COMPARING THE DIAGNOSTIC ACCURACY OF PRESEPSIN AND PROCALCITONIN FOR SEPSIS IN CRITICALLY ILL PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

THESIS

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DECLARATION

I hereby declare that the thesis titled **"COMPARING THE DIAGNOSTIC ACCURACY OF PRESEPSIN AND PROCALCITONIN FOR SEPSIS IN CRITICALLY ILL PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY"** embodies the original work carried out by me at All India Institute of Medical Sciences, Jodhpur

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CERTIFICATE

This is to certify that the thesis titled **"COMPARING THE DIAGNOSTIC ACCURACY OF PRESEPSIN AND PROCALCITONIN FOR SEPSIS IN CRITICALLY ILL PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY"** is the bonafide work of **DR. SHIPRA ROY** carried out under our guidance and supervision, at Department of Anaesthesiology and Critical Care, All India Institute of Medical Sciences, Jodhpur.

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“When eating fruit, remember the one who planted the tree”

Vietnamese Proverb

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Dr. Shipra Roy

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LIST OF ABBREVIATIONS

1. SIRS: Systemic Inflammatory Response Syndrome
2. ICU: Intensive Care Unit
3. MODS: Multi Organ Dysfunction Syndrome
4. CRP: C-Reactive Protein
5. IL: Interleukin
6. TNF: Tumor Necrosis Factor
7. CD: Cluster of differentiation
8. SOFA: Sequential Organ Failure Assessment
9. qSOFA: quick Sequential Organ Failure Assessment
10. PCT: Procalcitonin
11. ELISA: Enzyme Linked Immunosorbent Assay
12. APACHE: Acute Physiology and Chronic Health Evaluation
13. ED: Emergency Department
14. CI: Confidence Interval
15. CR: Clearance Ratio
16. QUADAS: Quality Assessment for Studies of Diagnostic Accuracy
17. AUC: Area under the curve
18. ACCP/SCCM: American College of Chest Physicians/Society of Critical Care Medicine
19. WBC: White Blood Cell
20. ROC: Receiver Operating Characteristic curve
21. NPV: Negative Predictive value
22. PPV: Positive Predictive Value
23. OR: Odds Ratio
24. GCS: Glasgow Coma Scale
25. AICU: Adult Intensive Care Unit
26. IEC: Institutional Ethics Committee
27. rpm: revolution per minute
28. MAP: Mean Arterial Pressure
29. STROBE: Strengthening the Reporting of Observational studies in Epidemiology
30. D1: Day 1
31. D7: Day 7

32. SPSS:Statistical Package for Social Sciences
33. AUROC: Area under ROC curve
34. AKI: Acute Kidney Injury
35. HR: Heart Rate
36. RR: Respiratory Rate
37. Hb: Hemoglobin
38. Hct: Hematocrit
39. TLC: Total Leukocyte Count

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SUMMARY

SUMMARY

Background: Sepsis is a problem that is the bane of all medicine. It can develop into severe sepsis, septic shock or multiple organ failure often having a lethal outcome. The burden of sepsis in hospitalized patients is high causing millions of deaths worldwide. Early diagnosis of sepsis is therefore crucial in order to be able to institute appropriate therapy and thence to avert a possible negative outcome.

Inflammatory biomarkers have provided an easy way to diagnose sepsis. Although procalcitonin is better than biomarkers used earlier, its reliability is a problem. It is at this juncture that Presepsin (soluble CD14-ST) is postulated as a novel biomarker for diagnosing sepsis.

Methods: A prospective observational study was designed to assess the diagnostic value of presepsin, its sensitivity and specificity for diagnosis of sepsis in critically ill patients, and its ability to prognosticate the outcome of sepsis. All patients getting admitted to the adult ICU at our institute were screened and those having features suggestive of sepsis were recruited into the study. Procalcitonin and presepsin were assessed on day of admission and day 7 of ICU stay apart from routine investigations. Patients were followed for outcome in terms of mortality till 28 days. Patients who/whose proxies refused to participate in the study were excluded.

Results and Conclusion: A total of 82 patients who met the inclusion criteria were included in the study. Sensitivity of presepsin for diagnosis of sepsis was determined to be 78% while that of PCT was determined to be 69%. This gave a combined sensitivity of presepsin and PCT of 93% when used in parallel for the diagnosis of sepsis. We concluded that a combination of both the biomarkers provides a higher sensitivity and can be used to screen for sepsis in ICU and emergency areas.


INTRODUCTION

INTRODUCTION

Inflammation is the body's response to microbial invasion. This inflammatory reaction has systemic consequences, which can lead to organ failure. Sepsis is the medical term for this condition. Sepsis is a life-threatening organ failure caused by a dysregulated host response to infection[1]. It's a form of systemic inflammatory response syndrome (SIRS) brought on by pathogens or conditional pathogenic microorganisms infiltrating the bloodstream. Severe sepsis, septic shock, and multiple organ failure can result[13].

Sepsis is a common occurrence in hospitals and intensive care units, resulting in millions of fatalities globally. According to studies, 23.8 percent of patients acquire sepsis during their ICU stay, with a 34 percent fatality rate[33].

The multiplication of microorganisms during sepsis causes them to produce a variety of pathogenic substances into the bloodstream. This causes endothelial cells, monocytes, macrophages, neutrophils, and plasma to release endogenous inflammatory markers.

Fever, tachycardia, tachypnea, and elevated white cell counts are all symptoms of sepsis, which are often accompanied by hypotension (septic shock) or end-organ dysfunction (Multi Organ Dysfunction or MODS).

The key to preserving lives in sepsis is early detection and treatment with antimicrobials as soon as possible. Early detection of sepsis is as important as it is difficult. It's critical to get a diagnosis as soon as possible so that life-saving treatments can begin. As previously mentioned, there are a variety of proteins generated by the body during the acute phase of sepsis that can help with early sepsis diagnosis. C-reactive protein, interleukin-1, interleukin-6, and cytokines like TNF-α have all been examined in the past, but while these markers are raised in sepsis, none of them is sensitive or specific enough to be used as biomarkers for the diagnosis of sepsis. Of course, blood and tissue cultures are the gold standard. It can both determine the cause of the infection and screen for antibiotic sensitivity. It is, however, a time-consuming process that will prolong the diagnosis of sepsis and, in its quest to provide an accurate diagnosis, will consume the patient's all-too-limited valuable time, negating the benefit of an early diagnosis of sepsis. As a result, a precise and timely biomarker for the identification of sepsis is required, one that can be measured easily, quickly, and accurately using point-of-care analysis.

Biomarkers of sepsis can include pro-inflammatory cytokines and chemokines, which are produced during the hyper-inflammatory phase of sepsis, or anti-inflammatory cytokines, which are produced during the immunosuppressive phase of sepsis[32]. A good biomarker should be able to diagnose with high precision.

Procalcitonin is one such biomarker that is being used for the diagnosis of sepsis. It is produced by thyroid C cells. It can be used to detect sepsis early on and to monitor antimicrobial therapy. Despite its unquestioned utility in the early detection of sepsis, procalcitonin can be elevated in a variety of non-infectious diseases, including major surgery, severe trauma without infections, and significant burns. Furthermore, due to its short half-life, procalcitonin rises quickly in response to any systemic inflammation and then drops just as quickly. As a result, its utility in predicting the prognosis of sepsis is limited.

While procalcitonin has been determined to be more reliable than the inflammatory markers employed previously, there is still a problem with reliability. In a systematic review done by Hoeboer *et al* sensitivity of procalcitonin for diagnosing sepsis is found to be 76% with a specificity of 69%[32]. It demonstrates that there is a lot of room for novel sepsis markers to be discovered. Presepsin appears to be a viable alternative.

Presepsin was discovered in the early 2000s and examined as a sepsis biomarker. It is expected to be a more sensitive and specific next-generation inflammatory marker. It is a glycoprotein that is a truncated version of CD-14's N-terminal fragment. Monocytes, macrophages, and granulocyte cells all have the CD-14 cluster of differentiation on their surfaces. The soluble region of CD-14 is split from the membrane bound portion during inflammation, and this is what is detected as presepsin. Presepsin production is thus linked to bacterial phagocytosis. According to certain research, it not only rises earlier after the commencement of infection, but it is also unaffected by severe trauma, burns, or major surgery, all of which cause systemic inflammation but not sepsis[5].

In several studies conducted around the world, presepsin has been demonstrated to be a very useful inflammatory indicator for sepsis. A meta-analysis performed by Zhang X *et al* found it to have high sensitivity and diagnostic accuracy in diagnosing sepsis[16]. In the only study conducted on the Indian population, Venugopalan *et al* reported that presepsin was superior to procalcitonin in detecting sepsis, with sensitivity and specificity of presepsin being 46.2 and 100 respectively while procalcitonin had a sensitivity of 46.2 and a specificity of 31.8[26].

However, samples were taken only at the time of suspicion of sepsis, and no further sampling was done to determine the prognostic value in the Indian population.

Presepsin could be a better alternative to established biomarkers for not only identifying sepsis but also guiding antibiotic therapy and predicting the patient's prognosis.

As a result, we performed an observational study to compare the diagnostic accuracy of presepsin with that of procalcitonin, a well-established biomarker utilized in our institution, and to try to correlate it with the patient's prognosis.

AIM & OBJECTIVES

AIM & OBJECTIVES

Aim:

The aim of this study is to evaluate the diagnostic accuracy, sensitivity, specificity as well as the prognostic value of presepsin & procalcitonin for sepsis in critically ill patients.

Objectives:

Primary Objective:

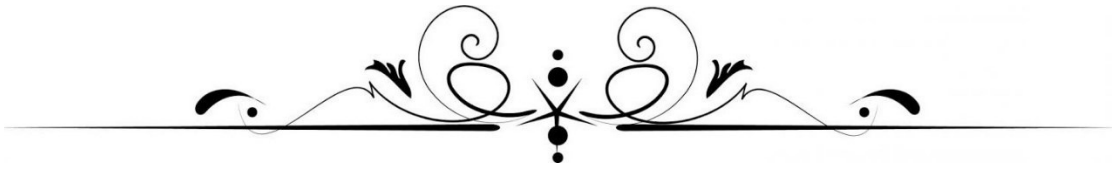
- The primary outcome is to evaluate sensitivity and specificity of presepsin and procalcitonin for detection of sepsis

Secondary Objectives:

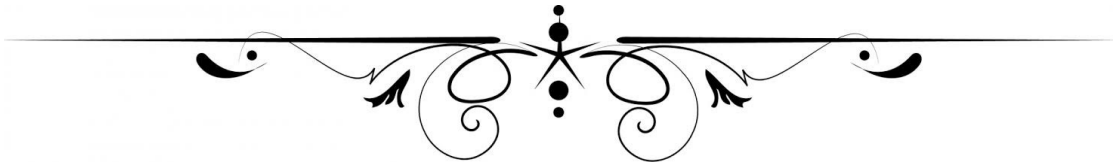
1. Ability of presepsin to prognosticate the multi-organ failure in critically ill patients as assessed by AKI.
2. To establish presepsin as a predictor of outcome of Sepsis in terms of 28 days' mortality.
3. To compare presepsin vs procalcitonin as a predictor of outcome of Sepsis in terms of 28 days' mortality.

HYPOTHESIS

- There is no difference in sensitivity and specificity of procalcitonin & presepsin in detection of sepsis and its prognosis in critically ill patients.



REVIEW OF LITERATURE



REVIEW OF LITERATURE

Singer *et al*[1] were appointed to a task force by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine in 2016 with the goal of evaluating and updating the definitions of sepsis and septic shock. The team revised the sepsis definitions and clinical criteria, which were then distributed to 31 professional associations around the world for peer review and approval. They established "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)" in this way. As per the experts, sepsis was defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. The clinical criteria for sepsis comprised a 2 point or more increase in the SOFA score, and it was linked to a mortality rate of more than 10%. They also developed the qSOFA score (respiratory rate greater than or equal to 22/min, altered mentation, or systolic blood pressure less than or equal to 100 mm of Hg) to help identify adult patients with sepsis in wards and emergency rooms. Patients who met at least two of the criteria above were more likely to have poor outcomes and so require intensive care.

There has long been an interest in using biomarkers to facilitate early diagnosis of sepsis. In 2015, **Arora S *et al***[30] did a meta-analysis to aggregate data from all known research on PCT levels in sepsis survivors and nonsurvivors. They did a thorough search of the literature using the terms "procalcitonin," "sepsis," and "prognosis." On days 1 and 3, data from the eligible trials were retrieved and evaluated to see if there was any significant pooled mean difference between survivors and nonsurvivors. The difference between survivors and nonsurvivors in day 1 PCT values was found to be statistically significant (P = 0.02). On day 3, the mean difference was statistically significant (P = 0.002). Day 1 difference was not found to be significant (P = 0.62) in a subgroup of research on patients with severe sepsis and septic shock. They came to the conclusion that procalcitonin levels in the early stages of sepsis are much lower in survivors than in nonsurvivors.

Even under the latest Surviving Sepsis Campaign, recommendation was made to use blood lactate levels to aid in the diagnosis of sepsis. **Evans *et al***[2] updated the global adult sepsis guidelines in 2021, establishing the International Guidelines for the Management of Sepsis and Septic Shock. They made a weak recommendation, proposing that blood lactate be assessed in persons suspected of having sepsis. They opined that in individuals with suspected sepsis, the presence of a high or normal lactate level considerably enhances or

decreases the likelihood of a definitive diagnosis of sepsis. Lactate alone cannot detect sepsis because it is not sensitive or specific enough; rather, it serves to raise the probability of identifying sepsis if found to be increased.

A systematic review was done by **Lan *et al***[3] in 2018 with the objective of comparing the performance of presepsin with procalcitonin and 7 other biomarkers in terms of diagnostic potential for sepsis as per Sepsis 3 guidelines as well as differentiation of infectious from non-infectious SIRS. A total of 108 studies representing 14,555 patients were included. When comparing presepsin to PCT, 0.13 (95% CI: [0.04,0.19]) higher sensitivity with significance and 0.09 (95% CI:[-0.02,0.22]) lower specificity were suggested for diagnosis of sepsis.

Yamamoto *et al*[4] conducted a prospective study at Osaka City University Graduate School of Medicine in Osaka, Japan, in 2018 to assess the diagnostic accuracy of presepsin for sepsis. The research took place over the course of 18 months, and a total of 91 patients were enrolled. They found that presepsin has 87 percent sensitivity and 86 percent specificity for diagnosing sepsis with a threshold of 508 pg/mL. Procalcitonin sensitivity was determined to be 68 percent and specificity to be 86 percent using a 1.5 ng/mL threshold. They concluded that presepsin appears to be helpful in distinguishing sepsis with shock or, more specifically, sepsis without shock from non-sepsis in patients with a change in SOFA score of 2 or more.

MY Memar *et al*[5] conducted a study in 2019 with the goal of reviewing the clinical applicability of presepsin in diagnosis and prognosis of infection. To achieve this goal, studies on diagnostic, prognostic, and clinical assessment of presepsin as an indicator of infection were reviewed in the PubMed and Scopus databases. Their review led to the conclusion that assessing presepsin has the advantage of being able to anticipate the severity of a bacterial infection. They also mentioned that measuring presepsin is a simple operation that takes less than 17 minutes. It was suggested that presepsin could be used in conjunction with other indicators and established methods of infection diagnosis to improve accuracy. They concluded that more research is needed to define presepsin cutoff values for detecting different types of infections in different patient categories.

The diagnostic accuracy of presepsin, procalcitonin (PCT), and C-reactive protein (CRP) in discriminating sepsis severity, as well as their relationship with the Sepsis-related Organ Failure Assessment (SOFA) score, was investigated by **A. Aliu-Bejta *et al***[6]**.** During two time periods, 100 septic patients from two university clinical facilities were enrolled in the

study. For sepsis stratification, new Sepsis-3 definitions were employed. During the illness, biomarkers and the SOFA score were assessed four times. The presepsin was measured using a sandwich ELISA kit. To evaluate the changes in biomarker concentrations and SOFA score values during the illness and to estimate the differences between severity groups, a generalized linear mixed effects model was utilized. The correlation of biomarkers with SOFA score was investigated using multivariate analysis. Presepsin concentrations were significantly higher on admission in patients with septic shock (n = 34) compared to patients with sepsis (n = 66), mean ± SD: 128.5 ± 47.6 ng/mL vs. 88.6 ± 65.6 ng/mL, respectively ($p < 0.001$). The same was not observed for PCT and CRP; their concentrations did not differ significantly between severity groups. There was also a substantial association between presepsin and SOFA score ($p < 0.0001$). In the study groups, they found that presepsin had an excellent diagnostic ability to distinguish septic shock from sepsis. PCT and CRP were unable to distinguish the severity of sepsis.

S. Endo *et al*[7] conducted a multicenter prospective study to compare the clinical efficacy of presepsin with other traditional sepsis biomarkers such as procalcitonin, interleukin-6, and C-reactive protein in assessing sepsis severity during follow-up. This study included 103 patients with sepsis who were admitted to the emergency room or intensive care unit and were divided into three diagnostic groups: sepsis, severe sepsis, and septic shock. On admission, blood samples were taken from each patient, as well as after 1, 3, 5, and 7 days. On the basis of multiple indicators of sepsis severity, the patients were further separated into good and bad prognosis groups (i.e., Sequential Organ Failure Assessment score, and Acute Physiology and Chronic Health Evaluation II score). On days 3 and 7, the individuals in the favorable prognosis group showed significant reductions in all biomarker values. Only presepsin levels did not drop appreciably throughout follow-up in the bad prognosis group. Antibiotic treatment took substantially longer in the adverse prognosis group than in the favorable prognosis group ($P < 0.05$). The group with a poor prognosis had a substantially greater 28-day mortality rate than the group with a good prognosis ($P < 0.05$). In comparison to other traditional sepsis biomarkers, the data revealed that presepsin levels correlated with the severity of sepsis during follow-up.

Ulla M. *et al*[8] studied the diagnostic and prognostic value of presepsin in patients with SIRS, suspected sepsis, or septic shock who presented to their ED. The study comprised 130 patients who presented to their ED with suspected sepsis or septic shock, an additional 52

patients who met at least two of the SIRS diagnostic criteria upon presentation as controls. Blood samples were taken at the time of the initial medical evaluation and again after 24 and 72 hours for certain patients; the samples were examined using the Pathfast® Presepsin test for sCD14 and commercial kits for other analyses (eg. PCT). After that, computerized medical data were analyzed to determine the definitive diagnosis and survival. Septic patients had higher presepsin concentrations at presentation (Mean, 95%CI: 2273 pg/ml, 1540-3005) than non-septic patients (1480 pg/ml, 696-2264); values were furthermore correlated to the severity of disease. The same trend was observed for mean values of PCT (13.98 ng/ml, 95%CI 8.1-19.9 in septic population; 0.85 ng/ml, 95%CI 0.26-1.46) in controls. According to preliminary findings from serial tests, presepsin levels were higher in septic patients at presentation and at T2 (i.e. after 72 hrs). There was no significant association between presepsin or PCT values and the primary site of infection (lung, urinary tract, or other sites). Presepsin levels were significantly greater (3100 pg/ml) in non-survivors of sepsis (30-day mortality) than in survivors (2010 pg/ml). They determined that in a complex group of patients with SIRS, Sepsis, Severe Sepsis, and Septic Shock, sCD14 was not inferior to PCT in early identification and assessing illness severity. In comparison to PCT, preliminary results for 30-day mortality prediction capacity demonstrated superiority. They suggested that more research be done on combining Presepsin with PCT or other biomarkers to see if this could improve sensitivity and specificity in the early detection of septic conditions.

Yu H *et al*[9] compared the utility of dynamic procalcitonin (PCT) and presepsin measures in determining therapy efficacy and prognosis for patients with severe sepsis in a study published in 2016. On the basis of 90-day survival, patients with severe sepsis (n=109) were enrolled and separated into survival and non-survival groups. On days 1, 3, 5, 7, and 12, the levels of PCT and presepsin were measured. The SOFA (sequential organ failure assessment) was computed. PCT was weakly to moderately favorably correlated with SOFA from day 5 onward, but presepsin was positively correlated from day 3 onward. The clearance ratio (CR) of PCT was weakly to moderately negatively connected with SOFA from day 5 onwards, but the CR of presepsin was substantially negatively correlated from day 3 onwards. There was no statistical difference in PCT levels between the survivors and non-survivors groups. Within 12 days, PCT levels in both survival and non-survival groups decreased synchronously. In comparison, presepsin levels in the survival group steadily declined, whereas they gradually increased in the non-survival group. On days 3, 5, 7, and 12, the survival group's PCT CRs were higher than the non-survival group's. PCT CRs, on the other

hand, increased in both groups at the same time. In comparison, presepsin CRs climbed steadily in the survival group, while they gradually declined in the non-survival group. They found that dynamic monitoring of presepsin and PCT indicated that presepsin and CR of presepsin are both continuous and superior markers for evaluating treatment efficacy and prognosis in patients with severe sepsis than PCT and CR of PCT.

A systematic review and meta-analysis conducted by **J Zhang *et al***[10] in 2015 combined data to better determine the efficacy of circulatory presepsin as a biomarker for sepsis. They considered studies testing the diagnostic accuracy of presepsin for sepsis from medical databases that were published in English before November 7, 2014. A revised Quality Assessment for Studies of Diagnostic Accuracy was used to assess the quality of qualifying studies (QUADAS-2). A bivariate model was used to evaluate the overall diagnostic accuracy of presepsin for sepsis. The Deek funnel plot asymmetry test was used to investigate publication bias. Eleven studies met the criteria for inclusion. The overall diagnostic sensitivity of presepsin for sepsis was 0.83 (95% CI: 0.77–0.88), and specificity was 0.78 (95% CI: 0.72–0.83). The area under the summary receiver operating characteristic curve was 0.88 (95% CI: 0.84–0.90).The pretest probability of sepsis was 0.56 among all subjects. When presepsin was introduced as the diagnostic test for sepsis, the post test probabilities were 0.81 for a positive result and 0.19 for a negative. Presepsin is a good auxiliary biomarker for the diagnosis of sepsis, but it is insufficient to detect or rule out sepsis when used alone, according to the authors.

In 2015, **Zhang X *et al***[11] conducted a meta-analysis to determine the diagnostic accuracy of presepsin in patients with systemic inflammation. They used PubMed, Embase, Web of Knowledge, and Cochrane to conduct a systematic search. Studies that evaluated the diagnostic accuracy of presepsin for sepsis in adult patients with SIRS were included. On the basis of these findings, a 2 x 2 contingency table was created. The studies were judged and data retrieved by two authors separately. A bivariate meta-analysis technique was used to calculate the diagnostic accuracy of presepsin in sepsis. Eight studies involving a total of 1,815 patients were included in the present study. The pooled sensitivity, specificity, diagnostic odds ratio, positive likelihood ratio and negative likelihood ratio were 0.86 (95 % CI: 0.79-0.91), 0.78 (95 % CI: 0.68-0.85), 22 (95 % CI: 10–48), 3.8 (95 % CI: 2.6-5.7), and 0.18 (95 % CI: 0.11-0.28), respectively. The area under the summary receiver operator characteristic curve was 0.89 (95 % CI: 0.86–0.92). They concluded that presepsin exhibits

very good diagnostic accuracy (AUC=0.89) for the diagnosis for sepsis. Presepsin has a high diagnostic accuracy (AUC=0.89) for sepsis detection, according to the researchers. They suggested that for sepsis diagnosis, an overall assessment of all clinical indicators be performed, along with continual re-assessment of presepsin all through the course of the disease.

In 2019, **Kondo Y *et al*** conducted a comprehensive meta-analysis to determine the overall diagnostic value of procalcitonin and presepsin for sepsis diagnosis. They looked for relevant studies in three electronic databases (MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials). Articles were screened by two authors independently based on inclusion and exclusion criteria. We calculated the combined sensitivity, specificity, and summary receiver operating characteristic curves. They included 19 studies (19 observational studies and no randomized controlled trials) that had enrolled 3012 patients. Analyses of summary receiver operating characteristic curves revealed areas under the receiver operating characteristic curves of 0.84 for procalcitonin and 0.87 for presepsin. The pooled sensitivities and specificities were 0.80 (95% confidence interval 0.75 to 0.84) and 0.75 (95% confidence interval 0.67 to 0.81) for procalcitonin. For presepsin, these values were 0.84 (95% confidence interval 0.80 to 0.88) and 0.73 (95% confidence interval 0.61 to 0.82), respectively. There were no statistically significant differences in both pooled sensitivities ($p = 0.48$) and specificities ($p = 0.57$) between procalcitonin and presepsin. Their meta-analysis found that procalcitonin and presepsin have similar diagnostic accuracy in detecting infection and that both are effective for early detection of sepsis and consequent reduction of mortality in critically ill adult patients.

Venugopalan *et al*[12] did a prospective observational study in 2019 to evaluate the diagnostic value and prognostic use of presepsin versus procalcitonin in sepsis. They evaluated 48 patients who were diagnosed to have sepsis either on admission or during their hospital stay according to the ACCP/SCCM guidelines. The superiority of presepsin over procalcitonin was evident with presepsin having a sensitivity of 46.2 and specificity of 100 and procalcitonin having a sensitivity of 46.2 and specificity of 31.8 ($P < 0.001$). They also proved presepsin to be a reliable biomarker for 28 day mortality. They concluded that presepsin was superior to procalcitonin as it has a better specificity with similar sensitivity and is a better predictor of 28 day mortality.

Seo Hee Yoon *et al*[15] did a systematic review and meta-analysis on presepsin as diagnostic marker of sepsis in children and adolescents with the aim to assess the overall diagnostic accuracy of presepsin in pediatric sepsis and compare it to those for C-reactive protein (CRP) and procalcitonin (PCT). 4 studies were included in the final analysis that comprised 308 patients between ages of 1 month to 18 years. The pooled diagnostic sensitivity and specificity of presepsin were 0.94 (95% confidence interval [CI]: 0.74–0.99) and 0.71 (95% CI: 0.35–0.92), respectively. The pooled sensitivity of presepsin (0.94) was higher than that of CRP (0.51) and PCT (0.76), whereas the overall specificity of presepsin (0.71) was lower than that of CRP (0.81) and PCT (0.76). The AUC of presepsin (0.925) was higher than that of CRP (0.715) and PCT (0.820). They concluded that presepsin has higher sensitivity and diagnostic accuracy, but lower specificity than procalcitonin or CRP in detecting sepsis in children.

A systematic review and meta-analysis on the accuracy of presepsin in sepsis diagnosis was published in 2015 by **Jiayuan Wu *et al*[17].** They performed a comprehensive electronic search via internet retrieval system up to 15 December 2014. The analysis included 9 studies with 10 trials and 2159 patients. Presepsin had a pooled sensitivity of 0.78 (0.76–0.80) for sepsis and a pooled specificity of 0.83 (0.80–0.85). The area under curve of summary receiver operating characteristics curve was 0.89 (95%CI: 0.84 to 0.94). This meta-analysis showed that presepsin has certain advantages in patient management and may be a useful and beneficial biomarker in the early detection of sepsis. However, presepsin's diagnostic accuracy in distinguishing sepsis from non-sepsis was only modest, preventing it from being recommended as a definitive test for sepsis diagnosis.

Behnes *et al*[14] in 2014 did a prospective controlled study in order to evaluate the diagnostic and prognostic value of presepsin in patients with severe sepsis or septic shock during the 1st week of ICU treatment. In total, 116 patients with suspected severe sepsis or septic shock were included during the first 24 hours of ICU treatment. Blood samples for biomarker measurements of presepsin, procalcitonin (PCT), interleukin 6 (IL-6), C reactive protein (CRP) and white blood cells (WBC) were drawn at days 1, 3 and 8. All patients were followed up for six months. ROC analysis with calculation of the AUC was performed for prognosis of all-cause mortality in all patients after 30 days and 6 months for all biomarkers (that is presepsin, IL-6, PCT, CRP, WBC), APACHE II and SOFA score. Also, receiver-operating characteristic (ROC) curve analyses were performed with calculation of area under

the curve (AUC) for diagnosis of sepsis, severe sepsis and septic shock during the first week of ICU treatment at days 1, 3 and 8. Accordingly, accuracy, specificity, sensitivity, negative/positive predictive values (NPV/PPV), and relative risk of the biomarkers were calculated. They concluded that presepsin possessed valuable diagnostic capacity to differentiate sepsis severity compared to PCT, IL-6, CRP, and WBC. Additionally, presepsin and IL-6 had prognostic value with respect to 30 days and 6 months all-cause mortality throughout the first week of ICU treatment.

The goal of the study conducted by **Jereb M *et al***[18] in 2019, was to determine the diagnostic and prognostic value of presepsin (sCD14) in sepsis patients. This prospective observational study comprised 54 adult patients with sepsis and 26 patients with aseptic meningitis as a control group. C-reactive protein (CRP), presepsin, lactate, and a count of leukocytes and neutrophils were all measured on admission in all of the patients in the study. Two different blood cultures were taken from patients with a suspected bacterial infection, and the concentration of procalcitonin (PCT) was determined. Patients in the septic group had their plasma presepsin and PCT concentrations measured on days 2, 3, and 7 after enrollment. The median presepsin serum levels in sepsis patients was 1614 pg/mL, while it was 203 pg/mL in the control group ($p < 0.001$). Presepsin levels were greater in patients with septic shock than in patients with sepsis ($p < 0.014$). The mean presepsin concentrations in deceased individuals were higher than those in living patients ($p = 0.009$). The trend in presepsin concentrations in deceased individuals differed significantly from that in living patients ($p = 0.018$). In patients with Gram negative or Gram positive bacteria, there were no statistically significant changes in presepsin or other biomarker concentrations. They concluded that presepsin can predict the severity and outcome of sepsis and can be utilized as a diagnostic marker for systemic bacterial infection.

In a single-center, prospective, observational cohort study known as PREDI study of diagnostic accuracy published in 2019 by **Contenti J *et al***[19]**,** the author**s** attempted to compare the diagnostic accuracy of blood levels of presepsin, lactate, C-reactive protein (CRP), and procalcitonin (PCT) for predicting sepsis as defined by the Sepsis-3 criteria. The secondary goal was to see how accurate these indicators were at predicting bacteremia in the absence of sepsis or septic shock. Patients with at least two criteria for systemic inflammatory response syndrome were prospectively included if they were suspected of having an infection. In blood taken on admission, they assessed presepsin, PCT, CRP, and lactate.

Blood samples from 359 individuals were tested, and 228 (63.5%) of them satisfied the sepsis criteria, whereas 20 (5.6%) met the septic shock criteria. PCT and presepsin levels were the best predictors of sepsis and septic shock with areas under the receiver operating characteristic curve (AUC) of 0.711 (95% CI, 0.660-0.758) and 0.709 (95% CI, 0.658-0.756), respectively (P <.001, both comparisons). The AUCs for CRP and lactate concentrations were, respectively, 0.63 (95% CI, 0.58-0.69) and 0.61 (95% CI, 0.56-0.66) (P <.05, both comparisons). On applying the diagnostic cut points of 0.25 ng/mL for PCT and 500 pg/mL for presepsin, the odds ratios were 2.51 (95% CI, 1.53-4.12) for PCT and 3.19 (95% CI, 1.91-5.31) for presepsin. The diagnostic accuracy of the combination of presepsin and PCT results (AUC, 0.71; 95% CI 0.66-0.76; P <.001) was no better than the accuracy of PCT alone. The most accurate predictor of bacteremia was PCT (AUC, 0.835; 95% CI, 0.79-0.87; P <.001). Presepsin and PCT appear to be the strongest predictors of a diagnosis of sepsis or septic shock in emergency department patients, according to the investigators.

Miao-Yun Wen *et al*[20] did a study in 2019 to see if the presepsin level might predict the prognosis of sepsis patients who met the sepsis-3 criteria. Patients who were diagnosed with sepsis using the sepsis-3 criteria were enrolled and divided into two groups based on their in-hospital mortality: survivors and non-survivors. This study comprised a total of 138 patients. The non-survivor group had significantly greater presepsin levels than the other group (P=0.000). The presence of presepsin was found to be an independent risk factor for sepsis-related in-hospital death (OR =1.221, P=0.026) in patients. The level of presepsin was found to be positively related to the SOFA score (p=0.396, P=0.000). The presepsin level was highly accurate in predicting patients' in-hospital death from sepsis, according to ROC curve analysis (AUC =0.703, P=0.000). The AUC of a presepsin and SOFA score combination was considerably higher than the SOFA score alone (AUC: 0.817 vs 0.793, P=0.041). They came to the conclusion that presepsin is a predictive biomarker with a high accuracy in predicting sepsis prognosis using the sepsis-3 criteria.

AN Drăgoescu *et al*[21] published a study in 2020 with the goal of determining the efficacy of presepsin in sepsis prognosis. This was a single-center prospective study conducted in Craiova Emergency Hospital that included 114 patients who met the sepsis criteria and were admitted to the Intensive Care Unit (ICU) between 2018 and 2019. Patients were divided into two study groups based on disease severity: sepsis (76 patients) and septic shock (38 patients). The SOFA score and most of its components (PaO2/FiO2, platelets, and Glasgow

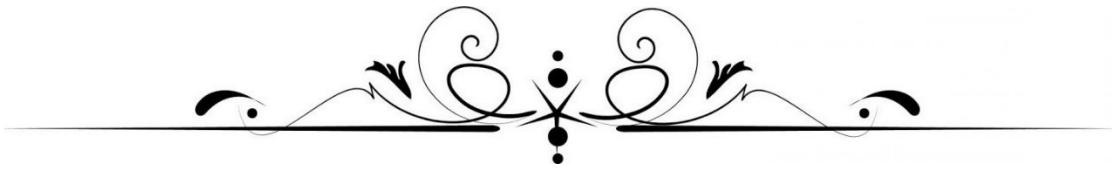
Coma Score (GCS)) were significantly altered in patients with septic shock compared to those with sepsis, and in survivors against non-survivors, as expected. The overall death rate was 34.2 percent, with septic shock patients having a significantly higher rate (55.3 percent vs. 23.7 percent, $p = 0.035$). The sepsis marker presepsin was considerably raised in all patients (2047 ng/mL), as well as in septic shock patients (2538 ng/mL, $p < 0.001$) and non-survivors (3138 ng/mL, $p < 0.001$) and non-survivors (3138 ng/mL, $p < 0.001$). The SOFA score and presepsin were found to have a significant relationship ($r = 0.883$, $p < 0.001$). According to their findings, presepsin could be a helpful marker for predicting sepsis severity and mortality risk under the updated definition of sepsis.

In 2021, **Abdelshafey EE *et al***[22] released a study comparing the role of presepsin and the systemic inflammatory response syndrome (SIRS) and the quick sequential organ failure assessment (qSOFA) score in early detection of sepsis and prediction of mortality in intensive care unit (ICU) patients. After being admitted to the adult ICU, forty patients were randomly selected. To construct the qSOFA score, SIRS criteria and SOFA score, data from emergency department (ED) triaging and preliminary laboratory results were acquired. Within 6 hours after ED triaging, a presepsin test was conducted. Based on clinical and microbiological criteria as well as SOFA score alterations, the patients were divided into sepsis and nonsepsis groups. Twenty-six patients were diagnosed as septic with an average age of 68.04 ± 18.60 years, while 14 patients were nonseptic with an average age of 51.71 ± 24.88 years.Presepsin with a cutoff value >640 pg/mL (area under the curve [AUC] of 0.848 ($p < 0.001$}) had a significant diagnostic accuracy of identifying septic cases with sensitivity of 73.08% and specificity of 92.86% as compared to the nonsignificant SIRS (AUC, 0.670; sensitivity, 69.23%; and specificity, 57.14%) or qSOFA (AUC, 0.652; sensitivity, 38.46%; and specificity, 78.57%) criteria.Prespsin with a cutoff value >640 pg/mL also significantly (AUC of 0.920 [$p < 0.001$]) predicted mortality with sensitivity of 100.0% and specificity of 66.67% compared to the nonsignificant SIRS (AUC, 0.540; sensitivity, 70.0%; and specificity, 43.33%) or qSOFA (AUC, 0.670; sensitivity, 60%; and specificity, 76.67%) criteria. They observed that, when compared to SIRS or qSOFA score, early presepsin testing in ICU patients is much more accurate in the diagnosis of sepsis and prediction of mortality.

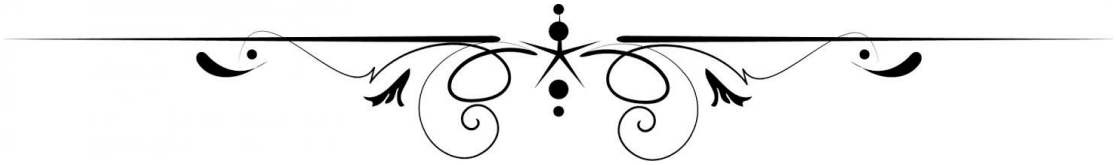
In the year 2021, **Jeong Suk Koh *et al***[24] published a study in Korea that looked into the utility of presepsin in predicting sepsis prognosis. Patients with sepsis who met the sepsis-3 criteria were enrolled in the study and were divided into two groups based on in-hospital mortality: survivors and non-survivors. Between July 2019 and August 2020, 153 patients (33 and 121 with sepsis and septic shock, respectively) were enrolled in the study. The survivor and non-survivor groups included 91 and 62 individuals with sepsis, respectively. The non-survivor group had higher levels of presepsin (p=0.004), lactate (p=0.003), and the sequential organ failure assessment (SOFA) score ($p < 0.001$). Presepsin and lactate performed poorly in predicting sepsis prognosis (area under the curve [AUC]=0.656, p=0.001; lactate: AUC=0.646, p=0.003), according to receiver operating characteristic curve analysis. The SOFA score had the best performance, with the highest AUC value (AUC=0.751, $p < 0.001$) and the highest AUC value (AUC=0.751, $p < 0.001$). The presepsin prognostic cutoff point was 1.176 pg/mL. In-hospital mortality was associated with presepsin levels greater than 1.176 pg/mL (odds ratio [OR], 3.352; $p < 0.001$), higher lactate levels (OR, 1.203; p=0.003), and a higher SOFA score (OR, 1.249; $p < 0.001$). They determined that non-survivors had higher levels of presepsin than survivors. As a result, presepsin could be a useful biomarker for predicting sepsis prognosis.

In 2021, **Sukyo Lee *et al***[27] released a prospective observational study with the goal of determining the therapeutic utility of presepsin for distinguishing sepsis from non-infectious organ failure and predicting mortality among sepsis patients in the emergency department (ED). According to the Sepsis-3 definitions, 420 patients were split into three groups: noninfectious organ failure (n=142), sepsis (n=141), and septic shock (n=137). The biomarker levels of presepsin, procalcitonin, and C-reactive protein were measured in the ED and compared between the groups. Presepsin levels (median [IQR]) were considerably greater in sepsis than in non-infectious organ failure (792 [450–1273] vs. 286 [170–417], p=0.001), and significantly higher in septic shock than in sepsis (1287 [589–2365] vs. 792 [450–1273], p=0.002). Presepsin's best cut-off value for distinguishing sepsis from non-infectious organ failure was 582 pg/mL (sensitivity, 70.1; specificity, 89.4; AUC, 0.877; $p < 0.001$), and for distinguishing sepsis from septic shock was 1285 pg/mL (sensitivity, 50.4; specificity, 76.6; AUC, 0.618; $p < 0.001$). In patients with sepsis and septic shock, the optimum presepsin cut-off value for predicting 30-day death was 821 pg/mL (sensitivity, 68.9; specificity, 50.5; AUC, 0.605; p=0.005). Patients with greater presepsin levels (821 pg/mL) had significantly higher mortality than patients with lower presepsin levels (821

pg/mL) (log-rank test; p=0.004), according to a Kaplan-Meier survival curve analysis. Presepsin levels might successfully distinguish sepsis from non-infectious organ failure and septic shock from sepsis, they concluded. Presepsin levels could aid clinicians in predicting death in sepsis and septic shock patients.



MATERIALS & METHODS



MATERIALS AND METHODS

Study setting:

- Department of Anaesthesiology & Critical Care**,** AIIMS Jodhpur (AICU)- case enrollment
- Department of Biochemistry- evaluation of presepsin and procalcitonin levels

Study design:

Observational Study: Prospective Cohort Study

Study Period:

The study was conducted in the Adult Intensive Care Unit at AIIMS, Jodhpur. Approval was taken from the Institutional Ethics Committee (IEC Reg No.- AIIMS/IEC/2019- 20/996 dated 01/01/2020) and the study was registered with Clinical Trial Registry – India (CTRI Reg. No. CTRI/2020/02/023337 dated 14/02/2020). The study was carried out in 82 patients admitted in the adult ICU. Enrolment of patients started in February 2020 and ended in July 2021.

Study Participants

Inclusion Criteria

1. Patients aged >18 years
2. Patients having clinical features suggestive of sepsis as defined by Sepsis-3 definition (2016) at the time of ICU admission

Exclusion Criteria

1. The patient/relatives who refused to give Informed consent
2. Age less than 18 years
3. Expired within 7 days of collection of 1st sample
4. Patients with terminal stage of disease (malignancy of any type, acquired immunodeficiency syndrome, end-stage liver or renal disease).
5. HIV/HBsAg/HCV.
6. Autoimmune disorders/Metabolic diseases
7. On long term steroids/ Immunosuppressants/ Chemotherapy

The study included adult patients admitted to the ICU with suspicion of sepsis throughout an

18-month period (February 2020 to July 2021). A total of 82 patients were enlisted.

Blood samples were collected as part of standard sampling on ICU admission for routine investigations, and five ml whole blood was taken from the same sample for serum procalcitonin and presepsin estimation, with no additional needle pricks or sampling done for the study (day 1). As a biomarker of sepsis in the ICU, serum procalcitonin is routinely measured on admission. These tests were then repeated seven days after the first sample was taken (day 7).

Five ml of whole blood sample was collected in plain vacutainers or gel separators from the recruited subjects. The sample was allowed to clot for one hour. Serum was separated by centrifugation at 3000 rpm for 10 minutes at room temperature. The serum was collected and stored at -80 degree Celsius in the biochemistry laboratory. When the desired sample size was achieved, the serum samples were processed. As presepsin is not a test that is routinely done at AIIMS Jodhpur, enzyme-linked immunosorbent assay (ELISA) kits were procured. The serum samples were used for Presepsin estimation by ELISA kit method according to the manufacturer's instruction

Patients enrolled in the study did not bear any cost or financial burden for participating in this study and all the tests were completed with the assistance of a research grant received as part of the thesis project.

Routine cultures were sent from blood, urine, trachea, and any drain site at the time of ICU admission to screen for the presence of any suspected bacteremia. All sent cultures were followed up on, and a definitive sepsis diagnosis was made based on the organisms that grew in the cultures.

Patient vitals, haemogram, urea and creatinine levels, bilirubin, partial pressures of O2 and CO2, bicarbonate, base excess, lactate, pH value, and the Glasgow coma scale (GCS) were all recorded on a daily basis.

Disease severity in the ICU was documented by the Acute Physiology and Chronic Health Evaluation II (APACHE II) and the Sequential Organ Failure Assessment (SOFA) scores. The values of presepsin and procalcitonin were correlated with SOFA scores at different points of time. Culture positivity was also compared with all these markers.

Patient outcome was noted in terms of death or discharge at 28 days from the time of admission

To achieve the aims and objectives of this study, the following parameters were observed for the study period.

Parameters that were observed every day for 7 days and the day of death or discharge:

1. Temperature
2. Heart rate
3. MAP
4. Respiratory rate
5. SOFA score
6. Serum PCT
7. Serum Lactate
8. Hemoglobin/hematocrit
9. TLC
10. Platelets
11. KFT
12. Na/K
13. Bilirubin
14. pH
15. pO2/pCO2
16. Base excess/HCO3
17. GCS score
18. Culture reports

Parameters that were observed on Day 1 and Day 7:

1. Serum Presepsin

Parameter observed at the time of admission:

1. APACHE score

SAMPLE SIZE CALCULATION

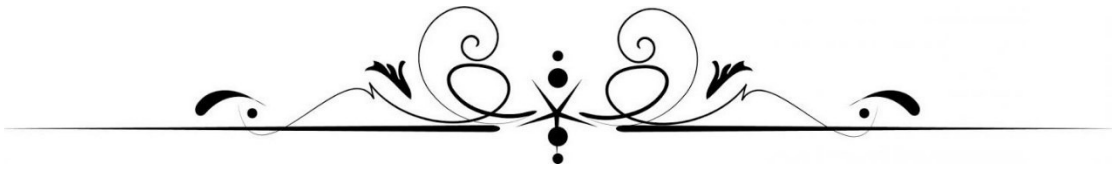
Sample size was calculated using OpenEpi software. Using data from Yoon SH et al[15], sample size as estimated was of 40 ICU patients at 95% confidence interval and 10% contingency.

$$n = Z^2pq/d^2 = (4^2x0.91x0.8)/0.091^2 = 35.2 \approx 36$$

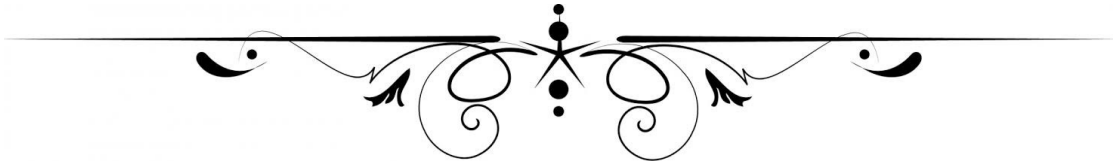
Adding 10% contingency, the final sample size is 40 ICU patients.

STATISTICAL ANALYSIS

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM Manufacturer, Chicago, USA, ver 28.0. Statistical significance was set at $p < 0.05$. Data was tested for normality using the Shapiro Wilk test. The quantitative data with normal distribution were presented as the means ± SE. The areas under the ROC curve (AUROC) were used to represent the discriminating abilities of the examined biomarkers (95 percent confidence interval [CI]). The Youden index was used to determine the best cutoff value for each ROC curve. (maximum of the sum 'sensitivity + specificity'). For presepsin and PCT, ROC curve analysis was used to predict 28-day mortality. The Youden index was used to identify the best cutoff value for predicting 28-day mortality. ROC curve analysis was finally performed for prognostication of organ failure (AKI). Paired t- test was applied to see any significant difference between day 1 and day 7 values of presepsin and PCT.



OBSERVATION & RESULTS



OBSERVATIONS AND RESULTS

Patient Data

Total number of patients admitted to the adult ICU at AIIMS Jodhpur during the study period was 768. Out of these, 126 patients were admitted with the suspicion of sepsis. Relatives of 12 patients out of these denied consent to participate in the study. Remaining 114 patients were assessed for eligibility to be recruited into the study. 8 patients were HIV or HBsAg positive and 3 were in terminal stages of malignant disease on chemotherapy, hence were excluded from the study. The remaining 103 patients were enrolled into the study. 21 patients died before day 7 of admission. Finally, 82 patients were recruited for the study.

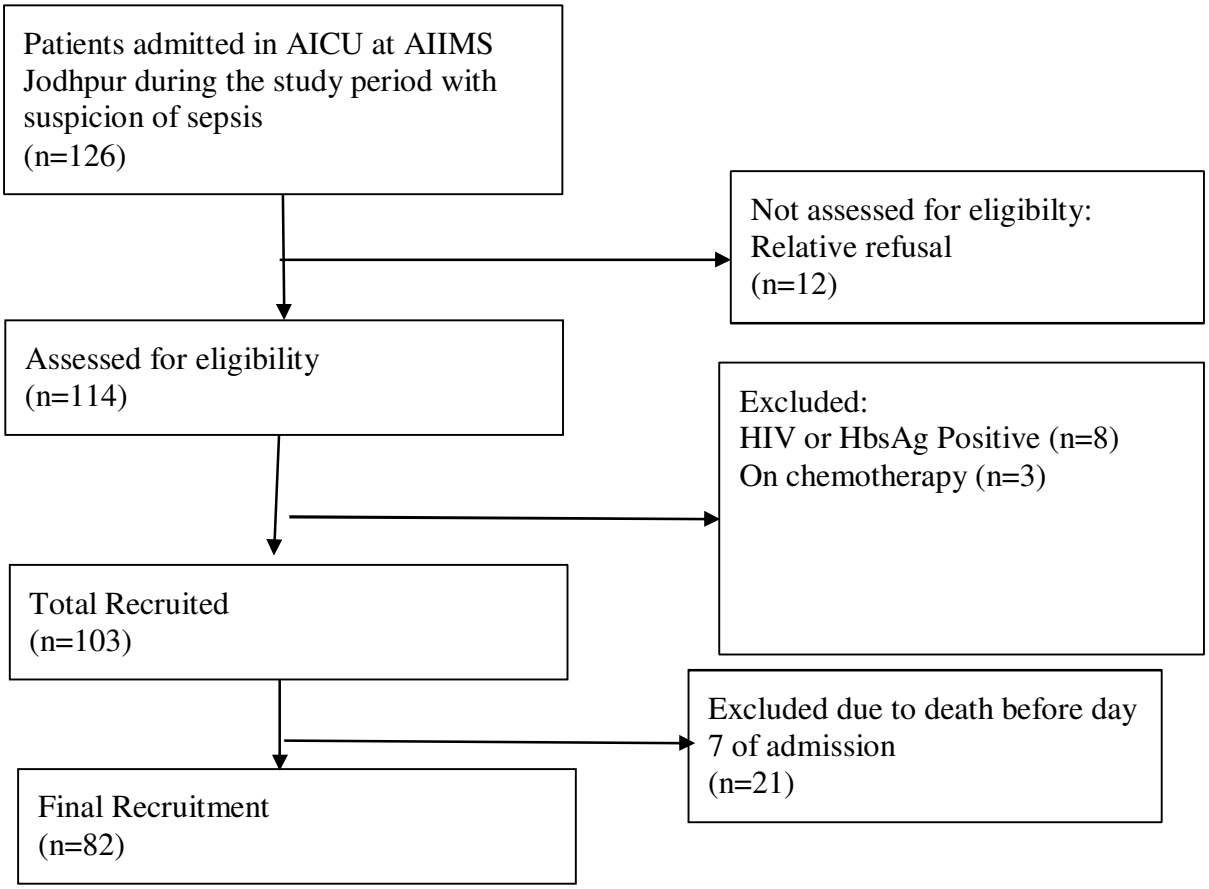


Figure 1: Flow diagram of **STROBES statement** is as follows:

Demographic Data

The mean age of the patients recruited in the study was 53.43±1.76 years (Mean±SE) with 95% confidence interval (95% CI) ranging from 49.86 to 57.26 years. Out of 82 patients in the study, most of the patients were in the age group ≥ 61 years constituting 37.80% of the total study population, 17 (20 %) were between 51 to 60 years, 15 (18%) were between 41 to 50 years, 9 (11%) were between 31 to 40 years (Table 1 & Figure 2). Out of 82 patients, 51 (62.20%) were males and 31 (37.80%) were females. (Table 2).

Table 1: Demographic distribution of patients.

Age	No. of Patients	Percentage (%)
21-30	10	12.20
31-40	9	10.98
41-50	15	18.29
51-60	17	20.73
≥ 61	31	37.80

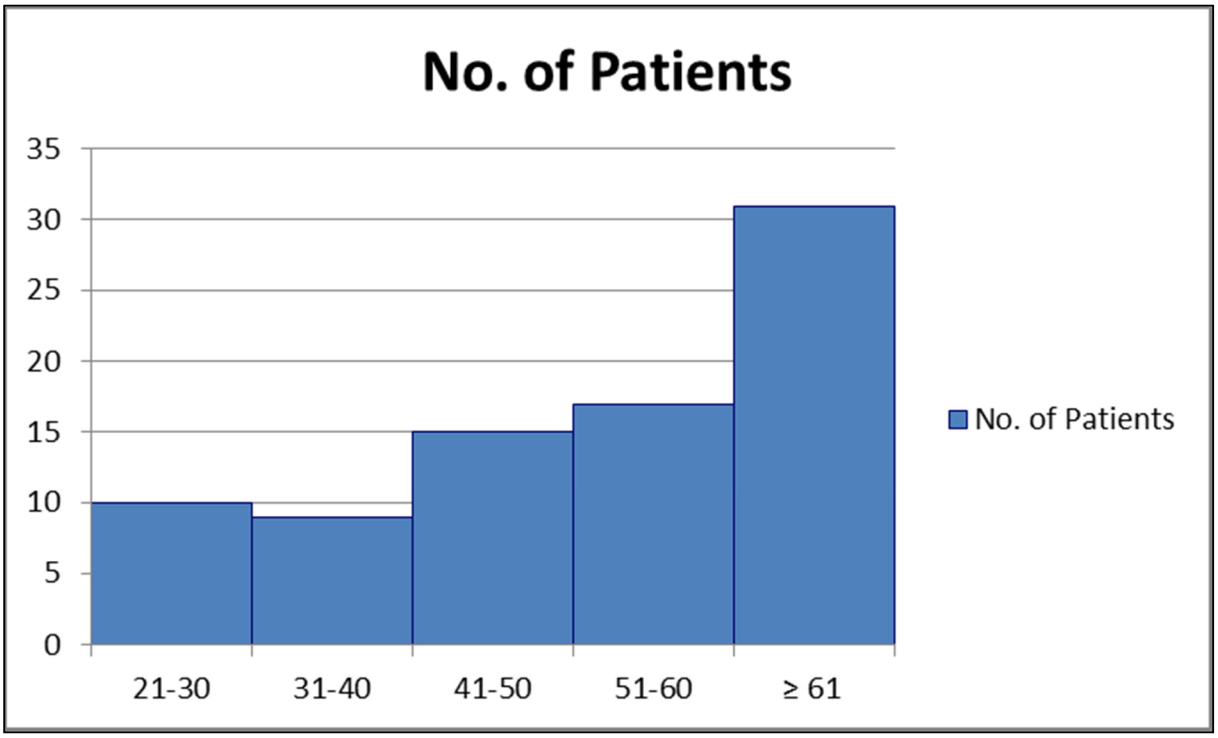


Figure 2: Bar chart of distribution of age group of patients

Table 2: Table representing gender distribution: Male patients presenting with features suggestive of sepsis were 62.20% as opposed to female patients who made up 37.80% of the study population.

Gender	No. of patients	Percentage
Male	51	62.20
Female	31	37.80

Microbiological Data

Out of 82 patents included in the study, 52 patients were found positive for culture test, accounting for 63.41 percent of the total number of patients included in the study. At the same time, there were 30 patients who had no culture positive during their hospital stay at the time the study was being conducted. They made up 36.59 percent of the total study participants (Table 3).

Table 3: The culture status of the patients.

Culture	No. of patients	Percentage
Positive	52	63.41
Negative	30	36.59

Mortality Data

In the study, 47 of the enrolled patients died within 28 days of onset of symptoms representing a 28 day mortality of 57.32% while 35 were discharged making up 42.68% of the study participants.

Table 4: Mortality of patients enrolled in the study.

Outcome	No. of patients	Percentage
Death	47	57.32
Discharge	35	42.68

Figure 3 shows the normal distribution of presepsin values measured on day 1 and figure 4 shows the normally distributed values of presepsin measured on day 7 of the study period. Hence mean ± SE was used to represent the data.

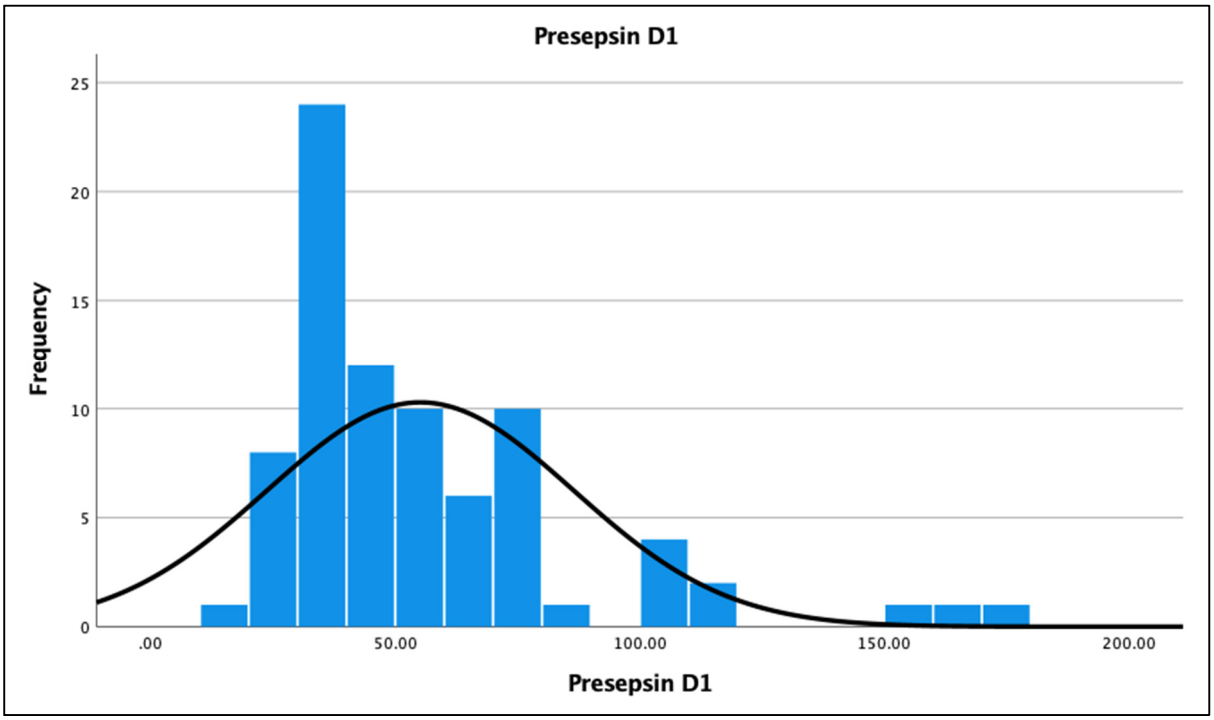


Figure 3 showing normal distribution of presepsin values measured on day 1

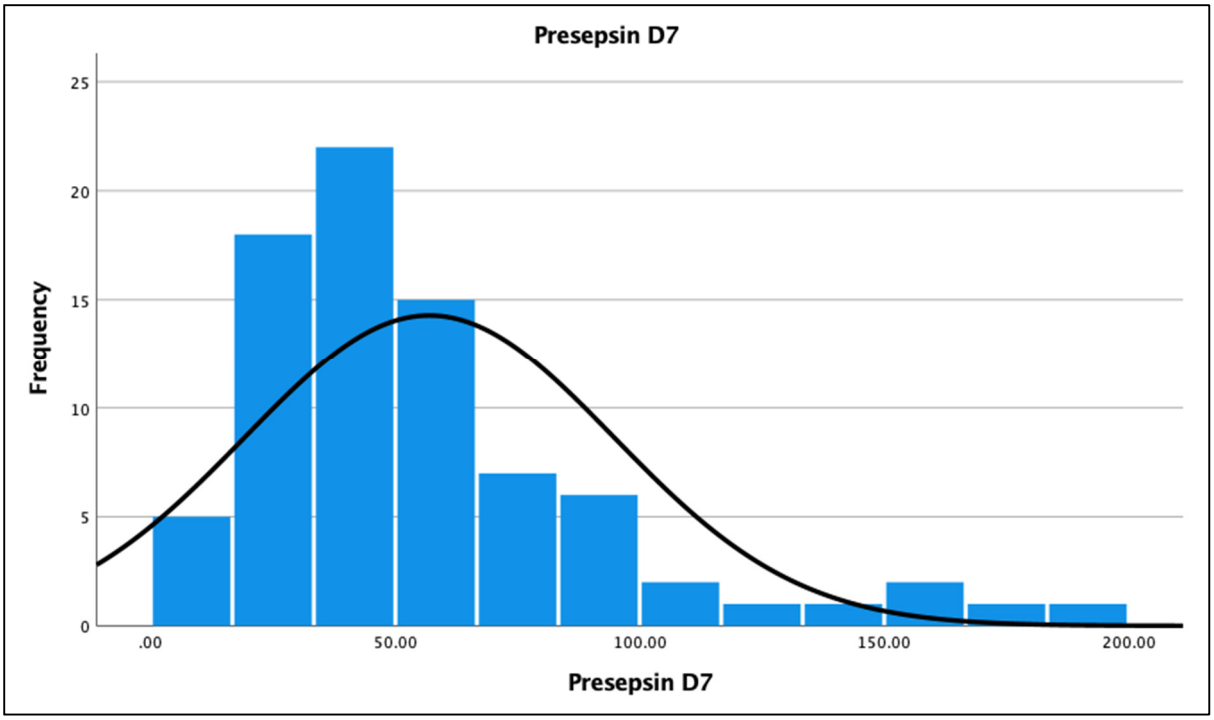


Figure 4 shows normal distribution of presepsin values measured on day 7.

Procalcitonin (PCT) was estimated in blood samples at the time of suspicion of sepsis during the ICU stay. This point was considered as day 1 (D1) and repeat estimation of PCT was done on the 7th day (D7). The mean value of PCT in patients who were culture negative was 5.04±2.15 ng/mL (Mean±SE) on D1 and the mean value of PCT on D7 was 5.95±2.97 ng/mL (Mean±SE). On the other hand, the mean value of PCT in patients who were culture positive was 10.34±2.94 ng/mL (Mean±SE) on D1 and 20.66±3.84 ng/mL (Mean±SE) on D7 (Table 5 & Figure 5).

Table 5: The mean value of PCT in ng/mL on day 1 & day7 in patients who were culture negative compared with those who were culture positive.

Cultures		**Mean**	**Standard error**	**95% CI**	
				Lower	**Upper**
Negative	D1	5.048	2.157	1.827	10.959
	D7	5.950	2.971	1.709	14.110
Positive	D1	10.345	2.941	5.271	17.099
	D7	20.661	3.847	14.177	29.426

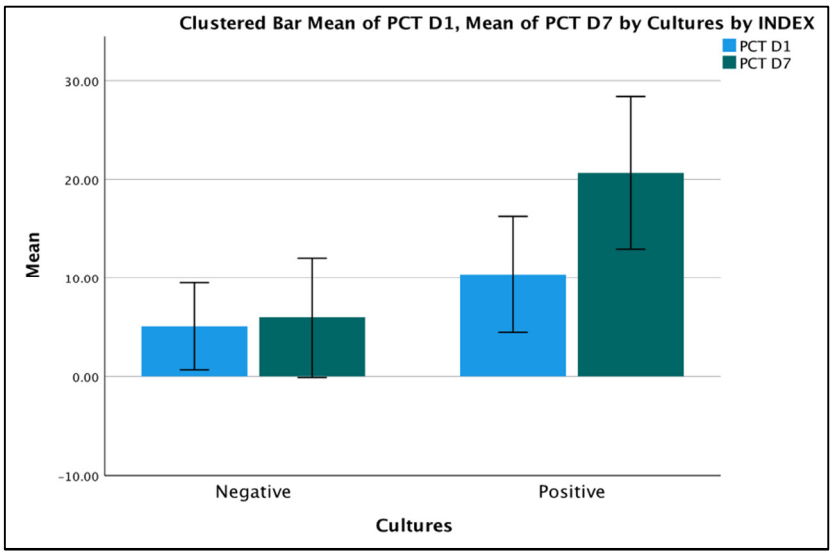


Figure 5: The mean value of PCT in culture negative and positive groups on D1 vs D7 during ICU stay.

The PCT values were also assessed by the outcome of patients either as death or discharge during 28 day follow up. The mean value of PCT in patients who died after 7 days during their ICU stay or during 28 days follow up was 4.77±1.16 ng/mL (Mean±SE) on D1 and the mean value of PCT on D7 was 25.44±4.20 ng/mL (Mean±SE). On the other hand, the mean value of PCT in patients who were discharged from ICU and were alive during 28 days follow up was 13.13±4.35 ng/mL (Mean±SE) on D1 and 1.21±0.22 ng/mL on D7 (Table 6 & Figure 6).

Table 6: The mean value of PCT in ng/mL on day 1 & day7 in patients who died vs the patients who were discharged.

Outcome		**Mean**	**Standard error**	**95% CI**	
				Lower	**Upper**
Death	D1	4.774	1.167	2.875	7.028
	D7	25.441	4.208	18.001	33.264
Discharge	D1	13.134	4.356	7.431	24.504
	D7	1.212	0.229	0.809	1.687

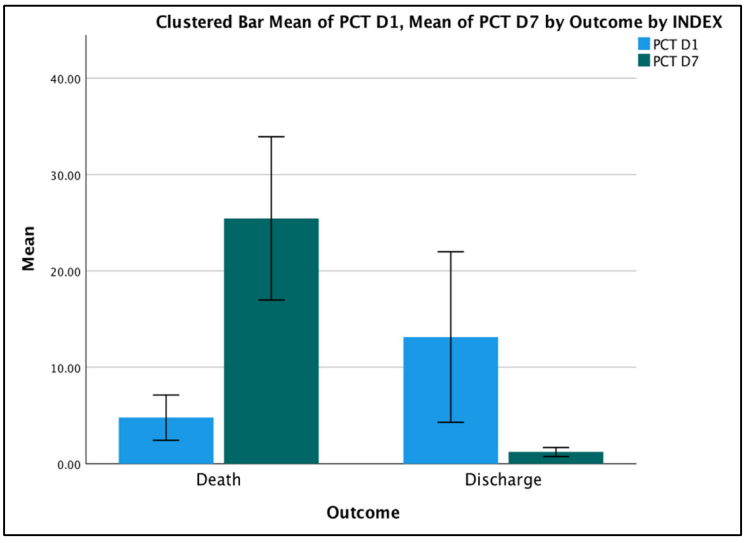


Figure 6: The mean value of PCT on D1 vs D7 in patients who died vs the patients who were discharged during ICU stay.

The subgroup analysis was done to see the procalcitonin (PCT) values in patients whose all cultures were negative but died during ICU stay and the group was compared with the PCT values of those whose cultures were positive and died during ICU stay or during 28 day follow up. Similar comparison was also done for the patients who were discharged from the ICU. The value of PCT on D1 in patients who were culture negative and died during ICU stay or during 28 day follow up was 2.35±0.761 ng/mL (Mean±SE) which was found increased on D7 to 12.145±6.8 ng/mL (Mean±SE) whereas the mean value of PCT in patients who were discharged was 6.99±3.65 ng/mL (Mean±SE) on D1 which was decreased to 1.47±0.32 ng/mL on D7 (Table 7).

Similarly, the PCT was estimated in blood of patients who were culture positive during their ICU stay. The value of PCT on D1 in patients who were culture positive and died during ICU stay or during 28 day follow up was 5.70±1.56 ng/mL (Mean±SE) which was found increased on D7 to 30.52±4.97 ng/mL (Mean±SE) whereas the mean value of PCT in patients who were discharged was 19.63±7.93 ng/mL (Mean±SE) on D1 which was decreased to 0.93±0.32 ng/mL on D7 (Table 7)

Table 7: The values of procalcitonin (PCT) on day1 and day 7 during ICU stay.

Cultures	Outcome	PCT	n	Mean	SE	95% Confidence interval	
Negative	Death	PCT D1	13	2.350	0.761	1.002	4.532
		PCT D7	13	12.145	6.850	2.672	30.870
	Discharge	PCT D1	18	6.996	3.650	1.723	15.603
		PCT D7	18	1.476	0.321	0.898	2.241
Positive	Death	PCT D1	34	5.701	1.566	2.555	9.064
		PCT D7	34	30.525	4.977	21.095	40.360
	Discharge	PCT D1	17	19.634	7.932	5.177	34.092
		PCT D7	17	0.932	0.322	0.512	1.670

Presepsin was measured in blood samples at the time of suspicion of sepsis during the ICU stay, just like PCT. Day 1 (D1) was chosen as the starting point, and the presepsin estimation was repeated on the seventh day (D7). The mean value of presepsin in patients who were culture negative was 62.70±8.76 ng/L (Mean±SE) on D1 and the mean value of presepsin on D7 was 58.08±7.67 ng/L (Mean±SE). On the other hand, the mean value of presepsin in patients who were culture positive was 66.21±5.30 ng/L (Mean±SE) on D1and 83.89±7.56 ng/L (Mean±SE) on D7 (Table 8 & Figure 7).

Table 8: The mean value of presepsin in ng/L on day 1 & day7 in patients who were culture negative compared with those who were culture positive.

Cultures		**Mean**	**Standard error**	**95% CI**	
				Lower	**Upper**
Negative	D1	62.709	8.766	44.517	84.967
	D7	58.080	7.674	42.635	72.653
Positive	D1	66.211	5.301	56.841	75.542
	D7	83.897	7.564	65.397	97.727

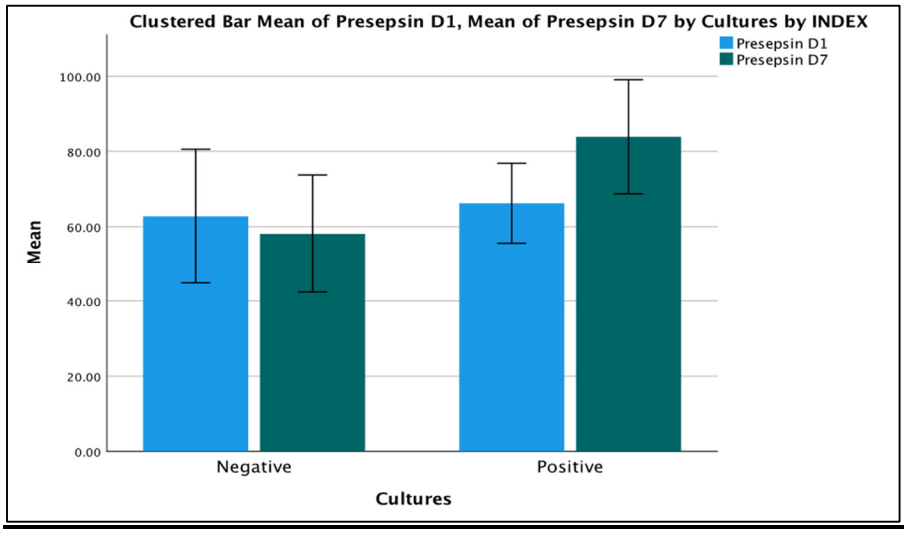


Figure 7: The mean value of presepsin in culture negative and positive groups on D1 vs D7 during ICU stay.

During the 28-day follow-up period, the presepsin values were also evaluated by the patients' outcomes, which included death or discharge. The mean value of presepsin in patients who died after 7 days during their ICU stay or during 28 days follow up was 64.85±5.59 ng/L (Mean±SE) on D1 and the mean value of presepsin on D7 was 99.48±7.38 ng/L (Mean±SE). On the other hand, the mean value of presepsin in patients who were discharged from ICU and were alive during 28 days follow up was 64.93±7.97 ng/L (Mean±SE) on D1and 40.10±4.57 ng/L on D7 (Table 9 & Figure 8).

Table 9: The mean value of presepsin in ng/L on day 1 & day7 in patients who died vs the patients who were discharged.

Outcome		**Mean**	**Standard error**	**95% CI**	
				Lower	**Upper**
Death	D1	64.854	5.594	52.946	74.556
	D7	99.483	7.385	84.877	116.560
Discharge	D1	64.933	7.976	51.851	81.424
	D7	40.102	4.572	32.795	52.930

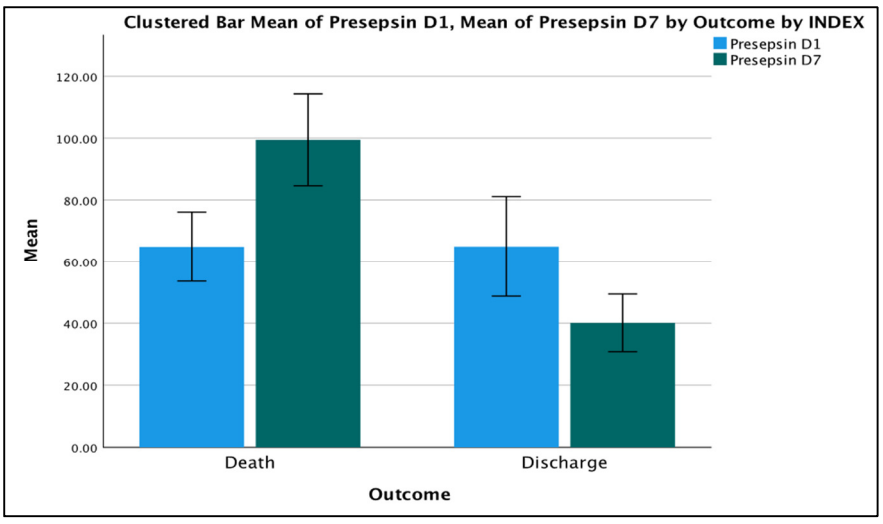


Figure 8: The mean value of presepsin on D1 vs D7 in patients who died vs the patients who were discharged during ICU stay.

The presepsin values in patients whose all cultures were negative but died during ICU stay were compared to the presepsin values in patients whose cultures were positive but died during ICU stay or during the 28-day follow-up period. Patients who were discharged from the ICU were compared in the same way. The value of presepsin on D1 in patients who were culture negative and died during ICU stay or during 28 day follow up was 58.75±13.78 ng/L (Mean±SE) which was found increased on D7 to 80.27±12.17 ng/L (Mean±SE) whereas the mean value of presepsin in patients who were discharged was 65.56±11.64 ng/L (Mean±SE) on D1 which was decreased to 42.05±8.21 ng/L on D7 (Table 10).

Similarly, the presepsin level in the blood of patients who had a positive culture during their ICU stay was determined. The value of presepsin on D1 in patients who were culture positive and died during ICU stay or during 28 day follow up was 67.18±5.76 ng/L (Mean±SE) which was found increased on D7 to 106.82±8.86 ng/L (Mean±SE) whereas the mean value of presepsin in patients who were discharged was 64.26±11.21 ng/L (Mean±SE) on D1 which was decreased to 38.03±3.88 ng/L on D7 (Table 10).

Table 10: The values of presepsin on day1 and day 7 during ICU stay.

Cultures	Outcome	Presepsin	n	Mean	Standard error	95% Confidence interval	
Negative	Death	Presepsin D1	13	58.757	13.783	35.550	96.031
		Presepsin D7	13	80.271	12.171	57.073	111.802
	Discharge	Presepsin D1	18	65.564	11.643	48.276	96.784
		Presepsin D7	18	42.053	8.212	30.046	62.295
Positive	Death	Presepsin D1	34	67.185	5.769	54.329	77.583
		Presepsin D7	34	106.828	8.865	88.491	128.855
	Discharge	Presepsin D1	17	64.264	11.214	47.030	87.779
		Presepsin D7	17	38.036	3.882	30.230	46.295

ROC Analysis

As with the coordinates of the ROC curve which is given in Figure 9, the presepsin value on day 1 enabling the best sensitivity and specificity in diagnosing sepsis is 36.9 ng/L while the cut off value of PCT to diagnose sepsis is 1.68 ng/mL (maximum Youden index)

The sensitivity at this value is 78% for presepsin as compared to PCT which is 69%.

The specificity of presepsin 53% while that of PCT is 56%.

The area under the curve (AUROC) for presepsin day 1 is 0.616 (p=0.06) and that for PCT is 0.590 (p=0.19). This suggests that day 1 values of presepsin are better able to discriminate between sepsis and non sepsis patients than PCT day 1 readings.

The combined sensitivity when the 2 tests are used in parallel is 93%.

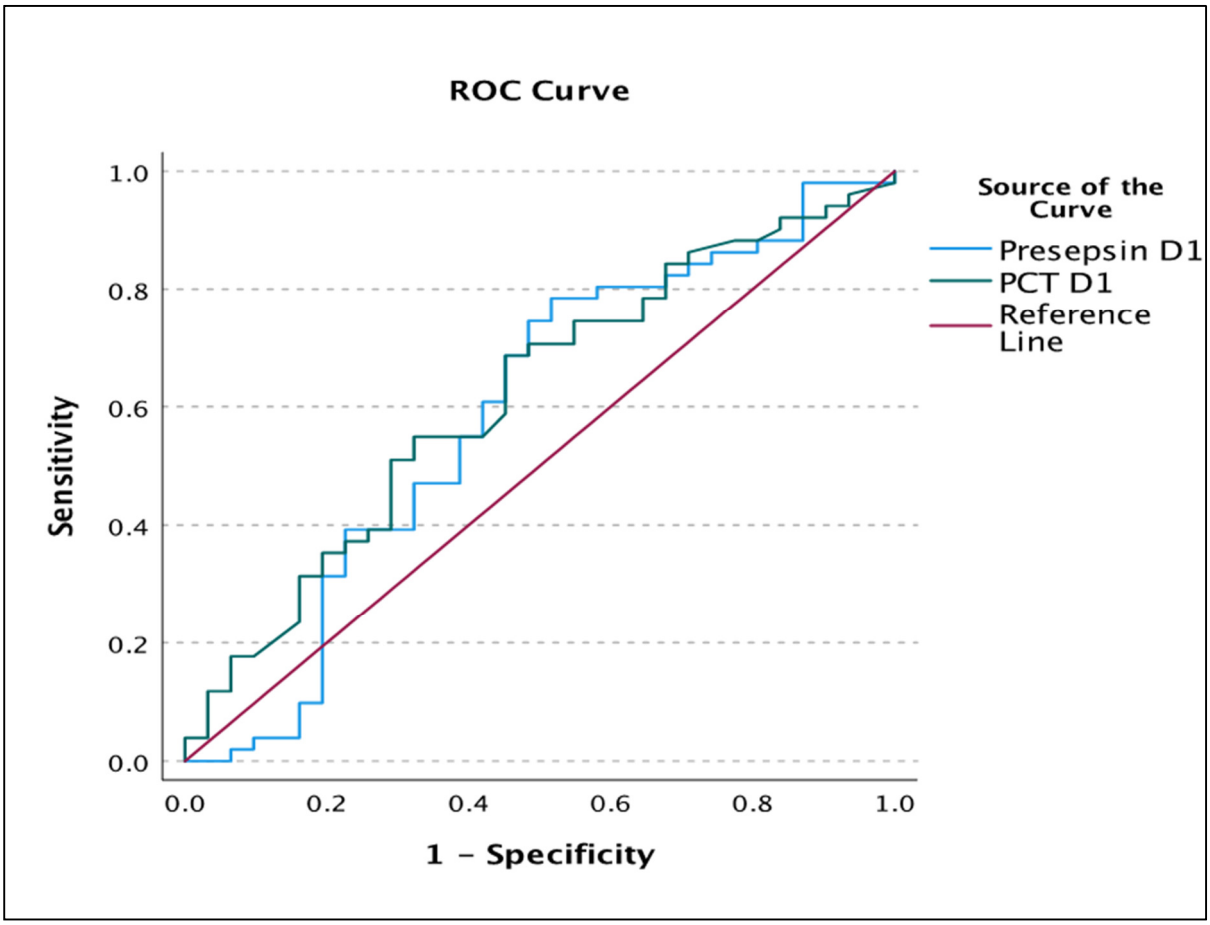


Figure 9: ROC curve of Presepsin and PCT values on D1 against culture positivity for diagnosis of sepsis

The sensitivity at this cut-off value on day 7 is 80% for presepsin as compared to PCT which is 66% as seen in figure 10.

The specificity is 39% for presepsin and 59% for PCT.

The area under the curve (AUROC) is 0.677 ($p<0.05$) for presepsin day 7 and 0.657 ($p<0.05$) for PCT and is a satisfactory indicator of the significance of the study.

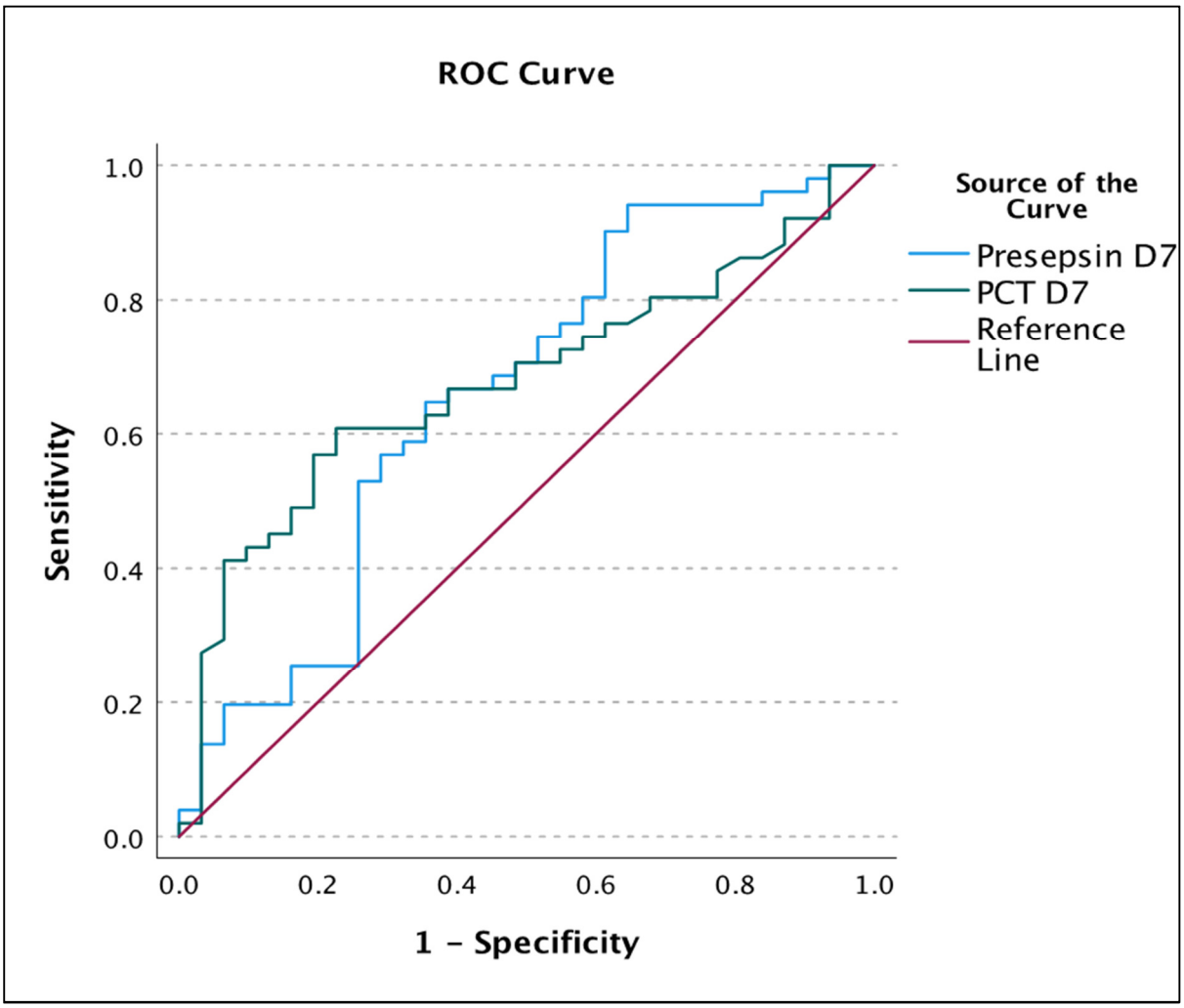


Figure 10: ROC curve of Presepsin and PCT values on D7 against culture positivity for diagnosis of sepsis

As with the coordinates of the ROC curve which is given in Figure 11, the presepsin value enabling the best prediction of mortality is 50.35 ng/L while the PCT value allowing best prognostication of 28 day mortality is 3.2 ng/mL (by maximizing Youden Index). The area under the curve (AUROC) is 0.896 ($p<0.05$) for presepsin and 0.894 ($p<0.05$) for PCT which denotes excellent discrimination between patients likely to die from those likely to survive. Thus, the sensitivity of presepsin for prognostication of 28 day mortality is 91% and specificity is 82% at this cutoff. The sensitivity of PCT at this cutoff for prognostication of 28 day mortality is 78% and specificity is 94%.

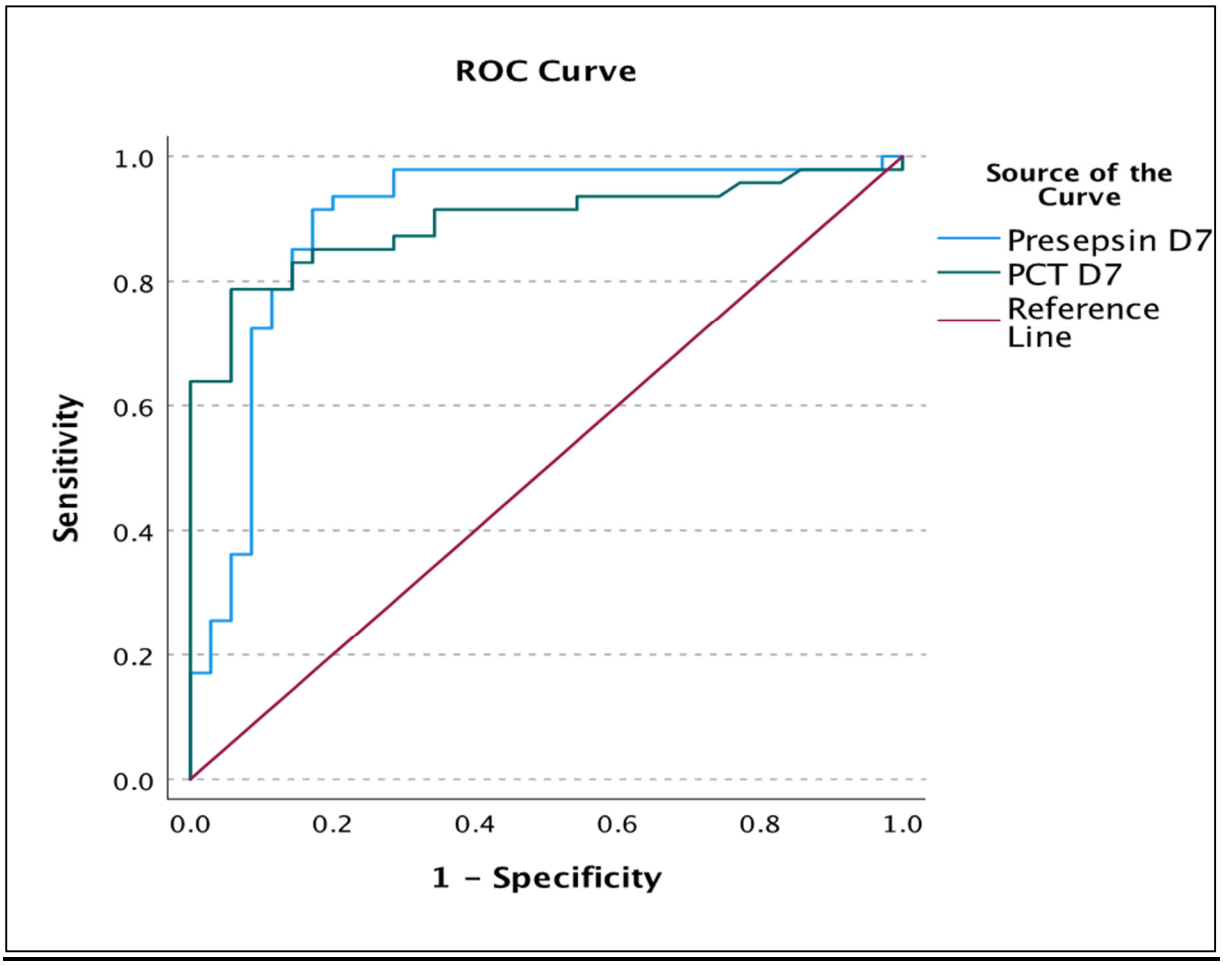


Figure 11: ROC curve of Presepsin and PCT values on D7 against outcome to prognosticate 28 day mortality

Paired t- test

Results of paired sample T- test shows that in the culture negative group there is no significant change in PCT as well as presepsin levels from D1 to D7. In the culture positive group, there is a significant change in PCT levels from D1 to D7 with a two tailed p value of 0.03. There is also a significant change in presepsin levels from D1 to D7 with a P value of 0.02 (Table 11)

Table 11: Paired t- test depicting trend of PCT and presepsin from D1 to D7 in culture negative and positive groups

Cultures			**Mean**	**Standard error**	**95% confidence interval**		**Two sided p value**
					Lower	**Upper**	
Negative	Pair 1	PCT D1- PCT D7	0.902	3.607	8.270	6.465	0.804
	Pair 2	Presepsin D1- Presepsin D7	4.629	7.008	9.684	18.943	0.514
Positive	Pair 1	PCT D1- PCT D7	10.315	4.832	20.022	0.608	0.038
	Pair 2	Presepsin D1- Presepsin D7	17.685	7.746	33.244	2.127	0.027

Similar to this, when PCT trends are seen from D1 to D7 in the mortality group, there is a significant change in levels of PCT with a P value of < 0.001. Even with presepsin, a significant change in level is seen from D1 to D7 with a P value of < 0.001. In the survivor group, significant change in PCT levels are seen from D1 to D7 with a P value of 0.01 while values of presepsin also showed a significant change fromD1 to D7 with P value of < 0.001 (Table 12).

Table 12: Paired t- test depicting trend of PCT and presepsin from D1 to D7 in death and discharge group

Outcome			**Mean**	**Standard error**	**95% confidence interval**		**Two sided p value**
					Lower	**Upper**	
Death	Pair 1	PCT D1-PCT D7	20.666	3.655	28.025	-13.308	<0.001
	Pair 2	Presepsin D1-Presepsin D7	34.628	6.657	48.029	-21.228	<0.001
Discharge	Pair 1	PCT D1-PCT D7	11.922	4.412	2.955	20.888	0.011
	Pair 2	Presepsin D1-Presepsin D7	24.830	5.908	12.822	36.838	<0.001

Organ Failure Data

43 patients suffered AKI out of 82 patients enrolled in the trial, accounting for 52.44% of the total number of patients. Simultaneously, 39 patients did not acquire AKI during their hospital stay at the time the study was being carried out. They made up 47.56% of all participants in the study. (Table 13 and figure 12).

Table 13: AKI in patients enrolled in the study

AKI	No. of patients	Percentage
Yes	43	52.44
No	39	47.56

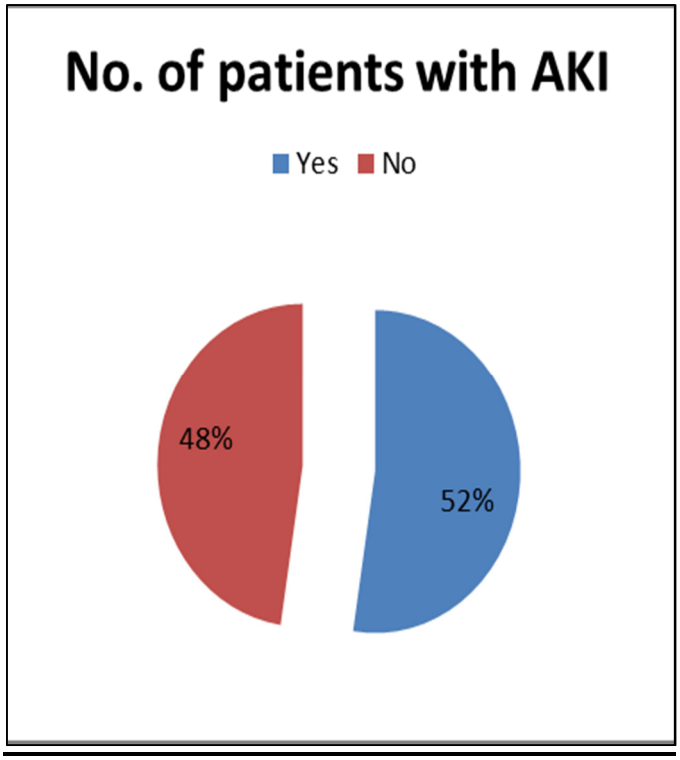


Figure 12: Percentage of patients with AKI

Twenty-five patients suffered shock out of the 82 participants in the study, corresponding to 30.49% of the total number of patients. Meanwhile, 57 patients did not develop shock during their hospitalization at the time the study was being done. They made up 69.51% of the total number of people that took part in the study.(Table 14 and figure 13)

Table 14: Shock in patients enrolled in the study

Shock	**No. of patients**	**Percentage**
Yes	25	30.49
No	57	69.51

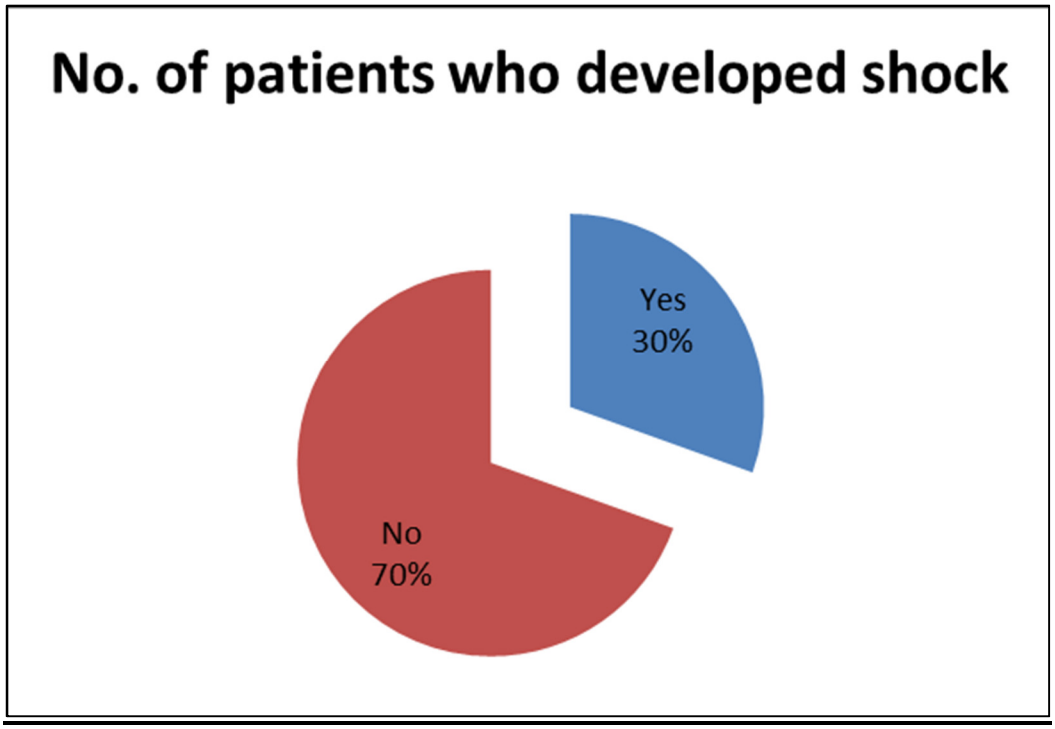


Figure 13: Percentage of patients who developed shock

The ability of presepsin to prognosticate multi organ failure was studied by considering acute kidney injury in patients.

As we see in this figure 14, AKI is taken as dependent variables. The AUC is 0.70 ($p<0.05$) for presepsin D1 and 0.71 ($p<0.05$) for presepsin D7. Presepsin is thus a good discriminator between patients likely to develop AKI and non AKI patients.

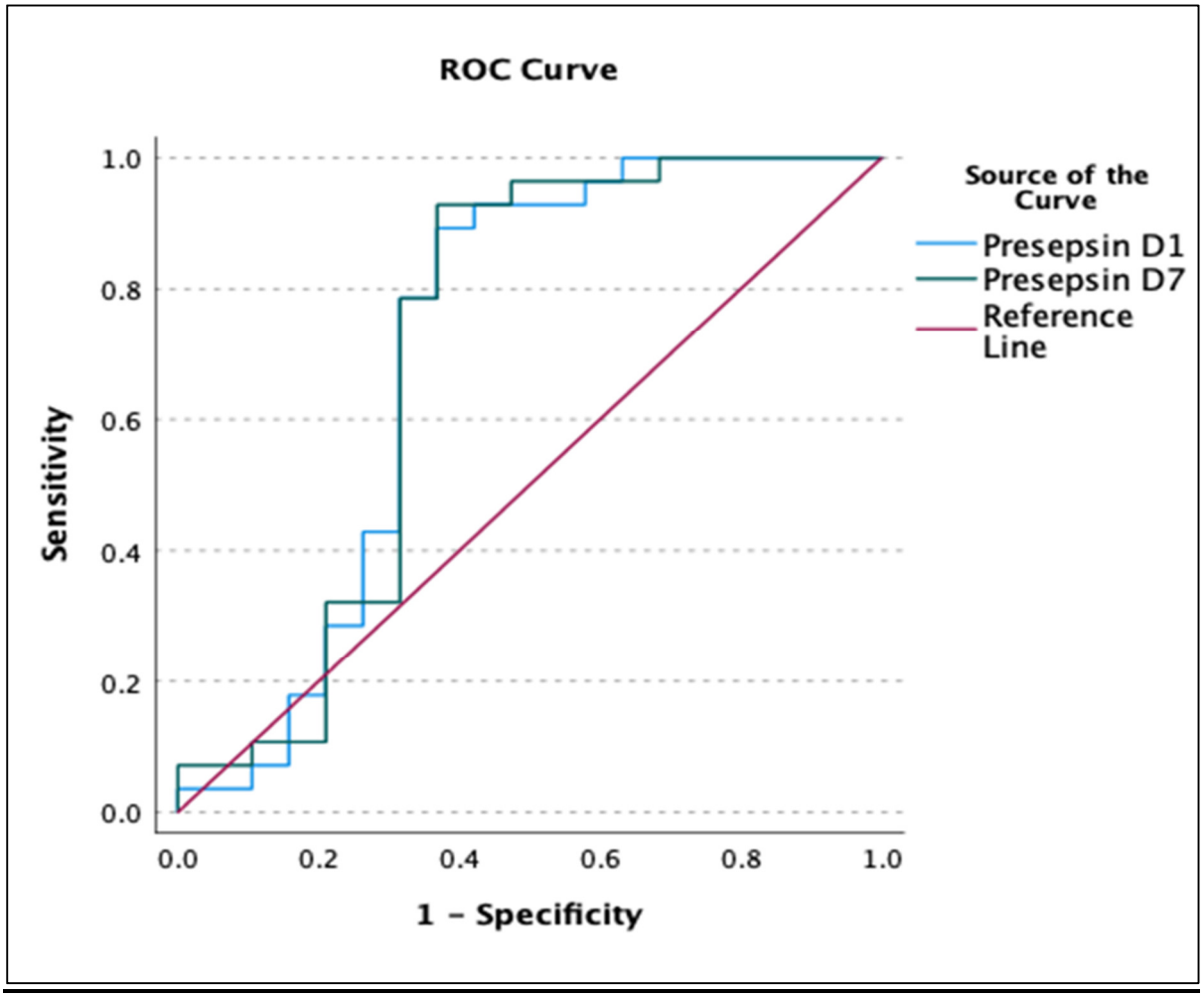


Figure 14: ROC curve of Presepsin values on D1 and D7 against AKI

SOFA scores were calculated as a means of measuring organ failure. The mean value of SOFA in patients who were culture negative was 7.61±0.62 (Mean±SE). On the other hand, the mean value of SOFA in patients who were culture positive was 8.64±0.50 (Mean±SE) (Table 15).

Table 15: The mean SOFA score in patients who were culture negative compared with those who were culture positive.

Cultures	**Mean**	**Standard error**	**95% CI**	
			Lower	**Upper**
Negative	7.612	0.621	6.404	8.994
Positive	8.647	0.500	7.336	9.729

APACHE score was calculated at the time of admission as an indicator of disease severity. The mean value of APACHE score in patients who were culture negative was 17.32±1.40 (Mean±SE). On the other hand, the mean value of APACHE score in patients who were culture positive was 18.98±0.86 (Mean±SE) (Table 16).

Table 16: The mean APACHE scores in patients who were culture negative compared with those who were culture positive.

Cultures	**Mean**	**Standard error**	**95% CI**	
			Lower	**Upper**
Negative	17.322	1.401	14.872	20.246
Positive	18.980	0.864	17.070	20.843

Similarly SOFA scores were also correlated with outcome The mean value of SOFA in patients who died was 9.78±0.52 (Mean±SE). On the other hand, the mean value of SOFA in patients who were discharged was6.20±0.37 (Mean±SE) (Table 17)

Table 17: The mean SOFA scores in patients who died vs the patients who were discharged.

Outcome	**Mean**	**Standard error**	**95% CI**	
			Lower	**Upper**
Death	9.787	0.524	8.623	10.694
Discharge	6.200	0.373	5.352	6.768

Likewise APACHE scores were also correlated with outcome The mean value of APACHE in patients who died was 22.46±0.79 (Mean±SE). On the other hand, the mean value of APACHE in patients who were discharged was 12.85±0.68 (Mean±SE) (Table 18)

Table 18: The mean APACHE scores in patients who died vs the patients who were discharged.

Outcome	**Mean**	**Standard error**	**95% CI**	
			Lower	**Upper**
Death	22.446	0.799	21.082	24.271
Discharge	12.857	0.684	11.612	14.109

DISCUSSION

DISCUSSION

Sepsis has long been considered a terrible disease with possibly fatal implications. Even as hospitals implement the Surviving Sepsis Campaigns' recommendations, sepsis mortality remains unacceptably high. As a result, it's critical to diagnose sepsis as soon as possible so that effective treatment may be started. Procalcitonin is a well-known biomarker while presepsin is a new biomarker that has received little attention in the Indian population. Our study comparatively evaluated the diagnostic as well as short- term prognostic value of sCD14-ST - that is - presepsin, with PCT in patients with sepsis during the first week of intensive care treatment at days 1 and 7.

As presepsin is a relatively new inflammatory marker and studies in the Indian population are rather limited, we first set out to define a cut off value for presepsin in the Indian population for the diagnosis of sepsis. For this, a receiver operating characteristic (ROC) curve was plotted against culture positivity which was considered the gold standard test for sepsis detection. The coordinates of the ROC curve were analyzed, and the presepsin value enabling the best sensitivity and specificity (maximum Youden index) was determined to be 36.9 ng/L. The sensitivity of presepsin for the diagnosis of sepsis at this cut off value was 78%. Similar analysis for PCT was done using ROC curve which defined a cut off value of 1.68 ng/mL as optimum (maximum Youden index). Sensitivity of PCT at this value was marginally less than presepsin at 69%. The specificities of both presepsin and PCT were moderate at 53% for presepsin and 56% for PCT.

Sukyo Lee *et al* [27] conducted a prospective observational study on 420 patients meeting Sepsis 3 criteria. Using a presepsin cutoff value of 582 pg/ml (ng/L) for diagnosing sepsis, the sensitivity was 70.1% and specificity was 89%. Using a cutoff value of 0.51 ng/ml for, the sensitivity was 75.5% and specificity was 93%. The sensitivity of presepsin as determined from their study is very similar to that from our study. However PCT is more sensitive as per their study.

Yamamoto *et al* [4] conducted a prospective study where a total of 91 patients were enrolled. They found that presepsin has 87 percent sensitivity and 86 percent specificity for diagnosing sepsis with a threshold of 508 pg/mL. Procalcitonin sensitivity was determined to be 68 percent and specificity to be 86 percent using a 1.5 ng/mL threshold. Our study similarly showed higher sensitivity for presepsin as compared to PCT.

The varying cut off values reported by different research studies is evident. This could be attributed to the difference in study design (retrospective versus prospective), sepsis severity, comorbidities, ELISA kit specifications, and population demographics (Indian population vs Western population) and in clinic settings (ED vs ICU)

Presepsin is a sensitive biomarker for sepsis diagnosis, and it can be used to screen for sepsis in the emergency room or intensive care unit. When PCT is administered as a supplement to presepsin, the combined sensitivity is high (93%).

Our studies showed an optimal cut off value of presepsin for prognostication of 28 day mortality to be 50.35 ng/L (maximum Youden index). At this cut off, presepsin had a high sensitivity of 91% and a high specificity of 82%. PCT value allowing best prognostication was 3.2 ng/L. The sensitivity of PCT at this cutoff for prognostication of 28 day mortality is 78% and specificity is 94%.

Jong Eun Park *et al* [35] in their study proposed a cut off value of 755 pg/mL for predicting 28 day mortality. This cut off had a sensitivity of 77.5% and specificity of 62%.

Ulla *et al* [8] demonstrated increased risk of death within 60 days in patients with increased presepsin levels ≥1,000 pg/ml.

Masson *et al* [31] demonstrated constantly increased presepsin levels in decedents and revealed significant prognostic value for both 28-day and 90-day all-cause mortality in a retrospective analysis of patients with severe sepsis and septic shock, whereas PCT failed to provide any prognostic information.

Therefore when compared to PCT, presepsin has consistently performed well in predicting 28-day mortality, as evidenced by multiple studies. This is comparable to our study, where in addition we also established a cut-off value for the Indian population for 28-day mortality prognosis.

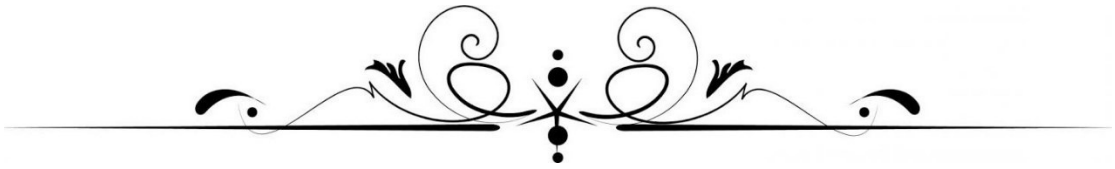
Next we have studied the ability of presepsin to prognosticate multi organ failure. Taking AKI as a dependent variable, the ROC curve was plotted. The AUC is 0.70 ($p<0.05$) for presepsin D1 and 0.71 ($p<0.05$) for presepsin D7. Presepsin is thus a good discriminator between patients likely to develop AKI and non AKI patients.

Most trials, so far, have focused on only single measurements of presepsin in patients

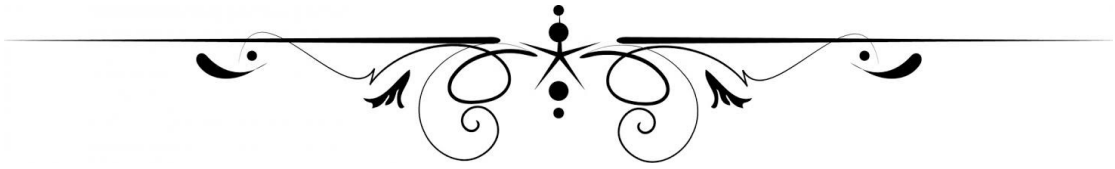
presenting to the emergency department or ICU, and have attempted to establish presepsin as an early single-shot biomarker for emergency care. However, during ICU care, a systematic diagnostic and prognostic evaluation of the individual patient with severe sepsis is indicated to establish treatment goals, monitor therapeutic effects, and guide clinical decision-making.

In our study, we measured both presepsin and PCT at 2 time points- day 1 and day 7. We found that a significant rise is seen from day 1 to day 7 in the value of presepsin in the decedents ($P < 0.001$). On the other hand, in the survivors, presepsin showed a significant decline from day 1 to day 7 ($P < 0.001$). This shows that presepsin trends could be utilized to assess the efficacy of therapy, be it etiologic, supportive, or both.

Although cultures are the gold standard for determining whether or not an infection exists in the body, they are not always accurate. Antibiotics, occult infections, and the type of organism that causes sepsis can all have an adverse effect on culture results. They are also time consuming. In this situation, having quick and reliable assays in our arsenal to diagnose sepsis is critical. Our study establishes presepsin as a robust predictive biomarker in patients with sepsis, especially when coupled with PCT. Presepsin is also an excellent marker for predicting 28 day mortality as compared to PCT especially at an early stage. Using presepsin in combination with PCT, it will be possible not only to diagnose sepsis early, but also to forecast the risk of 28 day mortality. This way, it may be possible to improve mortality rates or halt the progression to organ failure by identifying patients with risk of potentially adverse outcomes and enabling early and aggressive treatment. This is one of the first studies of presepsin in an adult Indian population in India. We have attempted to define a presepsin cut-off value in the Indian population with this study. More research in larger populations is needed to better identify cutoff values for diagnosis of sepsis and prediction of 28-day mortality in the Indian population.



CONCLUSION & LIMITATION



CONCLUSION

It can be concluded that complementary use of presepsin with procalcitonin is good for screening of sepsis in ICU and emergency departments. Presepsin has a high sensitivity for prediction of 28 day mortality which shows that it is a significant marker of mortality is sepsis. We also postulated a new cut off for presepsin for the Indian population. These findings can improve the outcome of sepsis by early institution of aggressive therapy in patients with high presepsin values thus potentially improving the mortality rates in sepsis. Further multicenter prospective studies with larger populations are needed to determine the optimal cut-off value of presepsin for the diagnosis and prognosis of sepsis.

LIMITATIONS

1. A relatively small number of patients were included, although the estimated power of the study was sufficient to detect significant reliable results.

2. This was a single-center study. A multi center study to evaluate the perfect cut-off point of such biomarkers in the Indian population is recommended.

3. PCT was measured by point of care testing while presepsin was measured by ELISA which may contribute to some error in the result.

4. Though serial rise in presepsin was measured by taking samples at day 1 and day 7, further multiple measurements at shorter intervals may yield more information especially pertaining to 28 day mortality.

5. Although cultures are probably the gold standard to confirm the presence of an infection in the body, it does not always yield accurate results. Previous treatment with antibiotics, occult infections and the organism involved in sepsis can all adversely affect the result of cultures

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ANNEXURES

ANNEXURE – 1

Ethical Clearance Certificate

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/2024

Date: 01/01/2020

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/996**

Project title: **"Comparing the diagnostic accuracy of presepsin and procalcitionin for sepsis in critically ill patients: A prospective observational study"**

Nature of Project:	**Research Project**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr.Shipra Roy**
Guide:	**Dr.Nikhil Kothari**
Co-Guide:	**Dr.Pradeep Kumar Bhatia, Dr.Praveen Sharma, Dr.Ankur Sharma & Dr.Shrimanjunath Sankanagoudar**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Enclose:
1. Annexure-I

Dr. Praveen Sharma
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Page 1 of 2

Basni Phase-2, Jodhpur, Rajasthan-342005, **Website:** www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
Email: ethicscommittee@aiimsjodhpur.edu.in

ANNEXURE - 2

Informed Consent Form

TITLE: COMPARING DIAGNOSTIC ACCURACY OF PRESEPSIN & PROCALCITONIN FOR SEPSIS IN CRITICALLY ILL PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

Name of PG Student: Dr. SHIPRA ROY

Telephone no: 9632692069 Patient Identification No: _____

I,_____S/o or D/o,_____r/o_____

give my full, free, voluntary consent for my patient to be a part of the study "**Title: Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study**" the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my patient's participation is voluntary, and I am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about my patient and any of my patient's medical records may be looked at by responsible individuals from AIIMS Jodhpur or from regulatory authorities. I give permission for these individuals to have access to my patient's records. I also give my consent for publication of my medical data for scientific and academic purposes.

Date: _____ _____

Place: _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date : _____ _____

Place : _____ Signature of PG Student

1. Witness 1 2. Witness 2

Signature Signature

Name: _____ Name: _____

Address : _____ Address : _____

ANNEXURE - 3

अखिल भारतीय चिकित्सा विज्ञान संस्थान, जोधपुर, राजस्थान

सूचित सहमतिप्रपत्र

थीसिस / निबंधकाशीर्षक: **Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study**

पीजी छात्र का नाम: डॉ शिप्रा रॉय रोगी / स्वयं सेवक पहचान संख्या: _____

नं..9632692069

मैं,_____एस/ओयाडी/ओ_____आर/ओ_____

_____ मेरे मरीज़ के लिए **"Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study."**अध्ययन का हिस्सा बनने के लिए मेरी पूर्ण, नि: शुल्क, स्वैच्छिक सहमति देता/देती हूँ।

मेरी पूर्ण संतुष्टि के लिए मेरी भाषा में प्रक्रिया और प्रकृति को मुझे समझाया गया है।मैं पुष्टि करता हूं कि मुझे प्रश्न पूछने का अवसर मिला है। मैं समझता हूं कि मेरी मेरे मरीज़ की भागीदारी स्वैच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय मेरे मरीज़ को अध्ययन से बाहर निकलने के मेरे अधिकार की जानकारी है। मैं समझता हूं कि मेरे मरीज़ के मेडिकल रिकॉर्ड के बारे में एकत्रित की गई जानकारी को _____ (कंपनी नाम) या विनियामक प्राधिकरणों से जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन लोगों के लिए मेरे मरीज़ के रिकॉर्डों तक पहुंच की अनुमति देता हूं। मैं इस बात की अनुमति देता हु की मेरे मेडिकल रिकार्ड्स को वैज्ञानिक और शैक्षिक प्रयोजनों के लिए इस्तेमाल किया जा सकता है

तारीख : _____.

जगह: _____ हस्ताक्षर / बाएं अंगूठे का छाप

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है

तारीख : _____

जगह: _____ पी जी छात्र के हस्ताक्षर

गवाह 1 गवाह 2

ANNEXURE – 4

Participant information sheet

All India Institute of Medical Sciences Jodhpur, Rajasthan

All India Institute of Medical Sciences

Jodhpur, Rajasthan

Patient name:

Patient id:

Title of study: Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study

Purpose of study: The purpose of this study is to compare the diagnostic accuracy, sensitivity, specificity as well as the prognostic value of presepsin & procalcitonin for sepsis in critically ill patients.

Study design: Prospective Cohort Study

I have been explained in my own understanding language by the Principal Investigator that they are doing this study and the risk and benefits associated with it.

I have been informed that I can withdraw my patient from the study at any time.

The data obtained from my patient will be used for the purpose of the study only. All records will be kept confidential .

Benefits of the study to the patients: Early diagnosis of sepsis and early institution of therapy

Any potential risks to the participants: No additional risks

Details of the candidate with phone number:

Dr. Shipra Roy
Post Graduate,
Anaesthesiology & Critical Care
AIIMS Jodhpur
9632692069

ANNEXURE – 5

रोगी सूचना पत्रक

रोगी का नाम:

रोगी आईडी:

अध्ययन का शीर्षक: **Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study**

अध्ययन डिजाइन: Prospective Cohort Study

प्रिंसिपल अन्वेषक द्वारा मुझे अपनी समझ भाषा में समझाया गया है कि वे"ये अध्ययन कर रहे हैं और इसके साथ जुड़े जोखिमों और लाभों को भी समझाया गया है। मुझे सूचित किया गया है कि मैं किसी भी समय अध्ययन से मेरे मरीज़ को हटा सकता हूं। मेरे मरीज़ से प्राप्त आंकड़ों का उपयोग केवल अध्ययन के उद्देश्य के लिए किया जाएगा मेरे मरीज़ के सभी रिकॉर्ड गोपनीय रखा जाएगा।

मरीजों के अध्ययन के लाभ: शीघ्र निदान और शीघ्र उपचार

प्रतिभागियों को कोई भी संभावित जोखिम: कोई अतिरिक्त जोखिम नहीं

डॉ शिप्रा रॉय
पीजी
अनैथीसिओलॉजी और क्रिटिकल केयर
एम्स जोधपुर
9632692069

ANNEXURE – 6

All India Institute of Medical Sciences (AIIMS), Jodhpur

Department of Anaesthesiology & Critical Care

Thesis Title: Comparing the Diagnostic Accuracy of Presepsin & Procalcitonin for Sepsis in Critically Ill Patients: A Prospective Observational Study

PROFORMA

Name:

Patient Id:

Age:

Gender:

Patient sticker

	D1	D2	D3	D4	D5	D6	D7	D_d
Temperature(F)*								
HR (beats/min)*								
MAP (mm Hg)*								
RR (/min)*								
APACHE II Score		---	---	---	---	---	---	---
SOFA Score								
Serum Procalcitonin								

Serum Presepsin		---	---	---	---	---		---
Serum Lactate								
Hb/Hct								
TLC								
Platelets								
Urea/Creatinine								
Na/K								
Bilirubin								
pH								
pO_2/pCO_2								
Base excess/HCO_3								
GCS								
CULTURE								
	D1	**D2**	**D3**	**D4**	**D5**	**D6**	**D7**	**D_d**
SAMPLE DATE								
TYPE OF SAMPLE								
REPORTING DATE								
TYPE OF ORGANISM								

Patient Outcome:

*Vitals to be recorded at the time of sample collection
D_d – Day of discharge or death.

ANNEXURE – 7

MASTER CHART