

A STUDY OF SERUM PROCALCITONIN AS A BIOMARKER IN SEPSIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Sepsis is reported to be the most common cause of death in Intensive Care Unit (ICU). It is an increasingly common cause of mortality and morbidity particularly in elderly, immunocompromised and critically ill patients. Approximately, 25-35% of patients with severe sepsis and 40-55% of patients with septic shock die within 30 days.

Aims and Objectives of the study-

To diagnose sepsis in early stages by measuring serum procalcitonin and to correlate with diagnosis of sepsis.

MATERIALS AND METHODS

Fifty patients of sepsis were included in the study and clinical assessment was made. Focus of infection was determined. Microbiological cultures of the focus of infection was asked for all the patients. Patients were classified into sepsis, severe sepsis and septic shock based on ACCP/SCCM guidelines. Serum procalcitonin levels of all the patients at admission were determined.

RESULTS

56% were females and 44% were males. 54% were in the group of sepsis; 34% were in the group of severe sepsis and 12% were in the group of septic shock. The Mortality rates were 3.7%, 23.5% and 66.7% respectively in the three groups of sepsis, severe sepsis and septic shock respectively 68% of patients had positive serum procalcitonin value and 32% had negative serum procalcitonin value. 48%, 88% and 100% of patients in the groups of sepsis, severe sepsis and septic shock respectively had positive procalcitonin level.

CONCLUSION

Serum procalcitonin was proven to be very good, cost effective biomarker for the early identification of sepsis better than cultures. It was in addition proven to be a simple prognostic marker when quantitatively estimated. This would warrant early initiation of effective treatment strategies. Thus, estimation of serum procalcitonin as a biomarker for identification and prognostication of sepsis should be practised.

KEYWORDS

Sepsis, Severe Sepsis, Septic Shock, Serum Procalcitonin, Biomarker.

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BACKGROUND

Septic response is a leading contributory factor for morbidity and mortality especially in intensive care settings. Recent data suggests that the incidence of sepsis worldwide is on the rise and at the same time the mortality rate remained high despite the ongoing advances in the management of sepsis. Partly this is attributable to the aging of the population, increasing longevity of patients with chronic diseases, indwelling catheters, misuse of antimicrobials and mechanical Devices^{1,2}

Accurate identification of sepsis aetiology in patients admitted to the emergency department is often unattainable, largely because their infections can have minimal or even no symptoms or signs. However, early diagnosis of bacterial infection is of primary importance, because early institution of an appropriate antimicrobial regimen after accurate diagnosis in infected patients is associated with a better outcome. Furthermore, not all patients who appear septic demonstrate an infection, and the widespread administration of antibiotics to all patients suspected of having an infection has problems, including selection for antibiotic resistance, drug toxicity, and high medical costs.³

An accurate, readily available test for bacteraemia would greatly facilitate medical decision making for in the ICU'S. The established biological markers of inflammation (leukocytes, C-reactive protein) may often be influenced by parameters other than infection and may only be slowly released during progression of an infection

Positive bacteriological results may be caused by contamination and negative results do not exclude sepsis.

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Since these common clinical and lab measurements lack sensitivity and specificity, other tests are needed to give an early marker of the infectious cause of a generalized inflammatory response to allow early diagnosis and for the use of specific treatment.⁴

One such marker of sepsis is serum Procalcitonin (PCT), PCT was found to be a promising biomarker of sepsis and provided valuable and early information before culture results were available. Hence this study has been undertaken to ascertain usefulness of procalcitonin in sepsis.⁵

MATERIALS AND METHODS

The study shall be Prospective Observational Study, where continuous data will be enumerated who fulfils the inclusion criteria.

Inclusion Criteria- All patients aged above 18 years with sepsis as diagnosed by-

1. Clinical or laboratory features suggestive of sepsis syndrome based on American college of chest physician guidelines.
2. Clinical presentation of sepsis with Positive blood or urine culture
3. Clinical presentation of Pneumonia with supporting radiological features or positive sputum culture.
4. Patients giving written informed consent.

RESULTS

PCT	Sepsis	Severe Sepsis	Septic Shock	Total	P – value
Negative (<0.5 ng/ml)	14 (87.5)	2 (12.5)	0 (0)	16	0.004
Positive (≥ 0.5 ng/ml)	13 (38.2)	15 (44.1)	6 (17.6)	34	
	27 (54.0)	17 (34.0)	6 (12.0)	50	

Table 1. Diagnostic Value of Serum PCT in the Study Population

*significant association between serum PCT for the diagnosis of the study population.

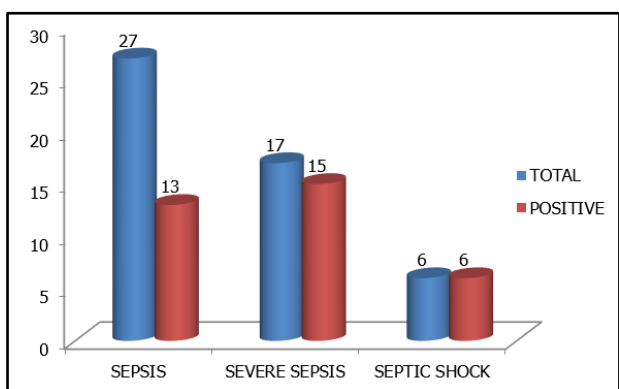


Figure 1. Diagnostic Value of Serum PCT

	Sepsis Median (IQR)	Severe Sepsis Median (IQR)	Septic Shock Median (IQR)	P-Value
PCT (Median)	0.5 (0.3, 1.8)	7.2 (1.7, 13.9)	10.6 (4.7, 20.8)	< 0.001

Table 2. Correlation Between PCT Levels and Sepsis

Exclusion Criteria

1. Patients with history of malignancy.
2. Trauma.
3. Recent surgery
4. Burns
5. Cardiogenic shock
6. Acute pancreatitis.

Routine CBC, routine urine analysis, renal function tests, random blood sugar, liver function tests, serum electrolytes, C-reactive protein, chest X-ray, ECG, sputum Gram's stain/AFB, cultures-blood/sputum/urine etc will be done where ever indicated and serum Procalcitonin will be done for all patients.

Statistical Analysis and Methods- Sample size: Was estimated using nMaster software version 1. N=50. SPSS software will be used for statistical analysis. Statistical Analysis- Descriptive analysis using mean, median and SD for continuous variables such as Age, duration of stay etc. Pearson correlation co-efficient to assess the association between Procalcitonin levels and categories of sepsis, severity of the infection and outcome will be studied. Parametric and non-parametric test will be applies where ever required.

*Significant association between serum PCT levels and study group. P Value <0.05.

With increase in severity of sepsis, levels of procalcitonin also increased.

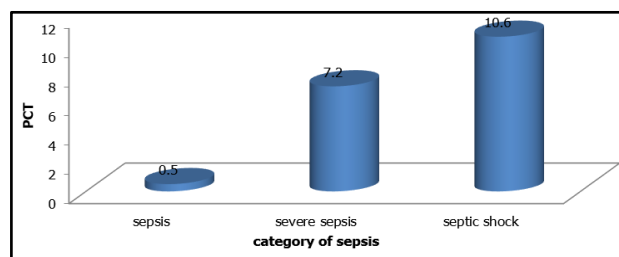


Figure 2. Correlation between PCT Levels and Sepsis

Sepsis Type	Death	Survived	Total	P - value
Sepsis	1 (3.7)	26 (96.3)	27	0.001
Severe Sepsis	4 (23.5)	13 (76.5)	17	
Septic shock	4 (66.7)	2 (33.3)	6	
	9 (18.0)	41 (72.0)	50	

Table 3. Outcome in the Study Population

Chi-square = 13.72, p = 0.001.

*significant association between outcome and study population. P Value = <0.05.

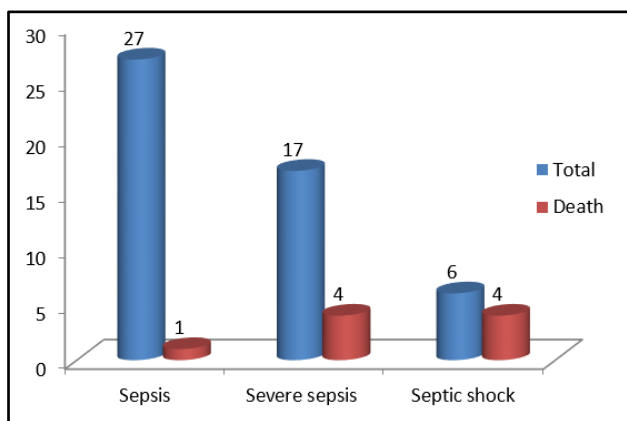


Figure 3. Mortality in Study Population

	Death Median (IQR)	Survivors Median (IQR)	P - value
PCT	8.5 (4.6, 19.2)	1.1(0.3, 6.0)	0.006

Table 4. Correlation of PCT Values with Outcome

*significant association between serum PCT and outcome. P Value = <0.05.

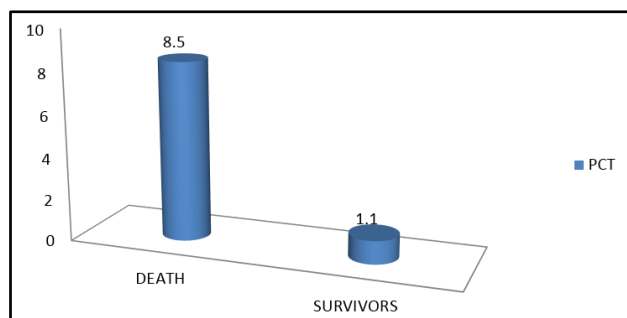


Figure 4. Correlation of PCT Values with Outcome

DISCUSSION

Outcome in the Study Population- In our study, 41 patients survived at the end of the study period and 9 patients did not survive with the mortality rate of 18%. Of the 27 patients in the sepsis group, 1 patient did not survive with the mortality rate of 3.7%. Of the 17 patients in the severe sepsis group, 4 did not survive with the mortality rate being 23.5%. Of the 6 patients in the septic shock group, 4 did not survive with the mortality rate of 66.7%. Thus, with the increasing severity of sepsis, mortality rate increased. There was significant association between severity of outcome and study population with the p value being less than 0.05.

In the study by Sudhir U et al⁶ mortality was seen in 23 patients (23%). A study by Martin et al⁷ showed that mortality in patients with sepsis from various centers varied between 16.8 and 31.8%. Sands et al⁸ who studied sepsis in eight academic medical centers reported a mortality rate of 34%.

Diagnostic Value of Serum PCT in the Study Population-

In our study, 34 patients had a positive procalcitonin level of more than 0.5 ng/ml whereas 16 patients had a negative procalcitonin level of less than 0.5 ng/ml. With the p value being 0.004, this correlated statistically with the presence of sepsis. Further it correlated the best in the groups with more severe forms of sepsis. All 6 patients (100%) in the group of septic shock had a positive procalcitonin level, whereas 15 of 17 patients (88%) in the group of severe sepsis and only 13 of 27 patients in the group of sepsis (48%) had a positive procalcitonin level.

Thus, inferring that more the severity of sepsis, more is the positivity rates of serum procalcitonin level.

PCT Levels Co-Relation in the Study Group-

In our study, median value of serum procalcitonin in the group of patients with sepsis was 0.5 ng/ml, in the group of severe sepsis was 7.2 ng/ml and in the group of patients with septic shock it was 10.6 ng/ml. Thus, inferring that higher median levels of serum procalcitonin were noticed in the groups with more severe forms of sepsis. Thus, quantitative correlation of higher values of serum procalcitonin with worse prognosis was established.

In the study by Sudhir U et al, 26.9% of patients in the group of sepsis, 40% in the group of severe sepsis and 47.8% of patients in the group of septic shock had high serum procalcitonin levels of more than 10 ng/ml. This is similar to the results obtained in our study. This was comparable to various studies done previously Meisner et al,⁹ Stucker et al¹⁰ in which there was significant statistical association between serum procalcitonin levels and categories of sepsis with p value = 0.001.

Focus OS Sepsis-

In our study, the most common focus of sepsis was lung (32%) followed by urinary tract (22%). Respiratory sepsis included lobar pneumonia and bronchopneumonia, infective exacerbation of COPD and some of the patients had ARDS. Urinary tract infections included mostly complicated infections like pyelonephritis. This is probably due to the higher incidence of our Diabetes mellitus in our study.

CONCLUSION

Sepsis is a major cause of admissions to ICU and emergency wards in any tertiary care centre with a significant mortality and morbidity. It also has a significant financial burden with arrays of serial investigations and various biomarkers. Cultures for the infecting organism take a lead among the set of investigations, which though are specific, sometimes less sensitive due to various reasons. Thus, there is requirement of a cost effective and single biomarker for early identification and aggressive treatment of patients with sepsis, who are potentially treatable.

Serum procalcitonin done once at the time of admission was proven to be very good, cost effective biomarker for the early identification of sepsis better than cultures. It was in addition proven to be a simple prognostic marker when quantitatively estimated. This would warrant early initiation

of effective treatment strategies. Thus, estimation of serum procalcitonin for identification and prognostication of sepsis should be practised since it is definitely accurate and not a compromise with the other costlier biomarkers.

SUMMARY

- Most of the patients in the study were in the age group of 15 to 30 years.
- 28 patients (56%) were females and 22 patients (44%) were males.
- 27 patients (54%) were in the group of sepsis; 17 patients (34%) were in the group of severe sepsis and 6 patients (12%) were in the group of septic shock.
- Fever was the most common symptom the study followed by breathlessness, cough and altered mental status.
- In the study, 41 patients survived at the end of the study period and 9 patients did not survive with the mortality rate of 18%.
- Mortality rates were 3.7%, 23.5% and 66.7% respectively in the three groups of sepsis, severe sepsis and septic shock respectively
- In the study, 68% of patients had positive serum procalcitonin value and 32% had negative serum procalcitonin value.
- In the study, 48% of patients in the group of sepsis, 88% in the group of severe sepsis and 100% of patients in the group of septic shock with positive procalcitonin level.
- It was inferred that more the severity, more is the positivity rate of serum procalcitonin levels.
- In the study, 58% of culture positive sepsis had positive serum procalcitonin level 71% who had culture negative sepsis had positive serum procalcitonin level, proving serum procalcitonin levels to be more sensitive in diagnosis of sepsis.
- Median length of stay in the group of patients with sepsis was 8 days, in the group of patients with severe sepsis was 7 days and that in the group of patients with septic shock was 5.5 days.
- More severe forms of sepsis had poorer glycemic control.

- More severe forms of sepsis having renal dysfunction inferred greater mortality in the study.
- The most common focus of sepsis was lung (32%) followed by urinary tract (22%).

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