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Comparison between Presepsin and Procalcitonin in Early Diagnosis and Prognosis of Sepsis

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ABSTRACT

Background: The introduction of pathogens or conditionally pathogenic microorganisms into the bloodstream triggers a systemic inflammatory response syndrome known as sepsis.

Objective: Comparison between Presepsin as well as procalcitonin in early diagnosis and prognosis of sepsis.

Subjects and Methods: In a prospective cohort study that was done on 90 cases with early sepsis, who admitted to ICU at Tropical Medicine Department, Zagazig University Hospitals. On admission, levels of procalcitonin and presepsin were assessed as well as after twenty-four and seventy-two hours.

Results: Regard cause of admission majority had confusion then drowsiness, regard sepsis causes majority had Urinary tract infection (UTI) then pneumonia. BCs, Cr, INR and CRP were significantly higher among +VE culture at all reading group but albumin at all reading, PLT in 2nd and 3rd reading and pH at all reading were significantly lower among -VE culture. Positive significant correlation was found between SIRS score and CRP at T0 and T2 and high significance at T1. CRP was highly significantly correlated with Modified SOFA score from T0 to T2. The correlation between SIRS score and procalcitonin was significant at T1 and T2. Procalcitonin was significantly correlated with Modified SOFA score at T1 and T2. Presepsin was significantly correlated with SIRS score from T0 to T2. The correlation between presepsin and Modified SOFA score was significant and highly significant at T1, T0 and T2 respectively.

Conclusion: Similar to procalcitonin, presepsin shows promise as a marker to detect sepsis. Compared to procalcitonin, presepsin is a more reliable biomarker for early sepsis diagnosis.

Keywords: Presepsin, Sepsis, Procalcitonin.

INTRODUCTION

An ineffective immunological response to infection causes sepsis, a potentially fatal organ failure. With an annual growth rate of 1.5%, sepsis is becoming an increasingly urgent problem in healthcare systems around the world. Sepsis is expensive to healthcare systems and has a human toll as well. More than $24 billion is spent annually on sepsis-related care, which may involve extended hospital stays, intensive care unit admissions, hospital readmissions, and intensive testing and patient monitoring [(1)].

Clinical indicators and presentation of sepsis can be deceptive and highly diverse due to the presence of frequent co-morbidities or the demographic characteristics of the patient population, making timely diagnosis challenging, consequently, there is a pressing requirement for a trustworthy diagnostic approach, enabling early differentiation between bacterial and non-bacterial illnesses[(2)].

High analytical costs stem from the complexity and expertise required for traditional methods of infection detection, like methodologies involving culture, biochemistry, antibodies, and molecular biology. As a result, there is always a call for cost-effective, accessible, user-friendly, rapid, sensitive, and time-efficient point-of-care analysis [(3)].

Along with the diagnostic criteria, the incorporation of biomarkers like C-reactive protein (CRP) and procalcitonin (PCT) may aid in the early diagnosis of patients with sepsis, severe sepsis, and septic shock who could benefit from prompt and appropriate medication [(2)].

Procalcitonin (PCT) has been widely acknowledged as a good biochemical diagnostic tool for separating sepsis from other non-infectious causes of systemic inflammation response syndrome (SIRS). Procalcitonin is widely used as a biomarker for sepsis; however, its specificity is low because it is also elevated in many conditions that are not infections [(4)].

Presepsin, or soluble CD14 subtype (sCD14-ST), is a biomarker that has showed promise as a unique, developing, early signal for the diagnosis of a wide range of disorders[(5)]. Although presepsin was able to distinguish sepsis from non-sepsis with moderate accuracy, its results should be regarded cautiously because of its lack of high diagnostic accuracy [(6,7)]. Monitoring the prognosis and survival rate of patients with severe sepsis or septic shock by changes in presepsin levels may be useful. Patients who had positive blood cultures and responded well to antibiotic treatment had reduced presepsin levels on day 7.

However, it was shown to be higher in people who had positive blood cultures and were given the wrong antibiotics. Infections caused by MDR bacteria accounted for the vast majority of cases of unnecessary antibiotic treatment[(8)]. Acute kidney injury and renal impairment, prolonged mechanical ventilation, and delayed weaning from vasopressors or inotropic agents have all been linked to elevated presepsin levels on day 1. Additionally, prolonged duration of the primary infection, incomplete resolution of the infection, and death have all been linked to prolonged ICU stays[(9)].

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We aimed at this work to compare between presepsin as well as procalcitonin in early diagnosis and prognosis of sepsis.

PATIENTS AND METHODS

90 adults diagnosed with sepsis or a similar illness and admitted to the intensive care unit at Zagazig University Hospitals' Tropical Medicine Department were the subjects of a prospective cohort research.

Inclusion Criteria: Aged 18 and up, A patient with a positive score on the Sepsis Indicator, Risk, and Severity Scale (SIRS) or Sequential Organ Failure Assessment (SOFA)[10], at minimum of two out of the three SOFA criteria [11].

Exclusion Criteria: who aged less than 18 years, failure to get patient/family member informed consent, patients with terminal illnesses such as cancer, liver or renal failure, AIDS, or a complication such as meningitis, thrombosis, hemorrhagic shock, etc., and prior corticosteroid or anti-inflammatory medication use in the patient.

All patients were subjected to:

Comprehensive medical background + minimum clinical standards: Biographical details (Name, age, sex and occupation), make a fuss, previous surgical experience, origins of blood transfusions, having a family history of diabetes, hypertension, or any other ailment, whether or not having a history of co-existing diseases like heart disease, and medically significant habits like smoking.

General examination focusing on:

Vital signs (Heart rate, blood pressure, respiratory rate as well as, temperature), signs of (Jaundice, cyanosis, pallor, as well as lymph node enlargement), SOFA as well as SIRS criteria.

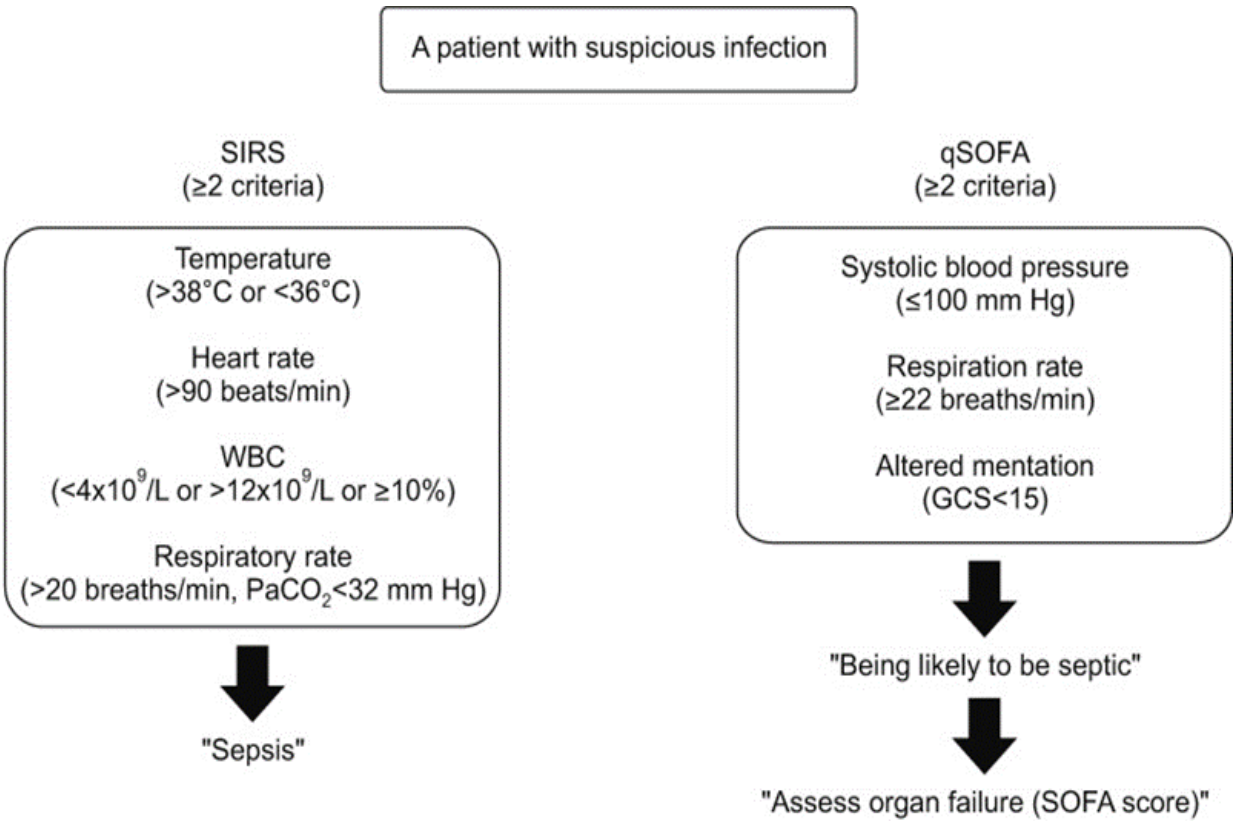

Figure (1): Patient with suspicious infection [12].

All patients in the ICU were required to have their heart rate, respiration rate, mean arterial pressure, oxygen saturation, central venous pressure, urine output, and temperature monitored continuously for the full 72 hours, and fluctuations in blood sugar.

Daily recorded laboratory parameters included:

Hemoglobin level, white blood cell count, platelet count, and red blood cell count all make up what is known as a "complete blood count.", partial thromboplastin time (PTT), international normalized ratio (INR), alanine transaminase, and aspartate transaminase levels in the blood; serum creatinine; sodium and potassium levels in the blood serum, the results of a blood gas test, C-reactive protein test, direct and total bilirubin, protein content, blood albumin.
On admission (T0), after 24 hours (T1), and 72 hours (T2), serum samples were taken and analysed for presepsin and procalcitonin levels (T2).

Ethical consideration:

Institutional Review Board of Zagazig University approved the study protocol (#9016/12-10-2021). All study participants gave their informed, signed agreement to take part in the study. At every stage of the research, participants' anonymity and confidentiality were protected. The study followed the principles outlined in the Declaration of Helsinki for studies involving humans.

Statistical analysis: The SPSS version 24 for Windows® was used to code, process, and analyse the obtained data. Using the Shapiro Wilk test, the distribution of the data was examined for normality. Frequencies and relative percentages were used to depict qualitative data. Mean ± standard deviation (SD), median, and range were used to express quantitative data. To compare two independent groups of regularly distributed variables (parametric data), the independent samples t-test was employed. P value less than 0.05 was regarded as significant.

RESULTS

Table (1) shows information about the study populations' demographics at baseline.

Table (1): Age and sex distribution among studied group (N=90)

		Age (years)	
Mean± SD		**44.26±8.6**	
Median (Range)		**42.0 (30-59)**	
		N	**%**
Sex	**Male**	**50**	**55.6**
	Female	**40**	**44.4**
	Total	**90**	**100.0**

Table (2) shows that the majority of the 90 septic patients in the case group (51.1%) had infections in their urinary tracts.

Table (2): Admission causes and sepsis distribution among studied group (N=90)

		N	%
Cause of admission	**Confusion**	**27**	**30.0**
	Delirium	**19**	**21.1**
	Drowsiness	**23**	**25.6**
	Respiratory failure	**21**	**23.3**
Sepsis cause	**Peritonitis**	**12**	**13.3**
	Pneumonia	**32**	**35.6**
	UTI	**46**	**51.1**
	Total	**90**	**100.0**

The diagnostic accuracy of various biomarkers for septic shock upon admission, and how they relate to the Sequential Organ Failure Assessment (SIRS) and the Modified SOFA score:

The sensitivity and specificity of the biomarkers tested were determined using the ROC curve to demonstrate their role in the diagnosis of septic shock upon patient admission; the AUC for procalcitonin and presepsin were 58 % and 83.3%, respectively, with the specificity for each being 62.2% and 78.3% (Figure 2 and table 3).

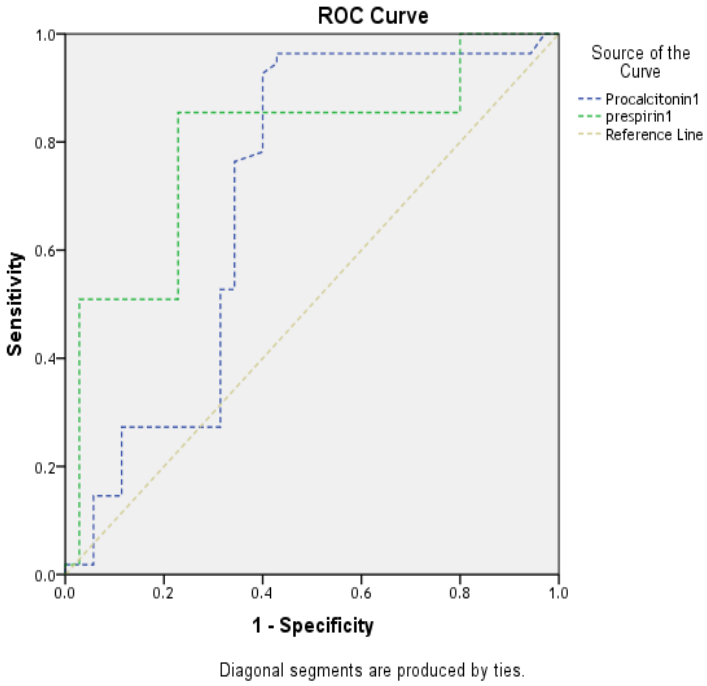

Figure (2): ROC curve for procalcitonin and presepsin cutoff regarding +VE culture

Table (3): The diagnostic accuracy of various biomarkers for septic shock upon admission

Test Result Variable(s)	Area	Cutoff	P	95% Confidence Interval		Sensitivity	Specificity
				Lower Bound	Upper Bound		
Procalcitonin	**0.698**	**>0.91**	**0.026***	**0.632**	**0.865**	**58.0%**	**62.2%**
Presepsin	**0.793**	**>82.5**	**0.001****	**0.546**	**0.780**	**83.3%**	**78.3%**

*: Significant, **: Highly significant

There was a highly significant positive connection between SIRS score and CRP at T1. CRP was highly significantly correlated with Modified SOFA score from T0 to T2. At admission, levels of PCT and presepsin were positively correlated with SIRS and Modified SOFA scores. Procalcitonin was significantly correlated with SIRS score and Modified SOFA score at T1 and T2. Presepsin was significantly correlated with SIRS score from T0 to T2. The correlation between presepsin and Modified SOFA score was significant at T1 and highly significant at T0 and T2 (Table 4).

Table (4): Correlations between SIRS and Modified SOFA scores with other parameters

		SIRS	Modified SOFA
Modified SOFA	**R**	**0.389****	**1**
	P	**0.000**	
CRP0	**R**	**0.297***	**0.343****
	P	**.003**	**.001**
CRP1	**R**	**.356****	**.381****
	P	**.000**	**<0.001**
CRP2	**R**	**.252***	**.312****
	P	**.019**	**.003**
Procalcitonin0	**R**	**.091**	**.205**
	P	**.393**	**.052**
Procalcitonin1	**R**	**.293***	**.258***
	P	**.009**	**.014**
Procalcitonin2	**R**	**.211***	**.235***
	P	**.040**	**.026**
Presepsin0	**R**	**.269***	**.337****
	P	**.010**	**<0.001**
Presepsin1	**R**	**.220***	**.269***
	P	**.038**	**.010**
Presepsin2	**R**	**.337***	**.350****
	P	**.002**	**<0.001**

*: Significant, **: Highly significant

Table (5) shows, diagnostic accuracy, association with the Sequential Organ Failure Assessment (SIRS) and the Simplified Organ Failure Assessment (Modified SOFA) scores, and the capacity of several markers to distinguish between death and survival (sepsis prognosis). Significantly higher SIRS and Modified SOFA scores, procalcitonin, presepsin, and CRP were seen in the group that died than the group that survived.

Table (5): Comparison between survived and died cases

	Survived	Died	T	P
Modified SOFA0	**5.22±1.36**	**9.52±1.18**	**10.786**	**<0.01****
Modified SOFA1	**5.14±1.25**	**9.80±1.46**	**13.316**	**<0.01****
Modified SOFA2	**4.45±1.34**	**10.20±3.89**	**10.767**	**<0.01****
Procalcitonin0	**2.79±0.81**	**5.44±1.45**	**2.448**	**0.016***
Procalcitonin1	**2.70±0.92**	**5.89±1.67**	**2.765**	**0.007***
Procalcitonin2	**2.59±0.82**	**5.34±1.72**	**2.565**	**0.012***
Presepsin0	**138.98±43.6**	**248.8±82.9**	**3.996**	**<0.01****
Presepsin1	**184.22±62.8**	**328.9±108.6**	**3.186**	**0.002***
Presepsin2	**187.01±58.2**	**359.7±113.6**	**3.842**	**<0.01****
CRP0	**90.27±32.6**	**114.6±34.9**	**3.430**	**<0.001****
CRP1	**85.56±26.7**	**153.7±50.8**	**3.443**	**<0.001****
CRP2	**83.47±25.5**	**145.1±47.7**	**3.040**	**0.003***

DISCUSSION

This study was set out to determine whether presepsin and procalcitonin were useful in the early diagnosis and prognosis of sepsis. Ninety ICU patients were enrolled in this trial, all of whom had been diagnosed with early sepsis.

As regard demographic data among the studied group, the current study showed that the mean age was 44.26±8.6 with minimum 30 and maximum 59 with male to female ratio was 55.6/44.4. **Abd El Latif *et al.*** [12] who included 62 adult critically ill patients who had sepsis, provided support for the current findings. Their ages ranged from 18 to 83, with a mean age of 55.45 16.264. There was a total of 60 patients, 37 male and 25 female (40 percent). In addition, 50 patients with sepsis (ranging in age from 18 to 60) were participated in the study by **Bahaa and Mohamed** [13]**,** with a mean age of (54.315.6) years. There were somewhat more female patients than male ones (52% to 48%). As well, **Mahmoud *et al.*** [14] looked at how well presepsin could foretell deaths from sepsis. There was a total of 83 sepsis patients included in the study; the average age was 58 (range, 47-65) and there were 33 (60%) men. Furthermore, the case-control study by **Sabry *et al.*** [15] included 60 sepsis patients in critical care and 20 healthy controls. There was no statistically significant difference in age or sex between the groups. One more case-control study by **El Shabrawy *et al.*** [16] covered both patients with and without sepsis who had been admitted to the critical care unit (ICU). No significant differences in age or sex were found between groups. A prospective observational study by **Lee *et al.*** [17] compared patients with noninfectious organ failure to those with sepsis and septic shock, the former were found to be older.

As regard vital signs among studied, we found that Temp, RR, HR, SBP and DBP were distributed as 38.95±0.57, 28.62±4.6, 120.71±13.6, 87.33±14.7 and 56.88±14.15 respectively.

Similar to our findings, **Mahmoud *et al.*** [14] found that the average values for temperature, pulse rate, heart rate, systolic blood pressure, and diastolic blood pressure were 38.5 (38-39), 21 (18-24), 100 (95-111), 80 (75-100), and 60 (50-60) mm Hg.

When at least 2 of the SIRS criteria are met, a diagnosis of sepsis can be made in adults (>18 years old) in intensive care. Increase in immature band formations (>10%) or a white blood cell count of >12,000/L or >4,000/L, and/or a temperature of 38°C or >36°C, a heart rate of 90 beats/min or >36 beats/min, a respiratory rate of 20 breaths/min or >32 mmHg of $PaCO_2$ while using mechanical ventilation [18].

In the present study we found that as regard cause of admission, the majority had confusion 30% then drowsiness 25.6%, and as regard sepsis causes majority had UTI 51.1% then pneumonia 35.6% The findings of **Sabry *et al.*** [15] corroborate our own: pneumonia accounts for nearly half (48.3%) of all infectious diseases, followed by urinary tract infections (23.3%) and diabetic foot infections (7.6%) (11.7 %).

Diabetes, high blood pressure, and respiratory disorders were found to be the most frequent comorbidities in the current study. 28 patients had diabetes (45.2%), and 35 had hypertension disease, as described by **Abd El Latif *et al.*** [12] (54.8 %).

In the current study we found that there were 61.1% of the studied patients had positive culture results. In agreement with our results **Bahaa and Mohamed** [13] findings from culture tests revealed that 60% of patients had positive results and 40% had negative results. This come also in agreement with **Osman *et al.*** [19] who showed that those with sepsis were more likely to have positive blood cultures (57.5%) than patients without sepsis (42.5%; patient/control ratio = 1.35). However, **Lee *et al.*** [17] found that 43% of patients with sepsis and 45% of patients with septic shock had a positive blood culture.

Regarding mortality rate among the studied cohort the present study showed that 11.1% died and 88.9% survived. However, **Abd El Latif *et al.*** [12] showed that there were 64.5% % died and 35.5 % survived. Also, **Mahmoud *et al.*** [14] reported that 39 of the patients died, with an in-hospital mortality rate of 70.9%. Similarly, **Sabry *et al.*** [15] reported that the 28-day mortality rate was 16 (26.7%) among patients with sepsis. As well, **El Shabrawy *et al.*** [16] reported that the death rate was (18/28, 64.3%). While, **Lee *et al.*** [17] reported that deaths from sepsis and septic shock occurred in 27% of patients (74/278) within 30 days. The difference of the mortality rate may be due to the differences in inclusion criteria and patients' characteristics including patient severity and comorbidities. Septic shock has a fatality rate of 40–70%, while severe sepsis has a 25%–30% mortality rate [20]**.**

In the current study we found that WBCs, Cr, INR and CRP were significantly higher among +VE culture at all reading group but albumin at all reading, PLT in 2nd and 3rd reading and PH at all reading were significantly lower among -VE culture. In line with our findings, **Yang *et al.*** [21] found that WBC and PCT counts, as well as albumin, were typically lower in patients with positive culture results. A higher danger of malnutrition and severe infections has been associated with positive blood culture results. White blood cell count and C-reactive protein levels were additional risk variables for culture-positive mortality, but ALB acted as a buffer.

A comparison of 415 culture-negative patients (41.5% of the total) and 586 culture-positive patients (58.5%) was made by **Phua *et al.*** [22]. There was no statistically significant difference in the numbers of white blood cells or C-reactive protein between the groups. **Nishimura *et al.*** [23] also found that patients with septic pulmonary embolism and a positive culture reported higher white blood cell and D-dimer counts, but no statistically significant alterations in potassium or chloride levels. Positive and negative culture findings were not statistically different in terms of white blood

cell count, hematocrit, platelets, and creatinine, according to **Sigakis *et al.*** [24] but there were significant variations in terms of bicarbonate and blood urea nitrogen.

Procalcitonin and presepsin levels were also found to be noticeably higher in the positive culture group. To back up our findings, **Bahaa and Mohamed** [13] found that presepsin levels were significantly higher in the "laboratory verified sepsis" group compared to the "suspected sepsis" group across all time points ($p<0.01$). In addition, they discovered that after 4 hours of admission, there was a statistically significant difference in procalcitonin levels between the two groups (p0.01), but early measures showed no change ($p>0.05$). These findings agreed with a meta-analysis and comprehensive review conducted by **Zou *et al.*** [25], which found that presepsin levels were elevated in septic patients as early as 2 hours after infection, peaked at 3 hours, and then declined gradually over the following 4-8 hours. However, procalcitonin levels began to rise 4 hours after infection, plateaued 8-24 hours after infection, and peaked at 48 hours.

In agreement with our results **Phua *et al.*** [22] reported that procalcitonin was significantly higher among positive culture. Similarly, **Yang *et al.*** [21] reported that procalcitonin was significantly higher among positive culture and was found to be a risk factors for culture-positive mortality. In addition, **Novelli *et al.*** [26] showed that presepsin levels correlate strongly with culture outcomes in perioperative patients, lending credence to our observations. Researchers found that patients in the emergency room had higher levels of presepsin when their cultures came back positive [27]. Furthermore, **Abd El Latif *et al.*** [12]**, Sabry *et al.*** [14]**, Mahmoud *et al.*** [15]**, El Shabrawy *et al.*** [16]**, and Lee *et al.*** [17]**,** reported that both presepsin and procalcitonin were found to be significantly increased in patients with confirmed sepsis.

The previously mentioned results suggested that both presepsin and procalcitonin were a potential biomarker for laboratory confirmed patients with sepsis. To test the diagnostic accuracy of their biomarkers ROC curve analysis was performed. We found that for procalcitonin at cutoff point of >0.91, 0.698 was the area under the curve, and 58 and 62% were the sensitivity and specificity. In addition, when using a presepsin threshold of >82.5, the AUC was 0.793, the sensitivity was 83.3%, and the specificity was 78.3%. Our data show that presepsin is more accurate as a diagnostic tool than procalcitonin.

These results corroborated those of prior research that had found presepsin to be superior to other biomarkers in the early detection of sepsis. **Bahaa and Mohamed** [13] corroborated this, reporting that an early presepsin level above a cutoff point of 379 correctly identified patients with negative cultures 82% of the time (sensitivity = 100%, specificity = 80%, p0.01). PCT's predictive usefulness in differentiating patients with positive cultures from patients with negative cultures was statistically insignificant, despite its similar sensitivity to presepsin but significantly lower specificity and poor (56 percent) accuracy. In addition, the meta-analysis by **Kondo *et al.*** [28] presented data demonstrating that procalcitonin and presepsin have comparable diagnostic accuracy for identifying infection and are both beneficial for early detection of sepsis and lowering mortality in critically unwell adult patients. **Wu *et al.*** [29] conducted another meta-analysis and reported that the pooled sensitivity and specificity of presepsin for sepsis diagnosis were 84% and 76%, respectively. In addition, they discovered no statistically significant distinction between presepsin and PCT (AUC 0.87 vs. 0.86). In intensive care unit investigations, however, presepsin was found to have a greater pooled sensitivity than PCT (88% vs. 75%), although having a lower pooled specificity (0.58 percent vs. 0.75 percent). Different cutoff values may account for the discrepancies in sensitivity and specificity seen between our study and others.

CONCLUSION

According to the findings of the current study, presepsin has as much potential as procalcitonin as a marker for the detection of sepsis. The results of the current study indicate that, compared to procalcitonin, presepsin is a more reliable biomarker for the early detection of sepsis. It is possible to tell bacterial infections apart from nonbacterial ones because presepsin levels rise rapidly on the first day of infection. Additionally, it is recommended to reevaluate sepsis patients frequently. To corroborate our findings and uncover risk factors of adverse outcomes, larger-scale, longer-term follow-up investigations are required.

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Competing interests: Nil.

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