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STUDY OF C-REACTIVE PROTEIN, TOTAL LEUKOCYTE COUNT AND PROCALCITONIN IN PATIENTS WITH SEPSIS ADMITTED IN MICU

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ABSTRACT

Introduction: One of the most common cause for morbidity and mortality in patients hospitalized to the intensive care unit is bacterial sepsis. In critically ill patients, sepsis can be difficult to distinguish in the early stages from non-infectious illnesses; patients with and without sepsis also have very different outcomes from diagnosis to treatment.

Objectives of the study: The study is intended to study the levels of c-reactive protein, leukocyte count and pro-calcitonin levels in patients with sepsis admitted in Medical ICU of our tertiary care hospital.

Methodology: The present study prospectively included all consecutive patients presenting with systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis or septic shock on admission to the MICU of our tertiary care hospital during the study period of November 2022 to October 2023.

Results and Conclusion:

In the present study, a total of 240 patients were included based on inclusion and exclusion criteria. Out of which 98 (40.8%) had SIRS, 74 (30.83%) had Sepsis, 48 (20%) had severe sepsis and 20 (8.33%) had septic shock. The mean age of the patients included in the study was 32.18 ± 8.24 years, out of 240 patients 164 (68.33%) were males and 76 (31.66%) were females. The mean levels of pro-calcitonin were 9.12 ± 12.64 ng/mL, c-reactive protein were 32.46 ± 18.36 mg/L and Total leukocyte count was 14000 $x10^6$/L. 142 patients had positive blood culture reports and 98 were negative. The most common isolates were E-coli, followed by klebsiella, pseudomonas and Acinetobacter. The diagnostic value of each marker was evaluated and it is found that sensitivity for PCT, CRP and TLC were 78.42%, 86.24% and 84.62% respectively. The specificity were 74.24%, 32.64% and 31.64% respectively. The NPV(Negative Predictive value) and PPV(Positive Predictive value) were 92.24%, 78.24%, 79.98%, 48.86%, 38.64% and 39.88% respectively for PCT, CRP and LC respectively. In the present study we found that the PCT has superior diagnostic value in sepsis as compared to other biomarkers, hence this biomarker can be employed as a routine diagnostic and prognostic biomarker in sepsis patients. However, further large scale studies are recommended to evaluate the diagnostic as well as prognostic utility of PCT in ICU setting of tertiary care hospitals.

Key-words: sepsis, c-reactive protein, leukocyte counts, pro-calcitonin and systemic inflammatory response syndrome.

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INTRODUCTION

One of the most common cause for morbidity and mortality in patients hospitalized to the intensive care unit is bacterial sepsis. In critically ill patients, sepsis can be difficult to distinguish in the early stages from non-infectious illnesses; patients with and without sepsis also have very different outcomes from diagnosis to treatment.[1] Biomarkers can reveal if sepsis is present or not, as well as its degree. Additionally, they influence the prognosis, direct the use of antibiotics, assess the effectiveness of treatment, forecast problems, and identify the onset of organ failure.[2] Sepsis is characterized by a number of indicators, including ferritin, lactate, interleukin-6, interleukin-8, serum procalcitonin (PCT), and C-reactive protein (CRP). Severe sepsis mortality ranges from 28% to 50% or more, despite the massive expenditure in critical care resources. Severe sepsis cases are also anticipated to increase in the future for a number of reasons, such as: more sensitivity and knowledge of the diagnosis; an increase in immunocompromised patients; a larger range of invasive procedures; an increase in resistant germs; and an aging population.[3] Currently in widespread usage are definitions for terminology such as "SIRS," "sepsis," "severe sepsis," and "septic shock," which were proposed by the ACCP/SCCM Consensus Conference in 1992. A range of intricate discoveries arising from the systemic induction of the innate immune response are together referred to as the "systemic inflammatory response syndrome" (SIRS). Two or more of the following are among the clinical parameters: hypothermia (below 36°C), or Fever (>38°C) or hyp), increased heart rate (>90 beats/min), tachypnea (>20 breaths/min) or hyperventilation ($PaCO_2$ < 32 mmHg), and altered Total white blood cell count (>12,000 cells/mm3 or <4000 cells/mm3) or presence of >10% immature neutrophils. Sepsis is defined as SIRS resulting from infection, whether of bacterial, viral, fungal, or parasitic origin. Severe sepsis is associated with at least one acute organ dysfunction, hypoperfusion, or hypotension. [4,5]

Traditional markers of systemic inflammation, such as CRP, erythrocyte sedimentation rate (ESR) and Total white blood cell count (WBC), also have proven to be of limited utility in such patients due to their poor sensitivity and specificity for bacterial infection. Moreover, microbiological cultures, the conventional gold standard diagnostic method for sepsis, are often time consuming, do not reflect the host response of systemic inflammation or the onset of organ dysfunction, and sometimes misleading with false positive or false negative reports. These shortcomings in both culture and available blood tests have driven researchers to find other more sensitive and specific markers. In recent years, PCT has been the focus of much attention as a specific and early marker for systemic inflammation, infection and sepsis, both in children and adults. [6,7]

Procalcitonin is the prohormone of calcitonin, secreted by different types of cells from numerous organs in response to proinflammatory stimulation, particularly bacterial stimulation; whereas calcitonin is only produced in the C cells of the thyroid gland as a result of hormonal stimulus. [8] Depending on the clinical background, a PCT concentration above 0.1 ng/mL indicate clinically relevant bacterial infection, requiring antibiotic treatment. [9] At a PCT concentration > 0.5 ng/mL, a patient should be considered at risk of developing severe sepsis or septic shock. [10,11] The study is intended to study the levels of c-reactive protein,

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leukocyte counts and pro-calcitonin levels in patients with sepsis admitted in Medical ICU of our tertiary care hospital.

MATERIALS AND METHODS

Study design: Hospital based prospective observational study.

Duration: 1 year.

Inclusion criteria: The present study prospectively included all consecutive patients presenting with systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis or septic shock on admission to the MICU of our tertiary care hospital, during the study period of November 2022 to October 2023.

Sepsis definition: Two or more of the following are among the clinical parameters: hypothermia (below 36°C), or Fever (>38°C) or increased heart rate (>90 beats/min), tachypnea (>20 breaths/min) or hyperventilation ($PaCO_2 < 32$ mmHg), and altered white blood cell count (>12,000 cells/mm3 or <4000 cells/mm3) or presence of >10% immature neutrophils.

Septic shock was defined as persistent hypotension, despite adequate volume resuscitation, requiring vasopressors to maintain a mean arterial pressure (MAP) $\geq$ 65 mm Hg and a lactate $\geq$ 2 mmol/l.

Exclusion criteria: Neurosurgical, traumatized, and elective surgical patients without complications were excluded.

Methodology: At the time of admission to the MICU the blood sample was collected and sent for Complete Blood hemogram analysed using five part fully automated haematology analyser, C-reactive protein by Nephelometric assay and pro-calcitonin by chemiluminescence immuno assay.

RESULTS

Table 1: Shows distribution of patients	
Total number of patients	240
SIRS	98 (40.8%)
Sepsis	74 (30.83%)
Severe sepsis	48 (20%)
Septic shock	20 (8.33%)

Table 2: Shows demographic profile and baseline parameters in patients with Sepsis	
Total number of patients	240
Males	164 (68.33%)
Females	76 (31.66%)
Age	32.18 ± 8.24 years
Pro-Calcitonin levels	9.12 ± 12.64 ng/mL
C-reactive protein	32.46 ± 18.36 mg/L
Total Leukocyte count	14000 $x10^6$/L

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Table 3: Shows mean values of PCT and CRP depending on culture sensitivity results		
	PCT	**CRP**
Culture positive (142/59.1%)	10.42 ± 11.68 ng/mL	34.46 ± 16.62 mg/L
Culture negative (98/40.88%)	7.86 ± 10.43 ng/mL	29.86 ± 14.53 mg/L
E-coli	60	42.25%
Klebsiella	42	29.57%
Pseudomonas	28	19.71%
Acinetobacter	10	7.04%

Table 4: Shows diagnostic validity			
	PCT	**CRP**	**Leukocyte counts**
Sensitivity	78.42%	86.24%	84.62%
Specificity	74.24%	32.64%	31.64%
NPV	92.24%	78.24%	79.98%
PPV	48.86%	38.64%	39.88%

DISCUSSION

In the present study, a total of 240 patients were included based on inclusion and exclusion criteria. Out of which 98 (40.8%) had SIRS, 74 (30.83%) had Sepsis, 48 (20%) had severe sepsis and 20 (8.33%) had septic shock. The mean age of the patients included in the study was 32.18 ± 8.24 years, out of 240 patients 164 (68.33%) were males and 76 (31.66%) were females. The mean levels of pro-calcitonin were 9.12 ± 12.64 ng/mL, c-reactive protein were 32.46 ± 18.36 mg/L and Total leukocyte count was 14000 $x10^6$/L. 142 patients had positive blood culture reports and 98 were negative. The most common isolates were E-coli, followed by klebsiella, pseudomonas and Acinetobacter. The diagnostic value of each marker was evaluated and it is found that sensitivity for PCT, CRP and LC were 78.42%, 86.24% and 84.62% respectively. The specificity were 74.24%, 32.64% and 31.64% respectively. The NPV and PPV were 92.24%, 78.24%, 79.98%, 48.86%, 38.64% and 39.88% respectively for PCT, CRP and LC respectively.

In the present study, plasma levels of PCT and CRP in patients with and without infection at different levels of SIRS were assessed. Patients with moderate to severe sepsis had higher PCT concentrations than patients with no/local infections ($P < 0.01$). These finding are similar to the studies reported by López *et al*.[11], Ruiz-Alvarez *et al*. [12] and Endo *et al*. [13]. Both serum PCT and CRP showed significant raise of the mean values along with increased severity of the clinical presentations in the study subjects. Significantly higher mean PCT and CRP values were observed in sepsis, severe sepsis and septic shock cases compared to SIRS and no SIRS when compared at the various severities of systemic inflammation and sepsis. However, a number of studies having not been able to demonstrate significant relations of PCT or CRP with severity, raised controversies regarding their utility as prognostic markers. [14]. International studies conducted in the past have reported the diagnostic performance for PCT with a sensitivity of 78% and a specificity of 94% comparing these values with CRP [15-18]. These studies have a more precise methodology towards the desired objectives and the sample number is much greater, for which the statistical significance was much better. In this study

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PCT showed highest level of accuracy (75.34%) with greater specificity (72.2%), positive and negative predictive values, positive likelihood ratio as well as the smaller negative likelihood ratio. However, sensitivity of CRP in the diagnosis of sepsis was found to be higher (85.45%) than PCT (76.36%). By convention, marked changes in prior disease probability can be assumed in PLR exceeding 10.0 and NLR below 0.1 [19] Procalcitonin had a higher PLR and lower NLR than did CRP and complement proteins. These results are in agreement with those of Clec'h *et al*. [18] and others.[15-17].

CONCLUSION

In the present study we found that the PCT has superior diagnostic value in sepsis as compared to other biomarkers. Hence this biomarker can be employed as a routine diagnostic and prognostic biomarker in sepsis patients. However, further large scale studies are recommended to evaluate the diagnostic as well as prognostic utility of PCT in ICU setting of tertiary care hospitals.

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Conflicts of interest

There are no conflicts of interest

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