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Original Research Article

Procalcitonin-A Marker of Sepsis

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Abstract

Background: Sepsis remains a significant health concern, particularly in resource-limited regions like Bangladesh. Despite available diagnostic methods, identifying bacterial infections in septic patients proves challenging, prompting the exploration of biomarkers. Procalcitonin (PCT) has emerged as a promising biomarker for bloodstream infections like sepsis. ***Objective:*** This study aims to evaluate the utility of measuring serum PCT levels in diagnosing and assessing the severity of sepsis, with a focus on enhancing early treatment in intensive care units (ICUs). ***Method:*** A prospective study was conducted on 50 patients admitted to the Combined Military Hospital, Dhaka ICU, exhibiting clinical manifestations of sepsis between April and September 2015. Patients of all ages and genders were included, while those with recent major surgery, trauma, or burn history were excluded. Detailed clinical assessments and laboratory investigations were performed, with data recorded on a standardized proforma. ***Result:*** Of the 50 patients evaluated, 64% were male, and 36% were female, with a mean age of 56.11±10.89 years. Sepsis was more prevalent in patients aged >50 years (60%) and in males (64%). Respiratory tract infection (RTI) was the most common source of sepsis (40% of cases), with Klebsiella pneumonia being the predominant organism. Higher Sequential Organ Failure Assessment (SOFA) scores correlated significantly with elevated serum PCT concentrations. Serum PCT demonstrated a significant difference between non-septic and septic groups (p-value <0.001), exhibiting sensitivity and specificity of 91% and 83.3%, respectively. ***Conclusion:*** Serum PCT emerges as a promising marker for sepsis in critically ill patients, enhancing diagnostic certainty and informing patient management. Its addition to routine work-ups could improve outcomes and patient care in ICUs.

Keywords: Sepsis, Procalcitonin, Biomarker, ICU, Diagnosis.

INTRODUCTION

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, remains a significant global health challenge, particularly in resource-limited settings such as Bangladesh [1]. Despite advances in medical science, sepsis continues to exact a heavy toll in terms of morbidity and mortality, with a reported mortality rate ranging from 20% to 50%. In Bangladesh, where healthcare resources are often limited and access to advanced diagnostic tools is constrained, the burden of sepsis is exacerbated, underscoring the urgent need for effective diagnostic and management strategies [2].

One of the challenges in managing sepsis is the timely identification of the causative pathogen. Even when microbiological diagnostics are available, bacterial infections are only identified in most patients presenting with sepsis and bloodstream infections [3]. This diagnostic gap not only delays appropriate antimicrobial therapy but also contributes to the high mortality associated with sepsis [4]. Thus, there is a critical need for adjunctive diagnostic tools that can aid in the early identification and management of sepsis.

Biomarkers have emerged as valuable tools in the diagnosis, prognostication, and monitoring of various disease processes, including infections [5]. Procalcitonin (PCT), a precursor peptide of calcitonin, has garnered considerable attention as a promising biomarker for bloodstream infections such as sepsis. Unlike traditional inflammatory markers like C-reactive protein (CRP) and white blood cell count (WBC), PCT exhibits a dynamic profile, with rapid elevation in response to bacterial infections and rapid decline upon resolution of the infection [6]. This unique kinetic profile enables PCT to discriminate between bacterial and viral etiologies of infection, aiding in early differential diagnosis and guiding appropriate antimicrobial therapy.

Several studies have demonstrated the utility of serum PCT levels in diagnosing and assessing the severity of sepsis. Elevated PCT levels have been shown to correlate with the presence of bacterial infections, the severity of sepsis-related organ dysfunction, and poor clinical outcomes [7]. Moreover, PCT levels are particularly useful in guiding antimicrobial therapy decisions, facilitating early initiation of appropriate antibiotics, and reducing unnecessary antibiotic exposure.

The significance of early recognition and treatment of sepsis cannot be overstated. Timely initiation of appropriate antimicrobial therapy and supportive care measures can mitigate the progression of sepsis, reduce the risk of complications, and improve patient outcomes [8]. In resource-limited settings like Bangladesh, where healthcare resources are often scarce, and access to advanced diagnostic tools may be limited, the role of biomarkers such as PCT becomes even more crucial in facilitating early diagnosis and guiding therapeutic interventions.

Against this backdrop, the present study aims to investigate the utility of measuring serum PCT levels as a diagnostic biomarker and assessing the severity of sepsis in patients admitted to the intensive care unit (ICU). By elucidating the relationship between serum PCT levels, clinical parameters, and outcomes in septic patients, this study seeks to augment early treatment strategies and improve patient management in resource-limited settings. In summary, sepsis remains a formidable challenge in healthcare, particularly in resource-limited settings where various factors hinder timely diagnosis and intervention. Biomarkers such as PCT offer a promising avenue for enhancing the early recognition and management of sepsis, thereby improving patient outcomes and reducing the burden of this devastating condition.

OBJECTIVES

General Objectives

- To determine Procalcitonin is a marker of sepsis.

Specific Objectives

- To assess the association between the level of Procalcitonin and the severity of sepsis.

MATERIALS AND METHODS

Study Design

The study employs a cross-sectional observational design with both descriptive and analytical components. This approach allows for data collection at a single point in time, facilitating examining relationships between variables and assessing outcomes within the study population. The observational nature of the design enables the investigation of associations between variables without intervention, providing valuable insights into the prevalence and characteristics of sepsis in the ICU setting.

Inclusion criteria

- Patients of any age and of both sexes.
- Patients with clinical manifestation of infection.

Exclusion criteria

- Patients without clinical presentation of infection.
- Patients with a history of recent major surgery, trauma, and burn.

Data Collection

Data collection involves comprehensive assessments of patients admitted to the Combined Military Hospital, Dhaka ICU presenting with clinical manifestations of sepsis. Detailed histories, clinical examinations, and laboratory investigations are conducted, with findings recorded on a standardized proforma. Patient demographics, clinical parameters, and laboratory results are documented to facilitate the analysis of the relationship between serum procalcitonin levels, severity of sepsis, and patient outcomes.

Data Analysis

Data analysis encompasses statistical processing of collected data using SPSS version 26 software. Descriptive statistics such as means, standard deviations, and percentages are computed to summarize patient demographics and clinical characteristics. Inferential statistics, including t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables, are employed to assess associations between serum procalcitonin levels, severity of sepsis, and other relevant parameters. Statistical significance is set at $p < 0.05$.

Ethical considerations

Ethical approval was paramount throughout this study. The Institutional Review Board of Combined Military Hospital, Dhaka, reviewed and approved the research protocol, ensuring compliance with ethical guidelines and standards. Informed consent was obtained from all participants or their legal guardians before their

inclusion in the study. Patient confidentiality was strictly maintained, and data were anonymized to protect privacy. The study adhered to beneficence, non-maleficence, and respect for autonomy.

RESULTS

Fifty patients with suspected sepsis who presented with symptoms and signs of infection/ or sepsis admitted to the ICU of CMH Dhaka between April 2015 to September 2015 were selected for this study. After a thorough physical examination, some routine and biochemical investigations were performed. Data analysis was performed by Statistical Package for Social Science (SPSS) with the help of a Statistician.

Table 1: Age group-wise distribution of subjects in the study (n=50)

Age in years	Number	Percentage
20- 29	5	10
30- 39	9	18
40- 49	6	12
50- 59	11	22
60- 69	5	10
70- 79	4	8
≥80	10	20
Total	50	100
Mean±SD	56.11±10.89	

The study showed a maximum number of patients (22%) were in the 50-59 years age group. The mean age of the study population was 56.11±10.89. The age of the study group ranged between 20- >80 years.

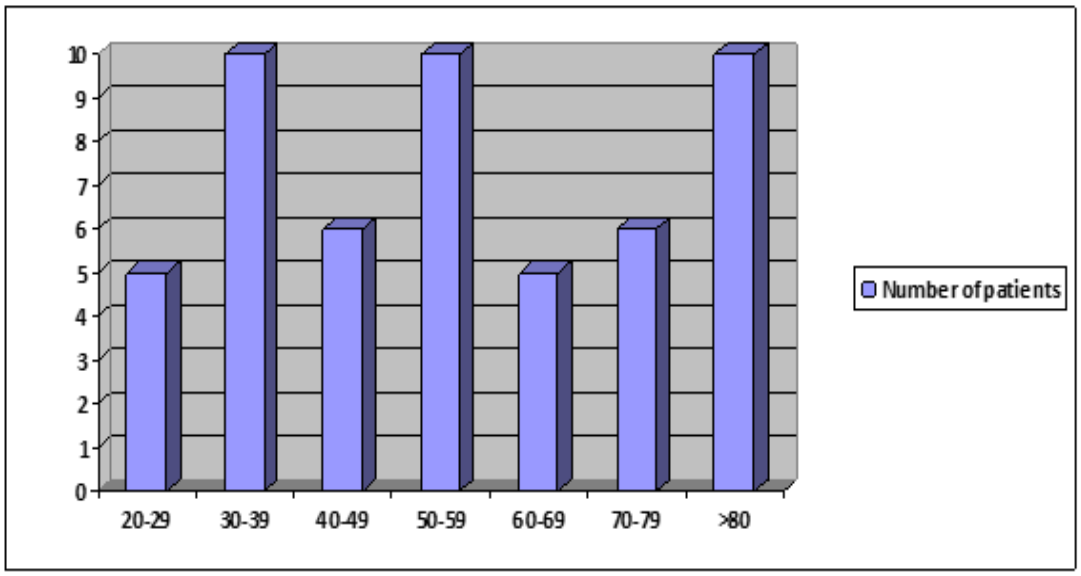

Figure 1: Age distribution of the study subjects

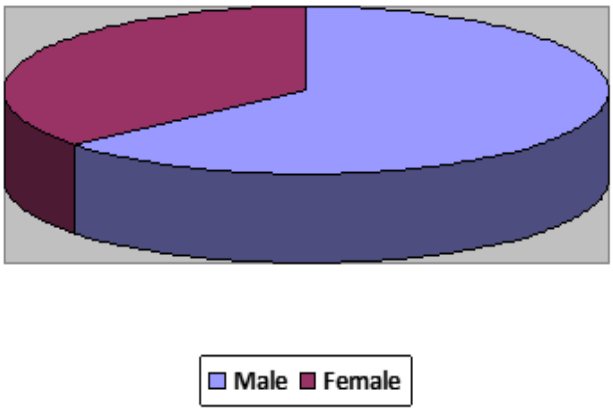

Figure 2: Pie chart representing gender distribution

In the study group of 50 patients, 32 (64%) were males and 18 (36%) were females.

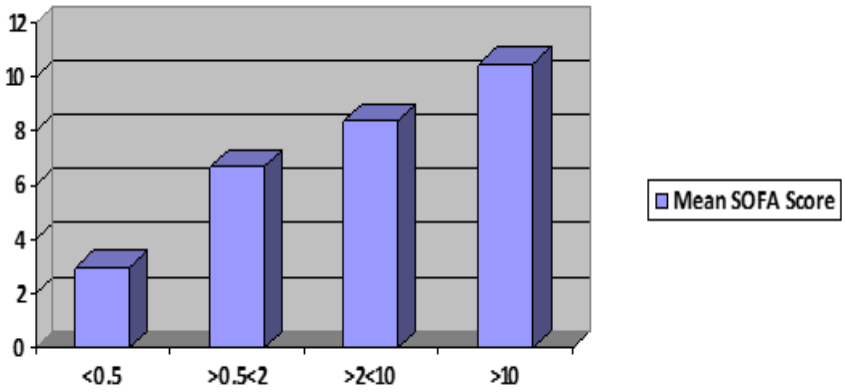

Figure 3: Comparison of serum PCT and mean SOFA score in local infection, sepsis, severe sepsis, and septic shock

The mean SOFA (Sequential Organ failure assessment) scores in local infection, sepsis, severe sepsis, and septic shock were 2.96, 6.7, 8.4, and 8.52, respectively. Higher SOFA score levels were associated with significantly higher serum PCT concentrations.

Table 2: Primary source of infection in sepsis

Source of infection	Local Infection	Sepsis	Severe sepsis	Septic shock	Total No. (%)
Respiratory tract	2	11	4	3	20 (40)
Urinary tract	1	4	2	2	9 (18)
GIT	1	3	0	1	5 (10)
Malaria		0	0	1	1 (2%)
Dengue		1	1	0	2 (4%)
Skin & Soft Tissue (Cellulitis)	1	1	1	0	3 (6%)
Central venous catheter tip			1		1 (2%)
Source not found	1	5	2	1	9 (18%)

The various sites of the primary source of infection are given in Table 3.3. Among 50, 41 (82%) patients had an identified source of infection; in 9 (18%) patients, no definite source was found. The commonest site of infection was the respiratory tract (40%), followed by the urinary tract (18%).

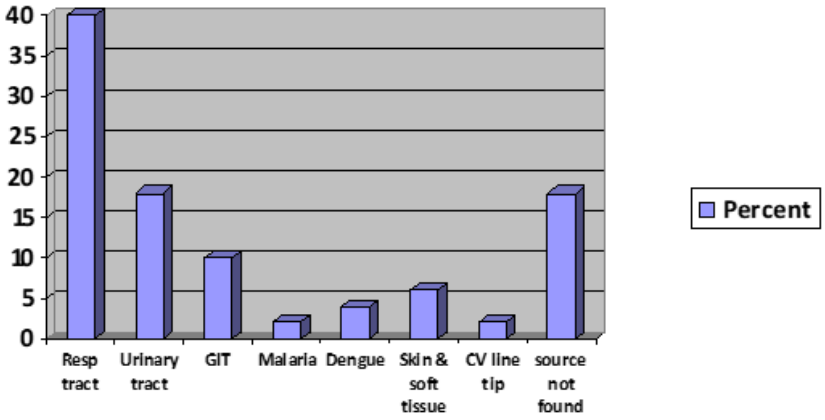

Figure 4: Graph represents the percentage of the site of infections

Table 3: Site of infection and microbiology

Site of infection	Microbiology
Respiratory tract (*n* = 09)	*Klebsiella pneumoniae* (5), *Streptococcus pneumoniae* (2), *Pseudomonas aeruginosa* (1), *Staphylococcus aureus* (1)
Urinary tract (*n* = 4)	*Escherichia coli* (3), *Pseudomonas aeruginosa* (1)
Wound and soft tissue (*n* = 2)	*Staphylococcus aureus (1), Klebsiella pneumoniae* (1),
Abdominal (gastrointestinal tract and biliary system) (*n* = 2)	*Proteus vulgaris* (1), Vibrio Cholerae (1)
Bacteremia (*n* =1)	*Pseudomonas aeruginosa*
Central venous catheter tip (1)	*Staphylococcus aureus*

Among 50 19 patients (18%), definite organisms were identified from various sites.

Table 4: Serum PCT level in local infection, Sepsis, Severe sepsis and Septic shock patients

Diagnosis	**Serum PCT range (ng/ml)**				
	<0.5	**>0.5 and <2**	**>2 and <10**	**>10**	**Total**
Local infection	5 (83.3)	1(16.7)	0 (00)	0 (00)	6 (100)
Sepsis	3 (12.0)	20 (80.0)	2 (8.0)	0 (00)	25 (100.0)
Severe sepsis	1 (9.1)	1 (9.1)	7 (63.6)	2 (18.2)	11 (100.0)
Septic shock	0 (00)	1 (12.5)	1 (12.5)	6 (75)	8 (100.0)

Patients were grouped into non-sepsis (local infection) and sepsis groups: sepsis group again reclassified as sepsis, severe sepsis, and septic shock by Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. Among 50, 6 (12%) patients were found to have features of local infection, 25 (50%)- sepsis,11 (22%) severe sepsis, and 8 (16%)- sepstic shock.

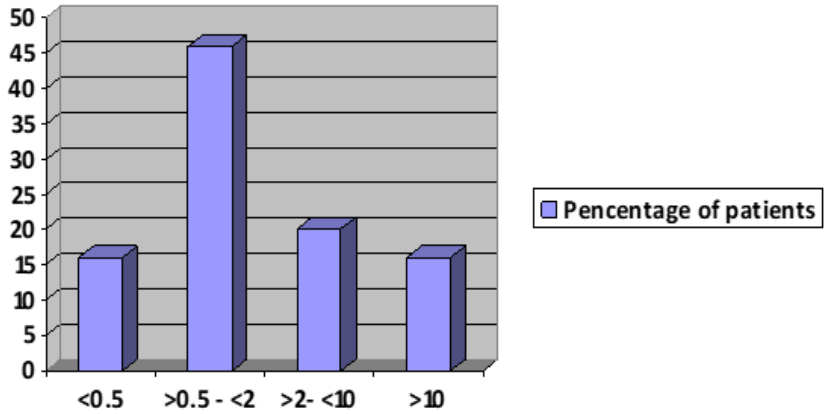

Figure 5: Percentage of patients in comparison to serum PCT level (ng/ml)

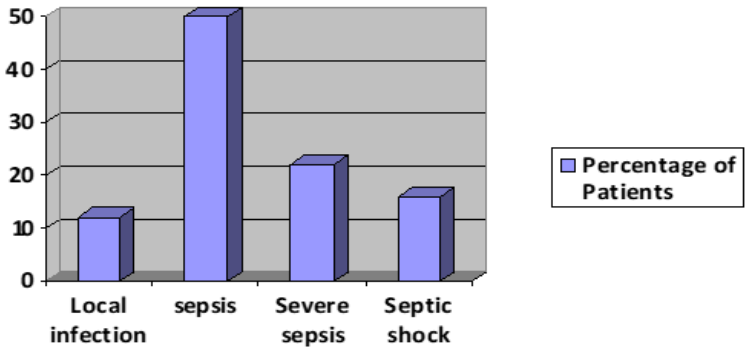

Figure 6: Percentage of patients with sepsis status

Table 5: Comparison of laboratory data of patients with a p-value

Variables	Non- sepsis Group (n=6)	Sepsis Group (n=44)	p-value
WBC, ×10³/mm³	8.3±5.1	10.9±11.8	0.249
Haemoglobin, ×g/dL	12.3±2.1	7.3±2.6	0.453
Platelet, ×10³/mm³	226.1±103.7	130.5±115.6	0.156
ESR, mm in 1st hour	10.4±4.6	32.3±11.7	0.248
Creatinine, mg/dL	0.9±0.8	1.3±1.4	0.004
CRP, mg/dL	6.9±7.4	8.0±9.3	0.396
Lactate, mmol/L	1.5±0.9	2.5±2.5	0.015
Procalcitonin, ng/mL	0.36±0.57	18.09±36.53	＜0.001

When comparing the subjects into non-sepsis and sepsis groups with laboratory tests, the item showed a significant difference between the two groups in serum creatinine, lactate, and procalcitonin. At the same time, the C-reactive protein (CRP) and white blood cell (WBC) counts did not show significant differences between the two groups.

DISCUSSION

Our study population was small; clinically suspected cases of sepsis were selected by Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012 [9]. We evaluated the combined role of serum PCT and other clinical indicators of inflammation as predictors of sepsis in which we explored the diagnostic accuracy of these different parameters from a clinical perspective. Incidence was higher in patients aged over 50 years (60%). The age distribution is similar to studies done around the world. A western study reported a higher incidence of sepsis in patients aged above 57 years. The mean age in an epidemiological study of sepsis in India was 54.9 years [10].

We found a higher percentage of males (64%) affected with sepsis than females (36%) in the present study. Studies by previous workers also indicated a higher incidence among men [11]. Martin *et al.*, reported that sepsis was more common in men, accounting for 48.1% of cases on average per year, and men were more likely to have sepsis than women with a mean annual relative risk of 1.28. Todi and group reported from a multicenter trial done at 12 centers in India that sepsis was more common in males. The mean SOFA (Sequential Organ failure assessment) scores in local infection, sepsis, severe sepsis, and septic shock were 2.96, 6.7, 8.4, and 8.52, respectively. Higher SOFA score levels were associated with significantly higher serum PCT concentrations. It was found that higher SOFA score levels were associated with significantly higher serum PCT plasma concentrations. Similar results have been found in various studies worldwide [12].

Respiratory tract infection (RTI) was found in 20 cases (40%), the most common source of infection in our study. Klebsiella pneumoniae (5 cases) was the most common organism causing community-acquired pneumonia in the present study. The primary source could not be identified in 9 (18%) cases. Urinary tract infection (UTI) was the second most common (9 cases-18%) focus, and Escherichia coli (3) was the most common organism, which may be partly due to the number of elderly patients with risk factors like diabetes [13]. A similar study identified six common infection sites in the causation of sepsis: pneumonia, bloodstream infections including infective endocarditis, intravascular catheter-related sepsis, intraabdominal infections, urosepsis, and surgical wound infections. Dengue was found to be the primary source of sepsis in three cases. Studies have shown a mild elevation of serum PCT in viral infections [14]. In contrast, two patients in our study had an elevation of serum PCT level. Malaria was the underlying cause of sepsis in 1 case. Mild elevation of serum PCT in malaria has been reported in the literature.

In this study, the infectious status of patients was grouped into a non-sepsis group (local infection) and a sepsis group (which was reclassified as sepsis, severe sepsis, septic shock) by Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. Among the biomarkers (ESR, CRP, lactate), PCT shows a significant difference between the non-sepsis and sepsis groups (p-value <0.001). Our study also shows serum PCT has sensitivity- 91%, specificity- 83.3%, positive predictive value-97%, and negative predictive value-56%. Harbarth *et al.*, reported a sensitivity of 97% [15]. The present results confirm earlier findings demonstrating serum PCT as among the most promising sepsis markers in critically ill patients, capable of complementing clinical signs and routine lab parameters suggestive of severe infection during ICU admission. Brunkhorst *et al.*, reported from their study that serum PCT levels increase with the increasing severity of the inflammatory response to infection [16].

Serum PCT levels are, therefore, undetectable (<0.1 ng/ml) in healthy humans. However, serum PCT levels may increase to over 100 ng/ml during severe infections with systemic manifestations. In these conditions, serum PCT is probably produced by extra-thyroid tissues. Patients who have previously undergone total thyroidectomy still produce high levels of serum PCT during severe infection. The exact origin of serum PCT during sepsis is uncertain. The (patho) physiological role of serum PCT during sepsis is unclear

[17]. Serum PCT is not a marker of infection since localized infections or infections with no systemic manifestation cause a limited, if any, increase in serum PCT levels. Although elevated serum PCT values during severe infections may decrease to very low levels with appropriate therapy, this does not always indicate complete eradication; only the generalization of the infection or the systemic response is under control [18,19]. Our study has several important implications for clinicians.

Although the present study population is small enough to commit to the importance of serum PCT in critical care, it indicates that serum PCT may be included in the battery of infections to help manage sepsis in critical care. In summary, the incidence of sepsis was higher in patients aged >50 years (60%) and males (64%). Respiratory tract infection (RTI- 40%cases) was the most common source of sepsis, and Klebsiella pneumonia was the most common organism. Serum PCT proved to be an excellent indicator of sepsis in critically ill patients, with a sensitivity of 91% and a specificity of 83.3%. Our results indicate that clinical variables are of modest diagnostic value for diagnosing sepsis in ICU-admitted patients.

CONCLUSION

our study underscores the potential of serum Procalcitonin (PCT) as a promising marker for sepsis in critically ill patients, enhancing diagnostic accuracy alongside clinical signs and routine laboratory parameters upon ICU admission. While the study sample size warrants cautious interpretation, serum PCT emerges as a superior predictor to conventional markers like blood cell counts, ESR, or CRP. The rapidity of PCT testing, providing valuable information before culture results, suggests its utility in guiding early clinical decision-making. Incorporating serum PCT into standard work-ups could enhance diagnostic certainty and ultimately improve patient management, signaling a promising avenue for optimizing outcomes in sepsis.

Recommendation

At the end of the study, the following recommendations:

- Large scale study should be carried out to determine the significance of PCT in early diagnosis of sepsis.
- A low serum PCT level cannot be used safely to exclude the presence of infection, especially in patients with sepsis.
- By measuring serum PCT, infectious severity can be evaluated.
- Serum PCT can be a good guide for the early treatment of antibiotics.
- A serial assessment of serum PCT levels can help evaluate the improvement and progression of sepsis.

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Abbreviations

ICU: Intensive Care Unit
CMH: Combined Military Hospital
PCT: Procalcitonin
CRP: C-Reactive Protein
ESR: Erythrocyte Sedimentation Rate

Article at a glance

Study Purpose: Evaluate serum PCT as a sepsis marker in the ICU.

Key Findings: Serum PCT is effective in diagnosing sepsis, correlating with severity.

Newer Findings: Serum PCT enhances diagnostic certainty and patient management in ICU settings.

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