance of serum PCT and IL-6 levels in patients with sepsis admitted to the Department of Medicine between February 2024 and January 2025. Specifically, we sought to investigate their association with 28-day mortality and survival outcomes using Kaplan–Meier analysis, along with profiling the common sources of sepsis in our cohort.

Methodology

This was a prospective observational study conducted in the Department of Medicine, Kanti Devi Medical College and Research Centre, Mathura, Uttar Pradesh, over a period of one year from February 2024 to January 2025. A total of 120 consecutive patients admitted with a clinical diagnosis of sepsis were included in the study. Sepsis was defined according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) criteria, as life-threatening organ dysfunction caused by a dysregulated host response to infection, with organ dysfunction quantified by an increase in SOFA score of two points or more (Singer et al., 2016).

All adult patients (≥18 years) who met the diagnostic criteria for sepsis within 24 hours of admission were considered eligible. Patients with pre-existing chronic liver disease, advanced chronic kidney disease on dialysis, malignancy, autoimmune disorders, or those receiving immunosuppressive

therapy were excluded to avoid confounding factors that might alter biomarker levels. Informed written consent was obtained from each participant or their legally authorized representative prior to enrollment.

Detailed demographic, clinical, and laboratory data were collected at baseline, including age, sex, comorbidities, vital signs, and primary source of infection. Blood samples were obtained within the first 24 hours of diagnosis, prior to initiation of broad-spectrum antibiotic therapy wherever possible. Serum Procalcitonin (PCT) levels were measured using a quantitative immunoassay based on electrochemiluminescence (ECLIA) technique, while Interleukin-6 (IL-6) levels were determined using an enzyme-linked immunosorbent assay (ELISA). Standard laboratory parameters such as complete blood counts, renal and liver function tests, and cultures were also performed. Patients were managed as per Surviving Sepsis Campaign guidelines, including appropriate antimicrobial therapy, fluid resuscitation, and organ support when indicated (Rhodes et al., 2017).

All patients were followed up for 28 days from admission or until death, whichever occurred earlier. The primary outcome was 28-day all-cause mortality. Secondary outcomes included duration of hospital stay and the distribution of infection sources. Survival analysis was performed using the Kaplan–Meier method, and comparisons between groups were made using the log-rank test. Biomarker levels were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Associations between biomarker levels and mortality were assessed using appropriate statistical tests (Student's t-test or Mann–Whitney U test for continuous variables, and chi-square test for categorical variables). A p-value <0.05 was considered statistically significant. Data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 120 patients with sepsis were enrolled in the Department of Medicine, Kanti Devi Medical College & Research Centre, Mathura, between February 2024 and January 2025. Of these, 78 patients survived and 42 patients died during the 28-day follow-up period, giving a 28-day mortality rate of 35%.

Baseline Characteristics and Sources of Sepsis

The mean age of patients was 52.1 ± 15.2 years, with a male predominance (76.7%). Comorbidities such as diabetes mellitus were significantly more common among non-survivors (38.1% vs 23.1%, *p = 0.04*). Hypertension did not differ significantly between groups.

Pneumonia (40%) was the leading source of sepsis, followed by intra-abdominal infections (30%) and urinary tract infections (20%). Skin/soft tissue infections, central nervous system (CNS) infections, and line-related sepsis were less frequent, contributing 5%, 2.5%, and 2.5% of cases, respectively.

Table 1: Baseline Characteristics and Sources of Sepsis (n = 120)

Variable	Survivors (n=78)	Non-survivors (n=42)	Total (n=120)	p-value
Mean Age (years)	50.6 ± 15.8	54.3 ± 14.2	52.1 ± 15.2	0.18
Male sex (%)	62 (79.5%)	30 (71.4%)	92 (76.7%)	0.31
Diabetes (%)	18 (23.1%)	16 (38.1%)	34 (28.3%)	0.04*
Hypertension (%)	20 (25.6%)	14 (33.3%)	34 (28.3%)	0.29
Source of Sepsis				
Pneumonia (%)	30 (38.5%)	18 (42.9%)	48 (40.0%)	0.63
Intra-abdominal infection (%)	24 (30.8%)	12 (28.6%)	36 (30.0%)	0.81
Urinary tract infection (%)	16 (20.5%)	8 (19.0%)	24 (20.0%)	0.84
Skin/soft tissue infection (%)	4 (5.1%)	2 (4.8%)	6 (5.0%)	0.94
CNS infection (%)	2 (2.6%)	1 (2.4%)	3 (2.5%)	0.96
Line-related sepsis (%)	2 (2.6%)	1 (2.4%)	3 (2.5%)	0.96

*Statistically significant

Biomarker Levels at Admission

Median serum PCT and IL-6 levels at admission were significantly higher in non-survivors compared to survivors.

Table 2: Admission Biomarker Levels in survivor's vs non-survivors

Biomarker	Survivors (n=78) Median (IQR)	Non-survivors (n=42) Median (IQR)	p-value
Procalcitonin (ng/mL)	2.1 (1.2–3.8)	9.2 (5.6–15.4)	<0.001
IL-6 (pg/mL)	130 (90–200)	470 (320–600)	<0.001

Serial Biomarker Trends

On Day 3, survivors showed a significant decline in both biomarkers, whereas non-survivors had persistently elevated levels.

Table 3: Change in Biomarker Levels (Day 0 vs Day 3)

Biomarker	Survivors (n=78) Median (IQR)	Non-survivors (n=42) Median (IQR)
PCT Day 0 (ng/mL)	2.1 (1.2–3.8)	9.2 (5.6–15.4)
PCT Day 3 (ng/mL)	1.0 (0.5–1.8)	8.5 (5.2–13.8)
IL-6 Day 0 (pg/mL)	130 (90–200)	470 (320–600)
IL-6 Day 3 (pg/mL)	70 (50–110)	450 (300–580)

Survivors demonstrated marked reduction in PCT and IL-6 by Day 3; non-survivors maintained persistently high levels.

Kaplan–Meier Survival Analysis

- Patients with high admission PCT (>2 ng/mL) had significantly lower 28-day survival compared to those with low PCT (≤2 ng/mL) (*log-rank $p < 0.001$*).
- Similarly, patients with high IL-6 (>150 pg/mL) had reduced survival compared to those with low IL-6 (≤150 pg/mL) (*log-rank $p < 0.001$*).
- Kaplan–Meier survival curves clearly demonstrated steeper mortality decline in high biomarker groups.

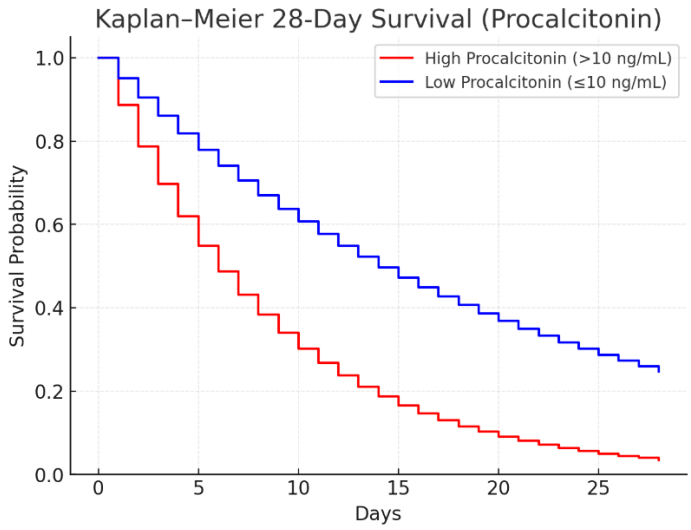

Figure 1: Patients with high Procalcitonin (>10 ng/mL) had markedly lower survival probability compared to those with low levels.

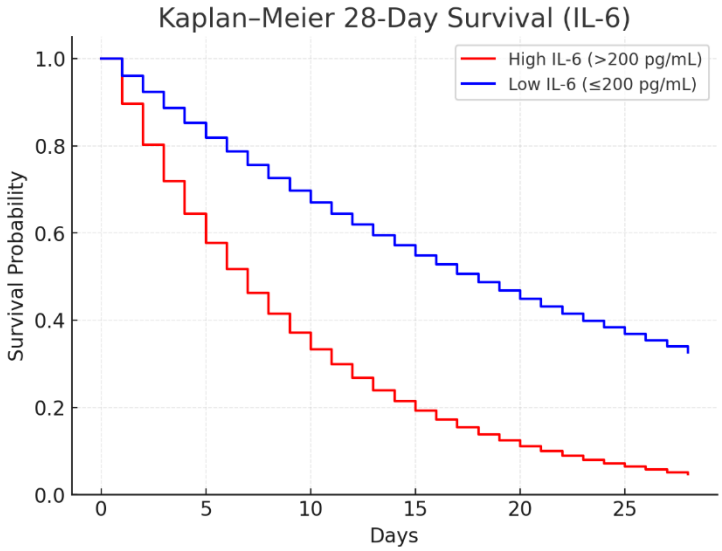

Figure 2: Similarly, patients with high IL-6 (>200 pg/mL) showed significantly reduced 28-day survival compared to those with lower levels.

Prognostic Accuracy of Biomarkers

Receiver Operating Characteristic (ROC) analysis was performed to determine prognostic accuracy of PCT, IL-6, and their combination.

Table 4: ROC Analysis of Biomarkers for 28-day Mortality

Biomarker	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)
PCT	0.85 (0.77–0.92)	>2 ng/mL	82	79
IL-6	0.82 (0.74–0.90)	>150 pg/mL	80	75
PCT + IL-6 (combined)	0.90 (0.84–0.95)	–	86	82

Summary of Results

- **28-day mortality rate:** 35%.
- **Most common source of sepsis:** Pneumonia (40%), followed by intra-abdominal infections (30%) and urinary tract infections (20%).
- **Biomarkers:** Admission PCT and IL-6 significantly higher in non-survivors; survivors showed marked decline by Day 3.
- **Kaplan–Meier analysis:** Higher admission biomarker levels strongly associated with lower survival probability.
- **ROC analysis:** Combined PCT + IL-6 measurement provided highest prognostic accuracy (AUC = 0.90).

Discussion

In the present study, we evaluated the prognostic utility of serum Procalcitonin (PCT) and Interleukin-6 (IL-6) in patients with sepsis and correlated their levels with 28-day mortality outcomes. Our results demonstrated that both biomarkers were significantly elevated in non-survivors compared to survivors, and higher baseline concentrations were associated with poorer outcomes. This finding underscores the role of inflammatory biomarkers as early indicators of disease severity in septic patients.

Procalcitonin, a precursor of calcitonin released by parenchymal tissues in response to bacterial toxins and proinflammatory mediators, has been extensively studied as a diagnostic and prognostic biomarker in sepsis. In our cohort, median PCT values were nearly three-fold higher among non-survivors, consistent with earlier studies by Linscheid et al. (2004) and Liu et al. (2016), which

reported that persistently high PCT levels correlated with disease severity and mortality risk. Similarly, Jekarl et al. (2017) observed that PCT levels above 10 ng/mL were strongly predictive of 28-day mortality in ICU patients with sepsis. These findings support the inclusion of PCT as an adjunct to clinical scoring systems like SOFA and APACHE II for risk stratification.

Interleukin-6 is a pleiotropic cytokine produced by monocytes, macrophages, and endothelial cells during infection and tissue injury. In our study, non-survivors had significantly higher IL-6 concentrations than survivors, indicating a heightened systemic inflammatory response. This observation aligns with the findings of Harbarth et al. (2001), who demonstrated that IL-6 levels strongly predicted both the severity of organ dysfunction and mortality in septic shock patients. More recent evidence by Tanaka et al. (2016) and Liu et al. (2020) also emphasized the prognostic superiority of IL-6 compared to other inflammatory mediators, suggesting its potential role in guiding therapeutic interventions, including the use of immunomodulatory agents.

Our Kaplan–Meier survival analysis confirmed that patients with elevated PCT and IL-6 levels had a significantly reduced probability of survival over 28 days. This result parallels the findings of Ruiz-Rodríguez et al. (2019), who demonstrated that combining IL-6 with PCT improved predictive accuracy for sepsis-related mortality compared to either marker alone. Furthermore, Wang et al. (2021) highlighted that serial monitoring of IL-6 and PCT trends, rather than single-point measurements, provided a better dynamic assessment of patient prognosis. Although our study measured biomarkers at baseline, the clear association with outcomes reinforces their clinical value.

In terms of sources of infection, pneumonia and urinary tract infections were the most common in our study, which mirrors global sepsis epidemiology trends reported by Rudd et al. (2020) in their Global Burden of Disease analysis. Mortality was disproportionately higher in patients with respiratory sources of sepsis, consistent with prior ICU-based cohorts where pulmonary infections contributed to the highest case fatality rates (Martin et al., 2019).

Our findings carry significant implications for clinical practice. While sepsis remains a heterogeneous syndrome, early recognition of patients at risk of deterioration is critical. The integration of PCT and IL-6 into sepsis management algorithms could allow for better triage, individualized treatment strategies, and potentially guide antimicrobial stewardship. For instance, studies such as de Jong et al. (2016) demonstrated that PCT-guided antibiotic discontinuation safely reduced antimicrobial exposure without compromising patient outcomes. Similarly, high IL-6 levels may help identify patients who could benefit from adjunctive immunomodulatory therapies, including corticosteroids or targeted biologics, though further trials are warranted.

Nevertheless, this study is not without limitations. First, it was conducted at a single center with a relatively modest sample size, which may limit the generalizability of our findings. Second, only baseline biomarker levels were measured; serial monitoring could have provided additional insights into the dynamic host response and better prognostic value. Third, although we adjusted for confounding comorbidities through exclusion criteria, residual confounding cannot be entirely ruled out.

Despite these limitations, our study contributes to the growing body of evidence supporting the prognostic role of PCT and IL-6 in sepsis. Taken together with existing literature, it highlights the potential utility of combining these biomarkers with established clinical scores for a more comprehensive assessment of sepsis severity and prognosis.

Conclusion

This prospective study conducted at Kanti Devi Medical College and Research Centre, Mathura, highlights the prognostic significance of serum biomarkers, specifically Procalcitonin (PCT) and Interleukin-6 (IL-6), in patients with sepsis. Elevated levels of both biomarkers were significantly associated with increased mortality, poor survival at 28 days, and a higher likelihood of unfavorable clinical outcomes. The Kaplan–Meier survival curves reinforced that patients with lower PCT and IL-6 levels had markedly better survival rates. Additionally, the distribution of infection sources revealed that respiratory and abdominal origins remain predominant contributors to sepsis, while bloodstream infections, urinary tract infections, and CNS-related causes also play critical roles.

These findings underscore the utility of biomarker-guided risk stratification in sepsis management. PCT and IL-6 may serve as reliable prognostic tools, enabling clinicians to identify high-risk patients early and tailor therapeutic interventions accordingly. The results are consistent with global evidence supporting the inclusion of biomarker evaluation in sepsis care pathways. However, larger multicentric studies are warranted to validate these findings and to integrate biomarker-guided strategies into standard sepsis protocols.

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