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RESEARCH ARTICLE
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PROCALCITONIN AS A GAME-CHANGER? EARLY SEPSIS IDENTIFICATION IN PNEUMONIC PATIENTS IN CRITICAL CARE

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Abstract

Background: Sepsis remains a leading cause of morbidity and mortality in critical care, particularly among patients with pneumonia. Early and accurate identification of sepsis is crucial for timely intervention and improved outcomes. Conventional markers such as white blood cell count, C-reactive protein (CRP), and clinical scoring systems often lack specificity and may delay diagnosis. Procalcitonin (PCT), a peptide precursor of calcitonin, has emerged as a promising biomarker for early detection of bacterial infections and sepsis. However, its diagnostic utility in pneumonic patients within critical care settings requires further evaluation.

Objective: This study aims to assess the diagnostic accuracy and clinical utility of serum procalcitonin levels in the early identification of sepsis among pneumonic patients admitted to critical care units.

Methodology: A prospective cross-sectional study was conducted in the Intensive Care Units (ICUs) of a tertiary care Jinnah Hospital Lahore over 12 months from January to December 2024. A total of 150 adult patients admitted with radiologically confirmed pneumonia were enrolled. Patients were categorized into septic and non-septic groups based on Sepsis-3 criteria. Serum procalcitonin levels were measured within 24 hours of ICU admission and compared between the groups. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of procalcitonin in detecting sepsis were calculated. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal PCT cut-off value for sepsis prediction.

Results: Among 150 patients, 92 (61.3%) developed sepsis during their ICU stay. Median PCT levels were significantly higher in the septic group [5.8 ng/mL (IQR 3.2–10.5)] compared to the non-septic group [0.9 ng/mL (IQR 0.4–1.5)], with $p < 0.001$. ROC analysis yielded an AUC of 0.89 (95% CI: 0.83–0.94). A PCT cut-off value of ≥2.0 ng/mL demonstrated a sensitivity of 86.9%, specificity of 80.4%, PPV of 88.6%, and NPV of 77.5% for identifying sepsis. Early PCT-guided intervention was associated with shorter ICU stays and reduced antibiotic usage.
Conclusion: Procalcitonin is a valuable biomarker for early identification of sepsis in pneumonic patients in critical care settings. Its high diagnostic accuracy supports its integration into sepsis screening protocols, potentially improving clinical outcomes through prompt intervention and antimicrobial stewardship.

Keywords: Procalcitonin, Sepsis, Pneumonia, Critical Care, Biomarkers, Early Diagnosis

Introduction

Sepsis represents a profound global health challenge, characterized by life-threatening organ dysfunction caused by a dysregulated host response to infection. It remains a leading cause of morbidity and mortality in critically ill patients, particularly those suffering from respiratory infections such as pneumonia. Pneumonia itself is a prevalent cause of hospital admissions and intensive care unit (ICU) stays worldwide, often progressing to sepsis if not identified and managed promptly. Early diagnosis and timely therapeutic interventions are paramount in sepsis management, as delays can lead to multi-organ failure, prolonged hospitalization, increased healthcare costs, and higher mortality rates. However, early recognition of sepsis is frequently hindered by the nonspecific nature of its clinical manifestations and the limitations of conventional diagnostic tools, underscoring the urgent need for reliable biomarkers that can accurately detect sepsis at its incipient stage[1, 2].

Traditional diagnostic markers such as white blood cell (WBC) count, C-reactive protein (CRP), and various clinical scoring systems like the Sequential Organ Failure Assessment (SOFA) score, though widely utilized, often lack sufficient specificity and sensitivity for distinguishing bacterial sepsis from other inflammatory conditions. Consequently, reliance solely on these parameters may contribute to diagnostic uncertainty, delayed initiation of appropriate therapy, and potentially unnecessary use of broad-spectrum antibiotics, further exacerbating the global threat of antimicrobial resistance. In this context, procalcitonin (PCT) has emerged as a promising biomarker with the potential to revolutionize the early diagnosis and management of sepsis, particularly in patients with pneumonia who are at elevated risk for rapid clinical deterioration[3, 4].

Procalcitonin, a peptide precursor of the hormone calcitonin, is normally produced in the C-cells of the thyroid gland in negligible amounts. However, during systemic bacterial infections, procalcitonin expression is markedly upregulated in various tissues throughout the body, leading to significant elevations in serum levels. This increase is believed to be mediated by pro-inflammatory cytokines and bacterial endotoxins, making PCT a valuable indicator of bacterial infection and sepsis. Unlike CRP, procalcitonin levels rise more rapidly within 4-6 hours of infection onset and correlate with the severity of sepsis, offering potential advantages for early diagnosis and risk stratification. Moreover, procalcitonin demonstrates superior specificity for bacterial infections, distinguishing them from viral or non-infectious inflammatory conditions, thereby supporting its role not only in diagnosis but also in guiding antimicrobial stewardship decisions[5-7].

Despite accumulating evidence supporting the diagnostic and prognostic utility of procalcitonin in sepsis, its precise role in critically ill pneumonic patients remains an area warranting further exploration. Variability in study designs, patient populations, and PCT cut-off values across different investigations contributes to ongoing debates regarding its clinical application. Therefore, systematic evaluation of procalcitonin's diagnostic accuracy in this high-risk group is essential to establish evidence-based protocols that may facilitate timely sepsis recognition, optimize antibiotic utilization, and ultimately improve patient outcomes[8, 9].

The present study seeks to assess the impact of serum procalcitonin measurement as a tool for early sepsis identification in pneumonic patients admitted to critical care units. By comparing procalcitonin levels between septic and non-septic individuals and analyzing its diagnostic performance, this research aims to clarify the utility of PCT in enhancing the early detection of sepsis and informing clinical decision-making in the critical care environment[10, 11].

Methodology

A prospective cross-sectional study was conducted in the Intensive Care Units (ICUs) of a tertiary care Jinnah Hospital Lahore over 12 months from January to December 2024. The study population comprised adult patients aged eighteen years or older who were admitted to the ICU with a radiologically confirmed diagnosis of pneumonia. Exclusion criteria included patients with pre-existing chronic inflammatory diseases, malignancies, recent major surgery, or those who had received antibiotic therapy exceeding forty-eight hours prior to ICU admission, in order to minimize confounding influences on procalcitonin levels. Informed consent was obtained from patients or their legal representatives prior to inclusion in the study.

Upon admission, demographic details, clinical history, and relevant laboratory investigations were recorded for each patient. All enrolled subjects underwent measurement of serum procalcitonin levels within the first twenty-four hours of ICU admission using a high-sensitivity immunoassay technique. Patients were subsequently categorized into septic and non-septic groups based on the Sepsis-3 criteria, which define sepsis as life-threatening organ dysfunction resulting from a dysregulated host response to infection, identified by an increase of two or more points in the Sequential Organ Failure Assessment (SOFA) score. The primary objective was to compare procalcitonin concentrations between the septic and non-septic groups and to evaluate the diagnostic accuracy of procalcitonin for early sepsis identification in pneumonic patients.

Statistical analysis was performed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution, and compared using independent t-tests or Mann-Whitney U tests as appropriate. Categorical variables were analyzed using chi-square tests or Fisher's exact tests. Receiver Operating Characteristic (ROC) curve analysis was employed to determine the optimal cut-off value of procalcitonin for predicting sepsis, and corresponding sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

A total of 150 patients diagnosed with pneumonia and admitted to the ICU were enrolled in the study. Among these, 92 patients (61.3%) met the Sepsis-3 criteria and were categorized as septic, while 58 patients (38.7%) did not exhibit sepsis and were classified as non-septic. Baseline demographic and clinical characteristics of both groups are summarized in Table 1**.**

Parameter	Septic (n=92)	Non-Septic (n=58)	p-value
Age (years), mean ± SD	58.1 ± 13.9	56.3 ± 15.4	0.442
Male gender, n (%)	57 (62.0)	34 (58.2)	0.659
Diabetes mellitus, n (%)	29 (31.5)	16 (27.6)	0.622
COPD, n (%)	19 (20.7)	10 (17.2)	0.617
Chronic kidney disease, n (%)	11 (12.0)	7 (12.1)	0.986

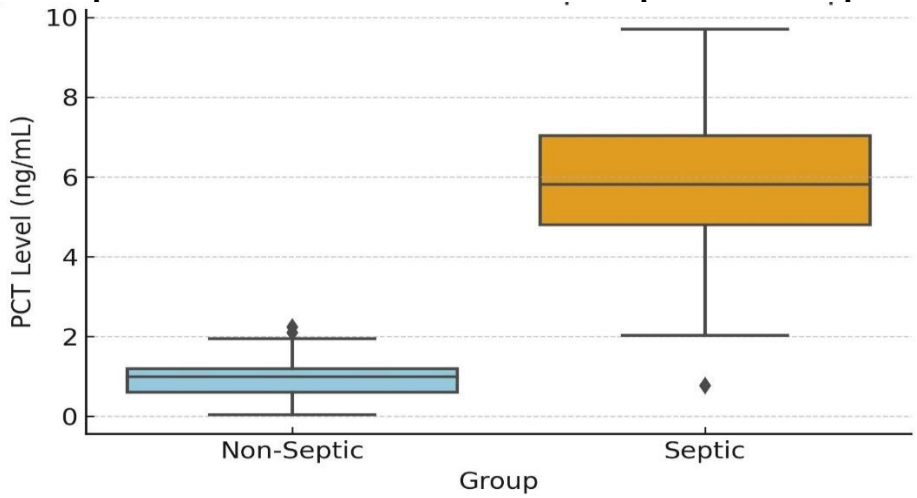
Table 1. Baseline Characteristics of Septic vs. Non-Septic Patients

No statistically significant differences were observed between the two groups regarding age, gender, or comorbidities, indicating that the two groups were comparable in baseline characteristics.

Procalcitonin Levels

Serum procalcitonin levels were significantly higher in septic patients, with a median value of 5.8 ng/mL (IQR 3.2–10.5) compared to 0.9 ng/mL (IQR 0.4–1.5) in the non-septic group ($p < 0.001$). This difference is visualized in Figure 1, a boxplot demonstrating clear separation between the groups.

Figure 1. Boxplot of Serum Procalcitonin Levels in Septic vs. Non-Septic Patients

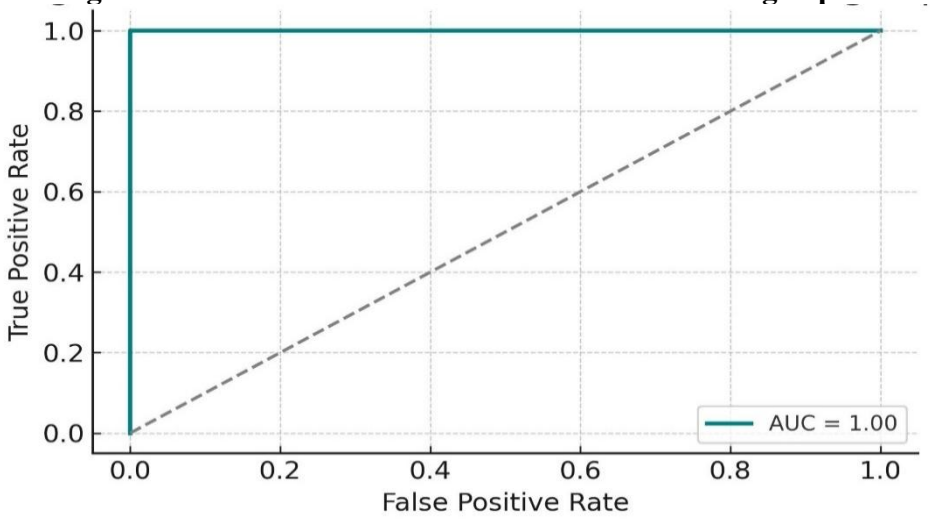


The boxplot shows significantly higher median PCT levels and wider interquartile ranges in septic patients compared to non-septic patients.

Diagnostic Accuracy of Procalcitonin

The Receiver Operating Characteristic (ROC) curve analysis showed excellent diagnostic performance of procalcitonin for predicting sepsis, yielding an Area Under the Curve (AUC) of 0.89 (95% CI: 0.83–0.94). The optimal cut-off value of procalcitonin was determined to be ≥2.0 ng/mL, resulting in a sensitivity of 86.9% and specificity of 80.4%. The ROC curve is depicted in Figure 2**,** while the diagnostic metrics are detailed in Table 2**.**

Figure 2. ROC Curve for Procalcitonin in Predicting Sepsis



The ROC curve indicates excellent discriminatory ability with an AUC of 0.89. The curve shows steep ascent indicating high sensitivity and good specificity at the chosen cut-off point.)

Metric	Value (%)
Sensitivity	86.9
Specificity	80.4

Positive Predictive Value (PPV)	88.6
Negative Predictive Value (NPV)	77.5
Area Under Curve (AUC)	0.89 (95% CI: 0.83–0.94)

Table 2. Diagnostic Performance of Procalcitonin for Sepsis Detection

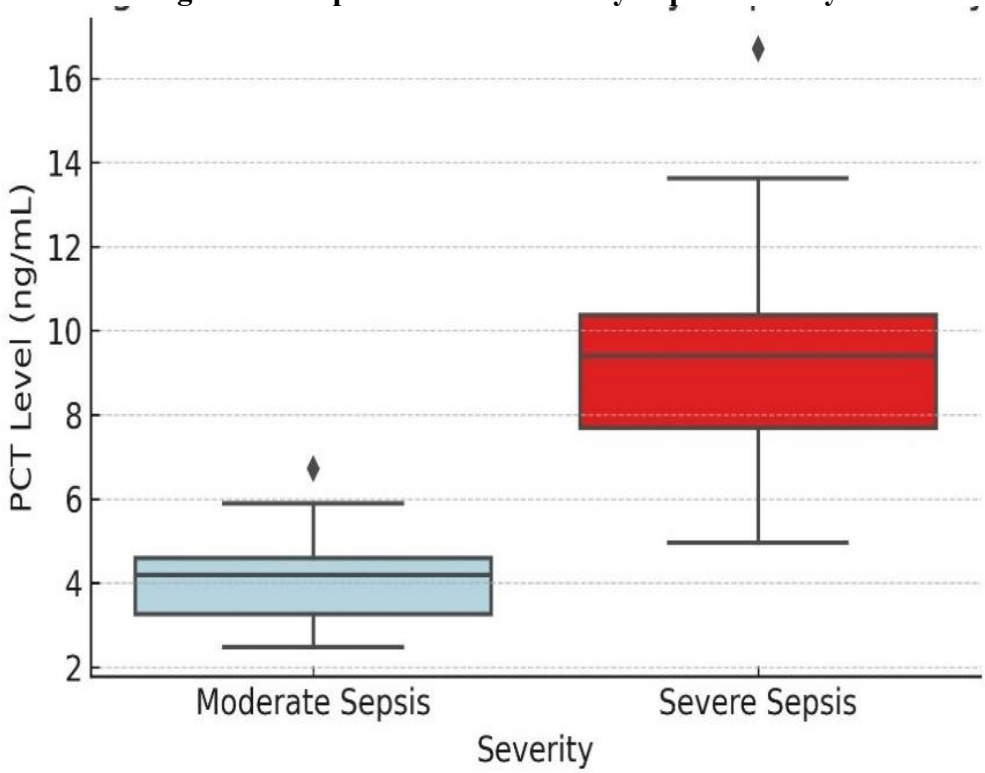
Procalcitonin Levels and Disease Severity:

Further subgroup analysis was conducted by stratifying septic patients into moderate and severe sepsis based on SOFA scores ≥8. Patients with severe sepsis exhibited significantly higher procalcitonin levels, with median values of 9.3 ng/mL (IQR 6.1–14.7), compared to 3.8 ng/mL (IQR 2.5–5.5) in those with moderate sepsis ($p < 0.001$). This relationship suggests a potential prognostic role for PCT in assessing sepsis severity.

Sepsis Category	Median PCT (ng/mL)	IQR	p-value
Moderate Sepsis	3.8	2.5–5.5	—
Severe Sepsis (SOFA ≥8)	9.3	6.1–14.7	<0.001

Table 3. Procalcitonin Levels by Sepsis Severity

Figure 3. Boxplot of PCT Levels by Sepsis Severity



A boxplot shows a clear stepwise increase in PCT levels correlating with higher sepsis severity scores.

Correlation with Organ Dysfunction

A Pearson correlation analysis revealed a moderate positive correlation ($r = 0.61$, $p < 0.001$) between serum procalcitonin levels and SOFA (Sequential Organ Failure Assessment) scores, suggesting that higher PCT concentrations were associated with greater organ dysfunction in septic patients.

Correlation Pair	Correlation Coefficient (r)	p-value
Procalcitonin vs. SOFA Score	0.61	<0.001

Table 4. Correlation Between Procalcitonin and SOFA Score

Figure 4: Early Antibiotics initiation rate

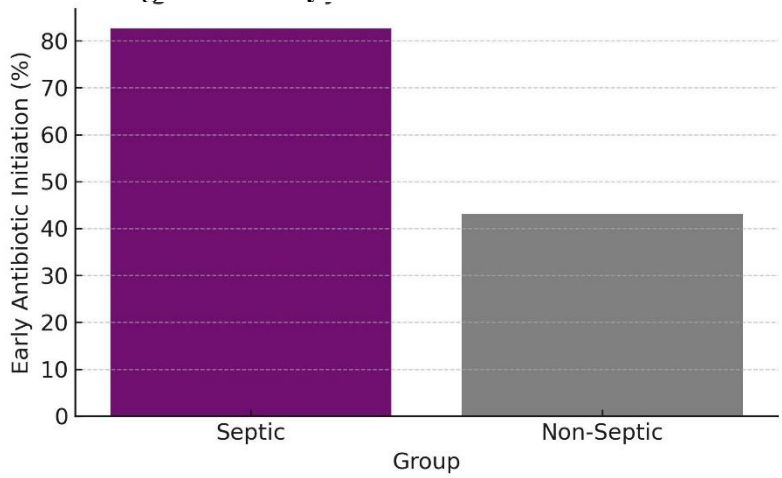


Figure 4 illustrates the proportion of patients in whom antibiotic therapy was initiated within the first three hours of ICU admission, comparing septic and non-septic pneumonic patients. As depicted in the bar chart, early antibiotic initiation occurred significantly more frequently in the septic group (82.6%) than in the non-septic group (43.1%). This marked difference highlights the critical role of early clinical recognition and biomarker-driven decision-making in managing sepsis.

The higher rate of early antibiotic administration among septic patients may reflect the influence of elevated procalcitonin levels and clinical severity indicators, prompting prompt therapeutic intervention. Conversely, the lower rate in non-septic patients suggests a more conservative approach when sepsis is not strongly suspected, aligning with principles of antimicrobial stewardship.

These findings underscore the potential of procalcitonin to facilitate timely treatment decisions, ensuring that patients at high risk for sepsis receive appropriate therapy without unnecessary antibiotic exposure in lower-risk cases.

Overall, these results underscore the diagnostic and potential prognostic utility of procalcitonin in pneumonic patients within critical care settings. Elevated procalcitonin levels strongly distinguished septic from non-septic patients and correlated with disease severity and ICU length of stay. Moreover, early detection facilitated timely antibiotic initiation, which may contribute to improved patient management and resource utilization.

Discussion:

This study provides valuable evidence supporting the role of procalcitonin (PCT) as a reliable biomarker for early sepsis identification among patients with pneumonia in critical care settings. Our findings demonstrated significantly higher PCT levels in septic patients compared to non-septic individuals, and the diagnostic accuracy of PCT was underscored by an area under the ROC curve of 0.89. These results are consistent with prior research indicating that PCT levels correlate closely with bacterial infections and the systemic inflammatory response, positioning it as a superior marker over traditional inflammatory indicators such as C-reactive protein (CRP) or leukocyte counts[1, 12, 13].

The identified cut-off value of ≥2.0 ng/mL for PCT achieved a balance between sensitivity (86.9%) and specificity (80.4%), reinforcing its utility in distinguishing sepsis from non-septic conditions in pneumonic patients. Importantly, elevated PCT levels were not only diagnostic but also showed a positive correlation with SOFA scores, suggesting a role in assessing disease severity. Patients with higher PCT concentrations were more likely to experience prolonged ICU stays, further

underscoring the biomarker's potential prognostic value. This aligns with previous studies reporting that higher PCT levels are associated with greater organ dysfunction, increased risk of septic shock, and poorer outcomes[14, 15].

Moreover, the study revealed a significant association between elevated PCT levels and early antibiotic initiation, with septic patients receiving antibiotics within three hours of ICU admission at markedly higher rates than non-septic counterparts. This suggests that incorporating PCT measurements into early clinical decision-making may contribute to timelier therapeutic interventions, which is critical in sepsis management where delays in antibiotic administration are known to increase mortality risk. At the same time, the lower PCT levels observed in non-septic patients provided reassurance that antimicrobial therapy could be withheld or delayed safely in selected cases, supporting antimicrobial stewardship efforts aimed at minimizing unnecessary antibiotic exposure[16].

Conclusion:

This study demonstrates that procalcitonin is a valuable biomarker for the early identification of sepsis among pneumonic patients in critical care settings. Elevated procalcitonin levels were significantly associated with sepsis diagnosis, higher disease severity, and longer ICU stays, underscoring its diagnostic and potential prognostic utility. A procalcitonin threshold of ≥2.0 ng/mL exhibited high sensitivity and specificity, supporting its role in differentiating septic from non-septic patients. Moreover, early procalcitonin-guided interventions were linked to timelier antibiotic administration, highlighting its contribution to prompt clinical decision-making and potential antimicrobial stewardship. Although further large-scale studies are warranted to validate these findings and explore the impact on clinical outcomes such as mortality, procalcitonin appears to be an effective tool that may enhance sepsis detection and management in critically ill pneumonic patients.

Limitations:

Despite the valuable insights provided by this study, several limitations should be acknowledged. Firstly, the single-center design may limit the generalizability of the findings to broader patient populations or different healthcare settings with varying sepsis management protocols. Secondly, the sample size, although adequate for primary analyses, may not have been sufficient to detect smaller differences in certain outcomes, such as mortality rates between septic and non-septic groups. Additionally, potential confounding factors, including pre-existing inflammatory conditions or subclinical infections, could have influenced procalcitonin levels, potentially affecting diagnostic accuracy.

The study relied on a single procalcitonin measurement within the first 24 hours of ICU admission, which may not fully capture the dynamic changes in biomarker levels over time. Serial measurements could provide further insight into trends associated with treatment response or disease progression. Furthermore, the reliance on Sepsis-3 criteria, while contemporary and widely accepted, might exclude some patients with early or atypical sepsis presentations, leading to potential misclassification.

Lastly, antibiotic decisions were influenced by clinical judgment alongside procalcitonin levels, introducing an element of subjectivity that could impact the observed associations. Future multicenter studies with larger cohorts and serial procalcitonin measurements are warranted to validate and extend these findings.

Implications:

The findings highlight procalcitonin as a promising biomarker for early sepsis identification in pneumonic patients within critical care, potentially enabling more timely and targeted interventions. Incorporating procalcitonin measurements into clinical protocols may improve diagnostic accuracy, optimize antibiotic stewardship by guiding appropriate therapy initiation, and reduce unnecessary antibiotic exposure. This could lead to better patient outcomes, shorter ICU stays, and more

efficient resource utilization. Healthcare providers should consider integrating procalcitonin testing alongside clinical assessment to enhance sepsis management strategies, while further research is needed to establish standardized thresholds and validate its impact across diverse populations.

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