Prognostic Value of Serum Procalcitonin in Patients with Sepsis in a Tertiary Level Hospital

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Abstract

Background: *Sepsis is a complex, life-threatening, heterogeneous infectious disease associated with increased rates of morbidity and mortality. Early assessment of the prognosis of sepsis is key to achieving a favorable outcome for the disease. This study aimed to identify the prognostic value of PCT for sepsis patients.*

Materials and Methods: *We conducted a prospective analytical study involving 100 adult patients with sepsis who were admitted to the Medicine dept and intensive care unit from 2019 to 2020. At least one blood test for PCT level was performed for all patients within the first 24 hours of suspecting an infection.*

Results: *Our study found that a maximum number of patients (43.0%) were between 51-60 years age group, mean age of the patient was 49.35 ± 11.7 years. Out of 100 cases, 65% were male and 35% were female. The male and female ratio was 1.85:1. In this study serum, procalcitonin levels 0.5-2.0 ng/were detected in 15.0% of patients with mean±SD 1.3±0.8. Serum procalcitonin levels 2.1-10.0 ng/mL were detected in 29.0% of patients with mean±SD 5.9±2.5 and >10.0 ng/mL was detected in 56 patients. Based on the receiver-operator characteristic (ROC) curves, procalcitonin had the area under curve 0.923, with 89.4% sensitivity and 87.5% specificity. In our study, procalcitonin showed the best predictive value for the short-term outcome of sepsis with a cut-off value of 14.8 ng/mL (AUC 0.923). Study shows that 76.0% of the patients recovered completely, but 24.0% of patients expired during the hospital stay.*

Conclusion: *There was a statistically significant correlation in serum procalcitonin with the outcome of sepsis ($p < 0.001$). So the effectiveness of serum procalcitonin has proven significant in the prediction of mortality in sepsis patients.*

Keywords: *Sepsis, Procalcitonin, multi-organ failure*

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Introduction

Sepsis is a potentially fatal organ failure that results from an unbalanced immune response to an infectious agent. Without immediate diagnosis and treatment, septic shock, organ failure, and death can result. The majority of the time, it is a consequence of an infection, and in middle and low-income nations, it is one of the leading causes of death and disability.

Effective treatment of sepsis requires both rapid diagnosis and administration of antimicrobials. Interleukin 1 is one of the standard markers used to diagnose sepsis along with inflammatory markers like erythrocyte sedimentation rate, C-reactive protein (CRP), and white blood cell count (WBC).

The gold standard for confirming bacteremia is a blood culture, which can isolate and identify the causal agent and then test the antibiotic sensitivity, but the time-consuming nature of bacterial culture highlights the importance of early detection of sepsis.[5] For a quick and precise diagnosis, a biomarker should have a high degree of diagnostic accuracy. Rediscovered biomarker procalcitonin precursor (PCT) meets

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several of these criteria, especially when compared to conventional and extensively used alternative biomarkers in sepsis. A positive bacterial culture test (PCT) can help in the early diagnosis of sepsis and in the monitoring of the antimicrobial treatment plan. Serum PCT levels increase quicker than CRP levels and reach their peak more quickly; if the patient responds well to treatment, PCT levels revert to normal more quickly than CRP levels do, making PCT a more accurate biomarker for sepsis.[6]

In reality, point-of-care testing (PCT) can be a helpful tool for antimicrobial stewardship, and its usage may safely lead to a large reduction in the needless administration of antimicrobial medication.[5] Therefore, the purpose of the current study was to evaluate the predictive usefulness of serum procalcitonin in patients with sepsis at a tertiary care facility.

Materials and Methods

This prospective analytical study included 100 patients with sepsis in an ICU of a tertiary care hospital in Dhaka from January 2019 to December 2020. All Patients above 18 years, either sex admitted to Hospital fulfilling sepsis criteria (SIRS + Documented infection). Patients with malignancy, transplantation, or hematological disorders and on antitumor drug therapy were excluded.

Ethical approval was obtained from the institutional ethical review board before the start of the study (BIRDEM/IRB/2019/182)

Data analysis: The data collected were statistically analyzed using (SPSS)/PC 22 software. Comparisons of the means of continuous variables for both groups were based on an analysis of variance. Receiver operating characteristic (ROC) curves were used to select the optimal cut-offs for procalcitonin in the diagnosis of sepsis and bacteremia with the cut-off value of 0.57 ng/mL (AUC 0.99) and 4.68 ng/mL (AUC 0.94), respectively. Serum procalcitonin level showed the in-hospital stay with the cut-off value of 14.8 ng/mL (AUC 0.92). Univariate logistic regression analyses were performed to examine the association between the outcome and each of the predictors separately. An odds ratio (OR) with 95% confidence intervals was calculated.

Recording of variables: Structured questionnaire with information (age, gender, resident, occupation, monthly income, level of education, etc.) and relevant information about co-occurring physical illnesses with laboratory test findings (basic biochemistry, PCT, CRP, complete blood count, microbiological results, number of days with antibiotics, main final diagnosis, patient condition at hospital discharge and cause of death) (related or unrelated to sepsis).

Procalcitonin assessment: 5 ml of venous blood was drawn, kept at room temperature for 2 h, and centrifuged at 3000 rpm for 10 min, and the supernatant was stored at "70°C until analysis. Serum levels were measured using an enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions. Procalcitonin level on the day of diagnosis of sepsis was assessed.

Procalcitonin cut-offs: Procalcitonin (PCT) is a peptide precursor of calcitonin seen in very low (<0.05ng/ml) or even undetectable amounts in healthy individuals. Over 0.5 ng/ml is pathological in infections.[8]

Regular follow-up was conducted and treatment & medication were titrated according to the clinical circumstances. Patients were divided into (I) survivors and (II) non-survivors.

Results

On the evaluation of the demographic profile, the maximum number of patients (43.0%) were between 51-60 years age group, mean age of the patient was 49.35 ± 11.7 years. (Table 1). Out of 100 cases 65% were male and 35% were female. The male and female ratio was 1.85:1. Maximum (64%) patients came from urban areas and 36% from non-urban.

Table 1. *Age distribution of the patients (n=100)*

Age (years)	Number of patients	Percentage (%)	Serum procalcitonin (Range)	Mean ± SD
≤40	4	4.0	1.8±0.8	49.35 ± 11.7
41-50	24	24.0	4.3±0.5	
51-60	43	43.0	10.7±0.5	
61-70	18	18.0	12.3±0.9	
>70	11	11.0	19.1±1.2	
Total	100	100	9.0±0.6	

The qSOFA score of 1 was found in 35.5% of sepsis patients followed by 2 in 32.5% and 3 in 25.6%. (Figure 1).

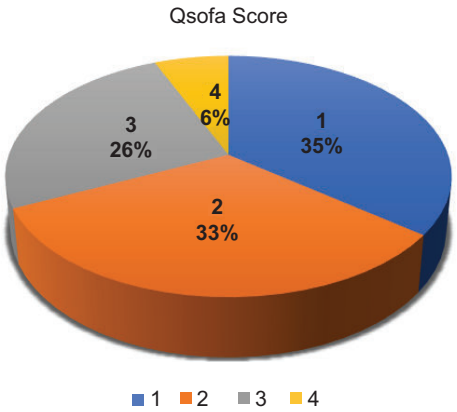

Figure 1. *Distribution of study subject by qSOFA Score (n=100)*

In our study respiratory tract was the main source of sepsis (71%) followed by the genitourinary tract (12%), skin and soft tissue (10%), and abdomen (7%). (Table 2).

Table 2. *The common source of sepsis as per the system involved.*

Source of sepsis	No of Patients	Percentage (%)
Respiratory tract	71	71
Genitourinary tract	12	12
Skin and soft tissue	10	10
Abdomen	7	7

Our Study shows that 76.0% of the patients recovered completely, but 24.0% of patients expired during their hospital stay. Serum procalcitonin levels 0.5-2.0 ng/were detected in 15.0%of patients, followed by 2.1-10.0 ng/mL detected in 29.0% of patients, and >10.0 ng/mL detected in 56 patients. Among the 76 survivor cases, serum procalcitonin correlates with 68 cases as below the cut-off value. In 24 cases of non-survivor, procalcitonin was predicted in 21 cases as raised cut-off value. There was a statistically significant correlation in the serum procalcitonin with the outcome of sepsis ($p < 0.001$). So, the effectiveness of serum procalcitonin has proven significant in the prediction of mortality in sepsis patients.

Patients' condition after proper treatment, symptoms, degree of abnormalities or dependence on the daily physiological activity, and the clinical outcome had evaluated and measured by follow-up and close monitoring. 76.0% of the patients recovered completely, but 24.0% of patients expired during the hospital stay. (Table 3)

Table 3. *Correlation between Serum procalcitonin and outcome of sepsis patients (n=100)*

Serum procalcitonin (ng/mL)	Patient Outcome Survivors *(n=76)*	Patient Outcome Non-Survivors *(n=24)*	p-value
<14.8 (*n=71*)	68	3	<0.001
>14.8 (n=*29*)	8	21	

Table 4: *Baseline clinical and laboratory parameters status of the subjects(n=100)*

Variables	(Mean±SD)	Range
Vital signs		
Temperature (C)	37.63 ± 1.27	36.3 6 38.2
HR (bpm)	95.43 ± 19.34	58 6 132
RR (breath/min)	31.23 ± 7.23	18 6 42
MABP (mmHg)	92.50 ± 28.43	64 6 98
ABGs (Arterial Blood Gases)		
pH	7.29 ± 0.17	7.25 6 7.47
$PaCO_2$ (mmHg)	49.01 ± 8.32	32.0 6 58.0
PO_2 (mmHg)	82.13 ± 22.15	62.0 6 108.0
HCO_3 (mEq/l)	18.86 ± 2.52	12.0 6 28.0
Complete blood count (CBC)		
Hb% (gm/dl)	10.8 ± 1.9	3.3 – 16.6
TC of WBC	24.2 ± 7.5	2.38 – 47.4
Platelet count	184401±100003	7000-599000
Others		
Lactate level	3.7 ± 18.3	12 – 112

Discussion

A total of 100 individuals with sepsis were enrolled according to the selection criteria. In our study the maximum number of patients (43.0%) were between the 51-60 years age group, mean age of the patient was 49.35 ± 11.7 years. Out of 100 cases, 65% were male and 35% were female. The male and female ratio was 1.85:1. However in a study by Jain *et al*[10] the mean age was 50.68 ±18.67 years and 55% were males.

In our study respiratory tract was the main source of sepsis (71%) followed by the genitourinary tract (12%), skin and soft tissue (10%), and abdomen (9%) whereas the study by Mustafiæ *et al* demonstrated the common source of sepsis as urinary tract, abdomen, and digestive system (29.3%), respiratory system (23.2%) skin and soft tissue (15%), and others (2.4%).[9]

In the present study, the mortality due to sepsis was 24% which is consistent with the reported wide range (18% to 56%) of overall mortality due to sepsis studied by Jain *et al* and Grozdanovski *et al*. Also, mortality increased with the severity of sepsis (61%) which was similar to the rates reported in previous studies by Jain *et al* and Grozdanovski *et al*.[10,11]

Based on (ROC) curves, procalcitonin had an area under curve 0.923, with 89.4% sensitivity and 87.5% specificity.

Procalcitonin showed the best predictive value for the short-term outcome of sepsis with the cut-off value of 14.8 ng/mL (AUC 0.923) similar to studies by Meng *et al.* and Clec'h *et al*.[12,13]

The level of procalcitonin declined significantly in survivors over the course of 28 days. A study by Karlsson et al, implicated that the level of serum procalcitonin increases with the severity of sepsis and organ dysfunction which could also be used to identify patients with a higher risk of adverse outcomes.[14] A study by Jain *et al* noted levels of serum procalcitonin were significantly higher in non-survivors compared to that of survivors (6.3-42) vs. 5.38 (3.48-12.8) ng/mL; p<0.01].[10] Procalcitonin levels were also significantly higher in patients with septic shock as compared to that with severe sepsis (34.6 ±36.7 vs. 15.0 ± 29.9 ng/mL; p=0.03) and sepsis (34.6± 36.7 vs. 3.8±1.6 ng/mL; p = 0.008)[10]

PCT's diagnostic capacity is superior to that of other infection and inflammation parameters due to its close correlation with the severity of systemic inflammation, its preferential induction during inflammation of bacterial origin, and its high concentration range, especially during sepsis and systemic inflammation.[15] In this study, serum procalcitonin correlated with sepsis prognosis (p 0.001) with 89.4% sensitivity and 87.5% specificity. Positive and negative predictive values were 95.7% and 72.4%. So, the effectiveness of serum procalcitonin has proven significant in the prediction of mortality in sepsis patients.

PCT is a reliable test to rule out bacteremia in febrile individuals.[16] Different marginal values of procalcitonin predict sepsis and bacteremia. for sensitivity and specificity. The sensitivity and Specificity were 97.5% and 95.8% respectively by Mustafiæ et al. It was also found that significant differences in PCT between SIRS-positive non-infected and SIRS-positive patients with documented sepsis, and between blood culture positive and blood culture negative sepsis. It has resulted in some higher marginal values (cut off: for sepsis 0.57ng/mL; for bacteremia 4.68ng/mL), but predictive significance was noticeably better due to higher marginal value. The rise in PCT concentration in patients with severe sepsis is much greater than in those with SIRS or sepsis alone, as was confirmed by Al-Nawas *et al*.[17] Mustafiæ *et al* reported that PCT concentrations were correlated with the severity of organ dysfunction defined by SOFA and APACHE II scores indicating that this biomarker, combined with a clinical score, could be useful for assessing the severity of infection.

The results of a randomized study by Jansen *et al* showed that monitoring PCT, unlike many other inflammatory markers, especially CRP, correlates better with clinical scoring systems for evaluating disease severity and some organ damages in sepsis (SOFA), especially later in the disease course, making it more effective in recognizing and treating severe sepsis than those parameters.[18] A study by Anand *et al* (2014) found a correlation between PCT values with the level of the SOFA score. PCT concentration was much higher in patients with fatal outcomes (89.3%) indicating that PCT is related to the severity of the disease and organic dysfunction and that it could be useful for the prediction of fatal outcomes in patients with sepsis.[19]

In the study of Zhang *et al* [20] PCT correlated well with SOFA score (r=0.406), and positive predictive value in comparison to fatal outcomes in patients with sepsis (AUC 0.81). Clech et al found a sensitivity of 87.5% and specificity of 45% in the prediction of the fatal outcome on the first day of septic shock at the marginal value of 6 ng/mL.[13] Besides the fact that PTC is a marker of sepsis, it could contribute to decreased survival in cases of patients with sepsis due to toxic proinflammatory effects on leukocytes and cytokine production.

Significant improvement in survival was evident after the early diagnosis and treatment of sepsis when immune neutralization was implemented as in the study by Becker *et al*.[21] Suberviola *et al* reported the prognostic reliability of procalcitonin is better than CRP and leukocytes. Those patients with increasing procalcitonin levels showed higher hospital mortality than those with a decreasing level (58.8% vs 15.4%, p<0.01). No such effect was observed in relation to C-reactive protein or leukocytes.[22]

Conclusion

Despite the use of optimal support and better strategy, the mortality rate in sepsis still remains high. An elevated level of procalcitonin at admission is a better predictor of mortality that helps in the stratification of patients and to identify patients at higher risk of adverse outcomes. This study has certain important observations which might guide clinicians in making early decisions since early diagnosis of sepsis and its associated complications are of utmost importance for greater clinical success. The observations definitely indicate that serum PCT measurement should be used as a part of the comprehensive clinical assessment, which would improve the management and consequently the survival of patients with sepsis.

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