Original Article

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Evaluation of Serum Procalcitonin Levels and Sequential Organ Failure Assessment Score in Assessing the Severity and Outcome of Sepsis

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Abstract

Introduction: Sepsis is a systemic condition with high mortality and morbidity in emergency medicine. The septic response is a complex chain of events involving inflammatory and anti-inflammatory processes. The diagnosis and assessing the severity of sepsis is complicated by non-specific nature of signs and symptoms.

Purpose: Early diagnosis and initiation of goal-directed therapies can prevent complications of sepsis. Furthermore, assessing the severity and outcome of sepsis can reduce mortality. The present study of evaluating procalcitonin (PCT) levels and sequential organ failure assessment (SOFA) score in various categories of sepsis was conducted.

Materials and Methods: The present cross-sectional study included 100 patients based on the defined inclusion and exclusion criteria's. The study subjects were divided into three groups: Sepsis, severe sepsis, and septic shock based on the American College of Chest Physicians/Society of Critical Care Medicine guidelines. Serum PCT levels were estimated, and SOFA score was calculated for all the patients. The statistical analyzes were done using one-way ANOVA.

Results: Of 100 patients studied, there were 30 patients in sepsis group, 40 in severe sepsis group, and remaining 30 in septic shock group. The serum PCT levels were positive in 84% of the total study population. Among the groups, PCT levels were 100% positive in both severe sepsis group and septic shock group. The SOFA score was significantly increased in severe sepsis and septic shock. The mortality was 60% in severe sepsis and 83.3% in septic shock group.

Conclusion: We conclude that PCT with SOFA score can be considered as indicators in assessing the severity and outcome of sepsis.

Key words: Inflammatory, Morbidity, Mortality, Procalcitonin, Sepsis, Shock

INTRODUCTION

Sepsis is one of the leading causes of death in emergency medicine despite the use of new antibiotics and advanced resuscitation therapies. Recent data have suggested that 18 million of new sepsis occurs each year with a mortality rate of 30%.[1] Hence, early diagnosis in assessing the severity of sepsis increases the possibility of initiating timely and specific treatment.[2]

The clinical diagnosis of sepsis and also assessing its severity is complicated due to non-specific and highly variable signs and symptoms. There are various biomarkers for assessing severity of sepsis, prognostication, guiding antibiotic therapy, evaluating response to therapy, and predicting sepsis complication like organ dysfunction.[3]

Procalcitonin [PCT] has been considered as a better biomarker of systemic inflammatory response to infection.[4] It is elevated in various severe infections and inflammations. However, the exact role of PCT in various stages of sepsis remains undefined.[5] Moreover, the sequential organ failure

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assessment (SOFA) score can assess the severity of sepsis and multi-organ failure at the beginning of sepsis and after 48 h.[6] Hence, the present study was conducted including both serum PCT levels and SOFA score in assessing the severity of sepsis.

MATERIALS AND METHODS

The present cross-sectional observational study was carried out in a tertiary health care center at Telangana, India. A total of 100 patients were included in the study.

Inclusion Criteria

- The patients with age above 18 years
- Clinical diagnosis of sepsis.

Exclusion Criteria

- Patients with acute inflammatory lesions, severe burns, heat stroke, and mesenteric embolism
- Patients on treatment with antibiotics and tumor necrosis factor-α inhibitors
- History of recent surgeries, cardiac surgery, recent trauma
- Patients with malignant neoplasm.

Informed consent and ethical clearance were taken from the patient attendants. A detailed clinical history, general physical examination, and systemic examination of the patients were carried out.

The study subjects were divided into three groups: (1) Sepsis, (2) severe sepsis, and (3) septic shock based on the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus guidelines.[5] The presence of organ dysfunctions (cardiovascular, neurological, respiratory, renal, hepatic, and coagulation) was assessed using a SOFA score (Table 1).[7]

Peripheral blood sample were collected from all the patients in sterile vacutainer and transported at room temperature to the central laboratory within 24 h of collection (as per the laboratory directions). Serum PCT levels were estimated, and SOFA score was calculated for all the patients.

Serum PCT was measured by semi-quantitative rapid assay (BRAHMS PCT-Q). It is an immunochromatographic test using monoclonal mouse anti-calcitonin antibody conjugated with colloidal gold (tracer) and a polyclonal sheep anti-calcitonin antibody (solid phase).[8]

Statistical Analysis

The statistical analysis was done using mean, standard deviation, and ANOVA.

RESULTS

Of the 100 patients studied, there were 30 patients in sepsis group, 40 in severe sepsis group, and remaining 30 belonged to septic shock group. The most common age group involved was 41-50 years (35.3%), 51-60 years (30%), and 31-40 years (34.6%) in sepsis, severe sepsis, and in septic shock groups, respectively. Males were more frequently affected than females with male:female ratio being 1.7:1%.

In the present study, serum PCT was positive in 84% and negative in 16% of the total study population (mean value 20.38 ± 35.49 ng/ml). Among the groups, PCT was positive in 46.7% of sepsis group, 100% in both the severe sepsis group and septic shock group ($P < 0.001$) (Table 2).

The SOFA score in the present study was analyzed between severe sepsis group and septic shock group based on SOFA score. The mean value of SOFA score among the total group was 2.03 ± 2.97. In severe sepsis group, SOFA score was 1.23 ± 1.29 while in septic shock group, the SOFA score was 5.92 ± 3.96. The mean levels of SOFA score were statistically significant for the diagnosis of severe sepsis and septic shock ($P < 0.001$*) (Table 3).

In our study among the three groups, the overall mortality was 50%. It was 3.3% in sepsis, 60% in severe sepsis, and 83.3% in septic shock group (Table 4). Mean serum

Table 1: SOFA score

SOFA score	0	1	2	3	4
Respiratory: PaO_2/FiO_2	> 400	≤400 221-300	≤300 142-220	≤200 67-141	≤100 <67
Hematology: Platelet count [10^3/mcL]	>150	≤150	≤100	≤50	≤20
Hepatic: Bilirubin (mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular: Hypotension	No Hypotension	MAP<70 mmHg	Dopamine ≤5[a] or dobutamine (any dose)	Dopamine >5[a] or epinephrine ≤0.1[a] or norepinephrine ≤0.1[a]	Dopamine >15[a] or epinephrine >0.1[a] or norepinephrine >0.1[a]
Renal: Creatinine (mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-5.9; urine output ≤500 mL/day	>5; urine output <200 mL/day
Neurologic: Glasgow coma scale score	15	13-14	10-12	6-9	<6

SOFA: Sequential organ failure assessment, PaO_2: Arterial oxygen tension, FiO_2: Fractional inspired oxygen, MAP: Mean arterial pressure, [a]Adrenergic agents administered for at least 1h (doses given are in μg/kg/min)

Table 2: Association of PCT with Diagnosis in patients studied

Procalcitonin	Sepsis	Severe sepsis	Septic shock	Total
≤1	16 (53.3%)	0 (0%)	0 (0%)	16 (16%)
1-10	14 (46.7%)	19 (47.5%)	0 (0%)	33 (33%)
10.1-50	0 (0%)	21 (52.5%)	23 (76.7%)	44 (44%)
50.1-100	0 (0%)	0 (0%)	3 (10%)	3 (3%)
>100	0 (0%)	0 (0%)	4 (13.3%)	4 (4%)
Total	30	40	30	100
Mean±SD	1.50±1.95	13.49±9.69	55.66±54.61	20.38±35.49

Variation between groups: *F* statistics: 26.57, df: 2, *P* value: 0.001*, SD: Standard deviation, PCT: Procalcitonin

Table 3: Association of SOFA score with diagnosis in patients studied

SOFA score	Sepsis	Severe sepsis	Septic shock	Total
0	30 (100%)	19 (47.5%)	0 (0%)	49 (49%)
1-5	0 (0%)	21 (52.5%)	15 (50%)	36 (36%)
6-10	0 (0%)	0 (0%)	12 (40%)	12 (12%)
>10	0 (0%)	0 (0%)	3 (10%)	3 (3%)
Total	30	40	30	100
Mean±SD	0	1.23±1.29	5.92±3.96	2.03±2.97

Variation between groups: *F* statistics: 81.75, df: 2, *P* value: 0.001*, SOFA: Sequential organ failure assessment, SD: Standard deviation

Table 4: Association of outcome with diagnosis in patients studied

Outcome	Sepsis	Severe sepsis	Septic shock	Total
Death	1 (3.3%)	24 (60%)	25 (83.3%)	50 (50%)
Recovery	29 (96.7%)	16 (40%)	5 (16.7%)	50 (50%)
Total	30	40	30	100

PCT levels in patients who succumbed to death were 43.78 ng/ml and patients who survived had 6.22 ng/ml.

DISCUSSION

Sepsis is a complex chain of events involving cell-mediated and humoral immunity, inflammatory and anti-inflammatory reactions, and also circulatory disturbances.[9] It has become a common problem in intensive care units of healthcare and also responsible for mortality and morbidity of the elderly population. Martin *et al.*[10] reported that sepsis more frequently occurred in men, which was similar with our study. The probable reason could be that men have more exposure to various environmental conditions and stress factors.

The diagnosis of sepsis remains a challenge, as both clinical and standard laboratory tests are not very much helpful. Based on ACCP/SCCM criteria, the most common observed group was severe sepsis group with 40% followed by sepsis group and septic shock group (30% each). Furthermore, the microbiological assessment appears unreliable because of many negative culture results. However, a multitude of potential biomarkers has been used in clinical studies.[11] Indeed, a few biomarkers have been assessed for their ability to distinguish septic patients from non-septic patients. Among the various biomarkers, PCT has been extensively used for diagnosis of sepsis but not for the severity of sepsis.[4] Hence, the present study was conducted to know the role of serum PCT in assessing the severity of sepsis. Previous documented reports suggest that raised PCT levels can be observed in trauma[12] and major surgery[13] and cardiac surgery.[14] Therefore, we excluded these patients in our study.

Harbarth *et al.*[15] and Brunkhorst *et al.*[16] reported high levels of PCT among severe sepsis and septic shock group. In the present study, we observed increased serum PCT levels in 84% of the total study population. There was a significant statistical association for PCT between the severe sepsis and septic shock groups ($P < 0.001$).

Although, a small amount of PCT is found in the peripheral circulation of healthy subjects, they are increased in infectious, non-infectious, and inflammatory conditions.[17] These various conditions release pro-inflammatory mediators (e.g., interleukin-1β, interleukin-6, and tumor necrosis factor-α) either by direct pathway (induced by lipopolysaccharides or toxins released by microbes) or indirect pathway (cell-mediated response). The pro-inflammatory mediators further may stimulate monocytes and can induce calcitonin mRNA expression in the non-neuroendocrine cells to release unprocessed PCT. Since, there are no specific storage secretory granules for PCT; the unprocessed PCT is released into the plasma resulting in increased PCT levels.[18] Thus, PCT appears to possibly aid in assessing the severity of sepsis, and also can support in predicting the prognosis of sepsis.

In the present study, SOFA score was increased among severe sepsis and septic shock groups ($P < 0.001$). Similar results were also observed by studies conducted by Bale *et al.*[7] and Moreno *et al.*[19] Among the three groups, mortality was high in septic shock group (83.3%) followed by severe sepsis group (60%). Thus, increased SOFA scores reflect the poor functioning of the organ systems during the course of severe sepsis and septic shock groups, mostly in non-surviving patients. Therefore, SOFA score can be a better predictor of mortality and also assess the severity of sepsis.

CONCLUSION

Serum PCT levels and SOFA score were significantly elevated in patients with severe sepsis and septic shock indicating their utility in predicting the severity of sepsis. Moreover, early identification of severity can prevent the fatal outcome of

sepsis. Therefore, Serum PCT levels with SOFA score can be considered as helpful indicators in assessing the severity of sepsis and outcome of sepsis complications.

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