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Original Research Article

Correlation between presepsin, procalcitonin, and c-reactive protein levels with sequential organ failure assessment scores in sepsis patients at the intensive care unit: A prospective observational study

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Abstract

Background: Sepsis is a life-threatening syndrome triggered by infection, frequently resulting in organ dysfunction and high mortality. Biomarkers such as presepsin, procalcitonin (PCT), and C-reactive protein (CRP) have emerged as valuable tools for early diagnosis and prognosis. This study aimed to evaluate the correlation between these biomarkers and the Sequential Organ Failure Assessment (SOFA) score in ICU patients with sepsis.
Materials and Methods: This prospective observational study included 40 adult patients with sepsis admitted to the ICU from March 2024 to October 2024 in Indonesia. Serum levels of presepsin, procalcitonin, and CRP were measured daily from day 1 to day 3 of ICU admission. SOFA scores were recorded concurrently. Statistical analyses were performed to assess correlations between biomarker levels and SOFA scores.
Results: All three biomarkers showed significant positive correlations with SOFA scores during the observation period ($p < 0.05$). Among them, presepsin demonstrated the strongest correlation, particularly on day 1 ($r = 0.951$, $p < 0.001$), indicating a superior prognostic value in assessing sepsis severity and organ dysfunction.
Conclusion: Presepsin appears to be a more reliable early biomarker for sepsis severity compared to procalcitonin and CRP, showing strong correlation with SOFA scores. These findings support its potential use in clinical settings for early risk stratification of septic patients. Larger-scale studies are warranted to validate its utility across diverse healthcare settings in Indonesia.

Keywords: Sepsis, SOFA score, presepsin, Procalcitonin, CRP, Biomarker, ICU.

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1. Introduction

Sepsis, a life-threatening condition caused by the host's dysregulated response to infection, remains a major challenge in clinical practice due to its high mortality and morbidity rates. It leads to organ dysfunction, with septic shock characterized by circulatory and metabolic abnormalities that significantly increase mortality.[1,2] Sepsis accounts for a substantial number of ICU admissions globally, with an estimated 750,000 cases annually in the U.S., resulting in over 210,000 deaths.[3] In Indonesia, the mortality rate for sepsis is reported at 59%, with pulmonary infections as the leading cause.[4]

Early diagnosis and effective management are critical for improving survival rates. Biomarkers such as procalcitonin (PCT), C-reactive protein (CRP), and presepsin have been widely studied.[5,6] CRP and PCT are commonly used in clinical practice but have limitations in sensitivity and specificity. For instance, CRP's sensitivity ranges from 35–100%, while PCT shows variability in non-infectious conditions like trauma or certain cancers.[7,8]

Presepsin, a novel biomarker, has shown promise for early sepsis detection.[9] Derived from the soluble CD14

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subtype (sCD14-ST), presepsin effectively distinguishes sepsis from non-infectious conditions, with levels rising within two hours of infection and peaking in three hours.[10] Its distribution in healthy individuals is 294.2 ± 121.4 pg/ml, compared to 817 ± 572.2 pg/ml in sepsis patients.[1] Studies have demonstrated presepsin's superior diagnostic and prognostic value compared to CRP and PCT.[11,12]

Despite its potential, presepsin testing faces barriers in Indonesia, including high costs and limited availability in healthcare facilities. Increasing awareness and integrating this technology into clinical practice could enhance sepsis management.

This study aimed to analyze the correlation between presepsin, procalcitonin, and CRP levels with SOFA scores in ICU patients with sepsis. The secondary objectives included determining the individual correlation strength of each biomarker and identifying which among them demonstrates the strongest prognostic value.

2. Materials and Methods

This study employed a correlational analytic approach with a cross-sectional design to examine the relationship between presepsin, procalcitonin (PCT), and C-reactive protein (CRP) levels and Sequential Organ Failure Assessment (SOFA) scores in ICU patients diagnosed with sepsis. The study was conducted from March 2024 to October 2024, and was approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, University of Riau (Approval No. B/045/UNI19.5.1.1.8/UEPKK/2024).

Sepsis was diagnosed based on clinical criteria in accordance with the Sepsis-3 guidelines, specifically defined as an acute increase of ≥2 points in the Sequential Organ Failure Assessment (SOFA) score from baseline in patients with confirmed or suspected infection. Due to limitations in access to definitive microbiological diagnostics (e.g., blood cultures), patient inclusion was determined based on the clinical judgment of ICU consultants. This assessment incorporated the presence of infection-related signs and symptoms, relevant laboratory markers, and hemodynamic instability. Patients were eligible if they were aged over 18 years and had a documented infection with a SOFA score >2. Exclusion criteria included acute myocardial infarction, cardiogenic shock, advanced-stage cancer, chronic kidney disease, or pregnancy. Patients who died within the first three days of ICU care were considered dropouts and excluded from the final analysis.

The sample size was calculated using a correlation analytical formula:

$$n = \left(\frac{Z\alpha + Z\beta}{0.5 \ln\left(\frac{l+r}{l-r}\right)} \right)^2 + 3$$

where:

$Z\alpha = 1.64$ (standard normal value at $\alpha = 0.05$, one-tailed)
$Z\beta = 1.28$ (standard normal value at $\beta = 0.10$, power = 90%)
r = minimum correlation considered significant (0.5)

Based on the formula, the minimum required sample size was 33. To account for a 10% dropout rate, the final target was set at 35 participants.

Between April and November 2024, 50 patients met the inclusion criteria. Of these, 2 patients died on the first day of ICU admission, 5 on the second day, and 3 on the third day. After applying the dropout criteria, 40 patients were retained in the final analysis—exceeding the minimum required sample size.

2.1. Statistical analysis

Statistical analyses were conducted to meet the study objectives and test the hypotheses. Data were presented as percentages (%) for categorical variables and as mean ± standard deviation (SD) for continuous variables. Univariate analysis was used to describe patient characteristics, including demographic data (age and gender). Normality of data distribution was assessed using the Shapiro-Wilk test, given the sample size was less than 50. If the data were normally distributed, a paired t-test was used. If the data were not normally distributed, the Wilcoxon test was applied. For comparisons involving more than two groups, if the data were normally distributed, repeated measures ANOVA was conducted dan if the data were not normally distributed, the Friedman test was used.

3. Results

A total of 45 patients were screened for eligibility and 5 participants were excluded. (**Figure 1**).

A total of 40 patients with sepsis in ICU were enrolled in this study. Their demographic and clinical characteristics are presented in **Table 1**. The average age of the patients was 51.53 ± 16.16 years, and there was an equal gender distribution, consisting of 20 male patients (50.0%) and 20 female patients (50.0%). The mean Body Mass Index (BMI) was 24.26 ± 4.39. In terms of surgical status, 13 patients (32.5%) had undergone surgical procedures, while the remaining 27 patients (67.5%) were classified as non-surgical cases.

Comorbidities were common among the patient population. Pneumonia was the most frequently observed condition, affecting 21 patients (52.5%). Type 2 diabetes mellitus was present in 11 patients (27.5%), while hypertension was identified in 8 patients (20.0%). Abdominal infections were observed in 7 patients (17.5%), and stroke infarction was found in 4 patients (10.0%). Less common comorbid conditions included intracranial hemorrhage in 3 patients (7.5%), chronic obstructive pulmonary disease (COPD) and pulmonary tuberculosis in 2 patients each (5.0%), and tuberculosis spondylitis, bronchial asthma, pleural empyema, and meningoencephalitis in 1 patient each (2.5%).

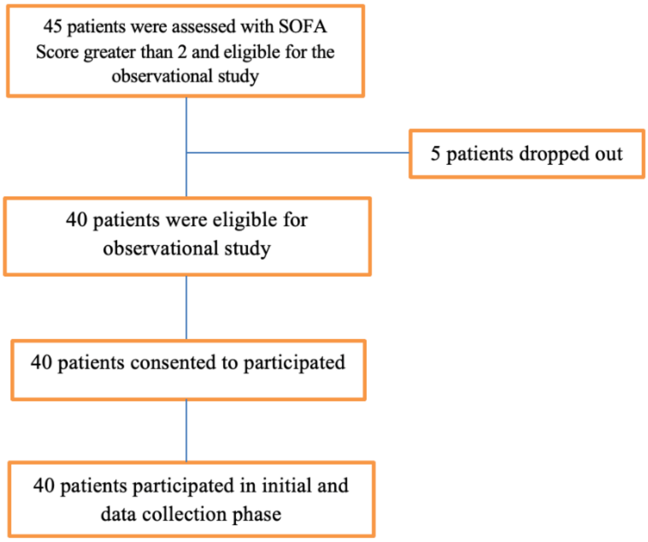

Figure 1: Consort flow diagram

In terms of clinical interventions, 26 patients (65.0%) required mechanical ventilation during their stay in the intensive care unit. Ventilation was administered using either pressure-controlled or volume-controlled modes, depending on the patient's respiratory status and clinical indication. Additionally, 21 patients (52.5%) received vasopressor therapy, predominantly norepinephrine, to maintain a mean arterial pressure (MAP) of at least 65 mmHg.

Data are presented as mean ± standard deviation (SD) for normally distributed variables, and as median with interquartile range (IQR) for non-normally distributed variables. Categorical variables are expressed as number and percentage (n (%)). Presepsin, procalcitonin, and C-reactive protein (CRP) levels were measured upon admission to the intensive care unit (ICU). The Sequential Organ Failure Assessment (SOFA) score reflects the baseline score at ICU entry.

On Day 1, the average SOFA score among patients was 7.83 ± 4.98, with a mean presepsin level of 1005.82 ± 1013.96 pg/mL, procalcitonin level of 16.79 ± 27.62 ng/mL, and C-reactive protein (CRP) level of 166.45 ± 89.98 mg/L. On Day 2, a slight increase was observed in all parameters, with the SOFA score rising to 8.03 ± 5.28, presepsin to 1039.20 ± 981.63 pg/mL, procalcitonin to 18.08 ± 26.90 ng/mL, and CRP to 171.12 ± 93.55 mg/L. By Day 3, further increases were noted: the SOFA score reached 8.33 ± 5.27, presepsin increased to 1050.50 ± 987.25 pg/mL, procalcitonin rose to 19.48 ± 28.55 ng/mL, and CRP to 178.83 ± 97.39 mg/L. A summary of these values across Days 1, 2, and 3 is presented in **Table 2**.

Table 1: Patient characteristics and baseline biomarker levels (n-40)

Variable	Value
Age (years), mean ± SD	54.2 ± 13.8
Male sex, n (%)	18 (52.9%)
Mechanical ventilation, n (%)	26 (76.5%)
Vasopressor support, n (%)	21 (61.8%)
Baseline SOFA score, median (IQR)	8 (6–10)
Presepsin (pg/mL), median (IQR)	850 (650–1,200)
Procalcitonin (ng/mL), median (IQR)	5.3 (3.1–8.4)
CRP (mg/L), mean ± SD	98.7 ± 45.2

IQR = interquartile range; SD = standard deviation; SOFA = Sequential Organ Failure Assessment.

Table 2: SOFA score, presepsin, procalcitonin, and CRP levels on days 1, 2, and 3 in ICU patients with sepsis (n = 40)

Variable	Mean ± SD	Median (Min–Max)
SOFA Score Day 1	7.83 ± 4.98	7.00 (2.00–22.00)
Presepsin Day 1 (pg/mL)	1005.82 ± 1013.96	748.50 (83.60–6204.00)
Procalcitonin Day 1 (ng/mL)	16.79 ± 27.62	3.37 (0.08–100.00)
CRP Day 1 (mg/L)	166.45 ± 89.98	142.09 (2.30–402.00)
SOFA Score Day 2	8.03 ± 5.28	6.50 (2.00–22.00)
Presepsin Day 2 (pg/mL)	1039.20 ± 981.63	713.00 (102.00–5824.00)
Procalcitonin Day 2 (ng/mL)	18.08 ± 26.90	3.75 (0.08–94.60)
CRP Day 2 (mg/L)	171.12 ± 93.55	169.60 (10.10–455.00)
SOFA Score Day 3	8.33 ± 5.27	7.50 (0.00–22.00)
Presepsin Day 3 (pg/mL)	1050.50 ± 987.25	817.50 (54.00–6020.00)
Procalcitonin Day 3 (ng/mL)	19.48 ± 28.55	3.54 (0.08–100.00)
CRP Day 3 (mg/L)	178.83 ± 97.39	153.17 (21.10–385.00)

3.1. Overview of SOFA scores, presepsin, procalcitonin, and CRP

The relationship between SOFA scores, presepsin, procalcitonin, and CRP levels over Days 1, 2, and 3 was analyzed using appropriate statistical tests (**Table 3**). CRP values, which followed a normal distribution, were evaluated using Repeated Measures ANOVA. While SOFA scores, presepsin, and procalcitonin variables that did not meet normality assumptions, were analyzed using the Friedman test. The results showed a statistically significant change in mean CRP levels across the three days ($p < 0.05$), indicating a meaningful variation over time. Conversely, the SOFA scores, presepsin, and procalcitonin levels did not exhibit statistically significant differences during this period, with p-values exceeding 0.05.

ROC analysis (**Figure 2**) demonstrated that presepsin consistently achieved the highest AUC values across all three days (Day-1 AUC=0.97, Day-2 AUC=0.95, Day-3 AUC=0.99), indicating excellent discrimination for predicting high SOFA scores. Procalcitonin showed moderate to good predictive value (AUC 0.77–0.91), while CRP demonstrated lower discriminatory ability (AUC 0.58–0.73) (**Table 4**). These findings confirm presepsin as the strongest biomarker for early identification of organ dysfunction severity in sepsis.

3.2. Correlation analysis between sofa score and presepsin, procalcitonin, and CRP on day 1

Bivariate analysis was conducted to evaluate the relationship between presepsin, procalcitonin, and CRP levels with the SOFA score on Day 1 (**Table 5**). Using Spearman's correlation test, a significant positive correlation was found for all three biomarkers with the SOFA score. Presepsin showed a very strong correlation with SOFA ($r = 0.951$, $p = 0.0001$), indicating a close association between presepsin levels and organ dysfunction severity. Procalcitonin demonstrated a moderate positive correlation with the SOFA score ($r = 0.561$, $p = 0.0001$), while CRP had a weaker yet statistically significant correlation ($r = 0.325$, $p = 0.041$).

In multivariate analysis, only presepsin (X1) exhibited a statistically significant effect on the SOFA score (Y) with a p-value of 0.000 ($p < 0.05$). Procalcitonin (X2) and CRP (X3) showed no significant influence on SOFA scores, with p-values of 0.577 and 0.712, respectively.

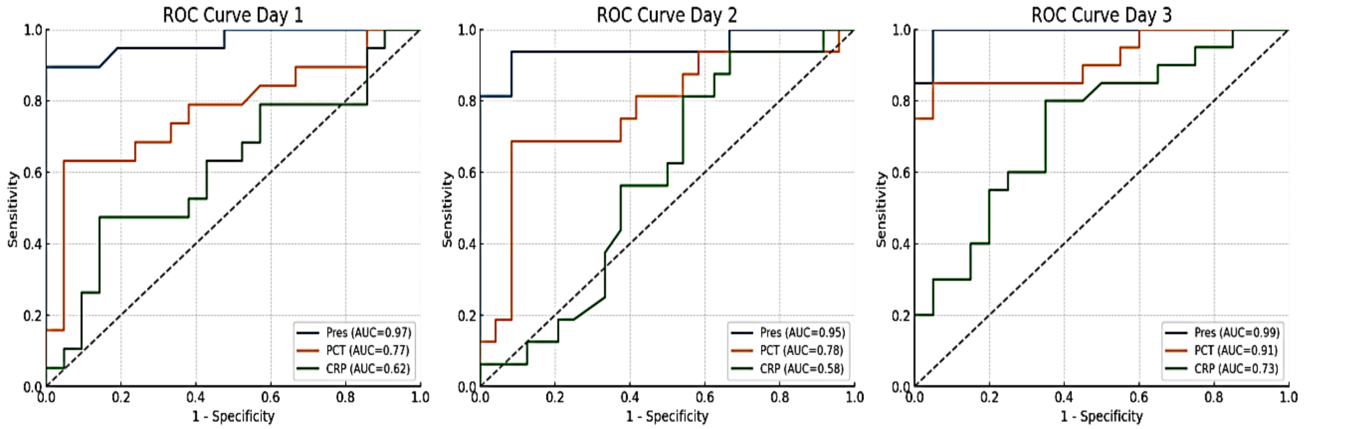

Figure 2: ROC curves for presepsin, procalcitonin, and CRP on day-1, day-2, and day-3 in predicting high SOFA score (≥8)

Table 3: Comparison of SOFA score, presepsin, procalcitonin, and CRP levels between day 1, day 2, and day 3 in sepsis patients (n = 40)

Variable	Day 1	Day 2	Day 3	p value
SOFA Score	7.83 ± 4.98	8.03 ± 5.28	8.33 ± 5.27	0.140
Median	7.00	6.50	7.50	
(Min–Max)	(2.00–22.00)	(2.00–22.00)	(0.00–22.00)	
Presepsin (pg/mL)	1005.82 ± 1013.96	1039.20 ± 981.63	1050.50 ± 987.25	0.497
Median	748.50	713.00	817.50	
(Min–Max)	(83.60–6204.00)	(102.00-5824.00)	(54.00–6020.00)	
Procalcitonin (ng/mL)	16.79 ± 27.62	18.08 ± 26.90	19.48 ± 28.55	0.903
Median	3.37	3.75	3.54	
(Min–Max)	(0.08–100.00)	(0.08–94.60)	(0.08–100.00)	
CRP (mg/L)	166.45 ± 89.98	171.12 ± 93.55	178.83 ± 97.39	0.0001*
Median	142.09	169.60	153.17	
(Min–Max)	(2.30–402.00)	(10.10–455.00)	(21.10–385.00)	

Table 4: Summary of AUC values for presepsin, procalcitonin, and CRP in predicting high SOFA score (≥8) across day-1, day-2, and day-3

Biomarker	Day-1 AUC	Day-2 AUC	Day-3 AUC
Presepsin	0.97	0.95	0.99
Procalcitonin	0.77	0.78	0.91
CRP	0.62	0.58	0.73

Table 5: Correlation analysis of SOFA score with CRP, procalcitonin, and presepsin on day 1

Variable	R	p *value*
Correlation Between CRP and SOFA Score	0.325	0.041*
Correlation Between Procalcitonin and SOFA Score	0.561	0.0001*
Correlation Between Presepsin and SOFA Score	0.951	0.0001*

*the significance value is $p < 0.05$. r: correlation coefficient

3.3. Correlation analysis between SOFA score and presepsin, procalcitonin, and CRP on day 2

Spearman correlation analysis between the SOFA score and biomarkers on Day 2 is summarized in **Table 6**. Presepsin demonstrated a very strong positive correlation with the SOFA score ($r = 0.933$, $p = 0.0001$), indicating a strong association between presepsin levels and organ dysfunction severity. Procalcitonin showed a weak but statistically significant positive correlation with the SOFA score ($r = 0.381$, $p = 0.015$). In contrast, the correlation between CRP and the SOFA score was weak and not statistically significant ($r = 0.184$, $p = 0.255$).

Regarding significance testing, only presepsin (X1) had a statistically significant effect on the SOFA score (Y) on Day 2 ($p = 0.000$, $p < 0.05$). Procalcitonin (X2) did not show a significant effect, with a p-value of 0.340.

Table 6: Correlation analysis between SOFA score and biomarkers on day 2 in sepsis patients (n = 40)

Biomarker	Correlation Coefficient (r)	p value
Presepsin (pg/mL)	0.933	0.0001*
Procalcitonin (ng/mL)	0.381	0.015*
C-Reactive protein (mg/L)	0.184	0.255

3.4. Correlation analysis between SOFA score and presepsin, procalcitonin, and CRP on day 3

Spearman correlation analysis on Day 3 showed that presepsin had a very strong positive correlation with the SOFA score ($r = 0.941$, $p = 0.0001$), indicating a strong association with organ dysfunction severity (**Table 7**). Procalcitonin demonstrated a moderate positive correlation ($r = 0.660$, $p = 0.0001$), while CRP also showed a moderate and statistically significant positive correlation with the SOFA score ($r = 0.468$, $p = 0.002$).

Despite these significant correlations, multivariate analysis revealed that only presepsin (X1) had a statistically significant effect on the SOFA score (Y) on Day 3 ($p < 0.05$). Procalcitonin (X2) and CRP (X3) did not have significant independent effects, with p-values of 0.922 and 0.240, respectively.

Table 7: Correlation analysis between SOFA score and biomarkers on day 3 in sepsis patients (n = 40)

Biomarker	Correlation Coefficient (r)	p value
C-Reactive Protein (mg/L)	0.468	0.002*
Procalcitonin (ng/mL)	0.660	0.0001*
Presepsin (pg/mL)	0.941	0.0001*

4. Discussion

This study evaluated the relationship between presepsin, procalcitonin, and CRP levels with SOFA scores in ICU patients with sepsis over the first three days of treatment. It aimed to determine which biomarker best correlates with organ dysfunction severity as measured by SOFA scores.

The results demonstrated a strong and statistically significant correlation between presepsin levels and SOFA scores on both Day 2 ($r = 0.933$, $p = 0.0001$) and Day 3 ($r = 0.941$, $p = 0.0001$), suggesting its superior prognostic value in assessing organ dysfunction in sepsis patients admitted to the ICU. These findings are consistent with the results by Lee et al.,[11] who reported that presepsin was more reliable than procalcitonin and CRP in early-stage sepsis, particularly in differentiating sepsis from systemic inflammation of non-infectious origin. Presepsin was recognized as a novel sepsis biomarker in 2004, although its utility in sepsis evaluation was first published in 2011.[13] The primary advantage of this measure compared to PCT is its early production following infection, achieving peak levels prior to PCT.[7,14,15]

In addition, procalcitonin also showed a moderate and significant correlation with SOFA score, especially on Day 3 ($r = 0.660$, $p = 0.0001$), supporting its role as an adjunct biomarker. These findings align with Galliera et al.,[1] who found that PCT concentrations correlated well with sepsis severity, albeit with a delayed response compared to presepsin. Procalcitonin serves as a valuable guide for antibiotic therapy, with evidence indicating that antibiotic treatment duration is markedly reduced when directed by PCT—6 days versus 8 days in non-PCT-monitored groups.[16] Shorter antibiotic courses are associated with decreased mortality and morbidity, reduced length of hospitalization, and lower healthcare costs, emphasizing the clinical benefits of PCT-guided therapy.

On the other hand, CRP demonstrated only a weak correlation on Day 2 ($r = 0.184$, $p = 0.255$; not significant) and a moderate but significant correlation on Day 3 ($r = 0.468$, $p = 0.002$). This limited performance is consistent with studies by Wu et al.,[7] and Moustafa et al.,[17] which showed that CRP lacks both specificity and sensitivity as a sole indicator of sepsis severity due to its delayed kinetics and nonspecific elevation in various inflammatory states. Unlike presepsin and procalcitonin, unlike presepsin and procalcitonin, CRP levels rise later in the inflammatory process and can be elevated in many non-infectious conditions such as trauma, surgery, or chronic inflammatory diseases. This nonspecificity reduces its prognostic utility in sepsis, as elevated CRP may not accurately reflect the severity or progression of infection-induced organ dysfunction.

Comparatively, our findings strengthen the position of presepsin as a superior biomarker for dynamic monitoring of organ dysfunction in septic ICU patients. The significantly higher correlation coefficients on days 2 and 3 highlight presepsin's rapid response kinetics and its strong association with sepsis pathophysiology, as also reported by Turgman et al.,[12] in an emergency department setting. Presepsin is released early after monocyte activation by bacterial components, allowing it to rise shortly after infection onset, which makes it a valuable early marker in critical care settings where timely diagnosis and monitoring are crucial.

Additional ROC/AUC analysis further supports these findings. Presepsin consistently demonstrated excellent predictive accuracy with AUC values of 0.97 (Day 1), 0.95 (Day 2), and 0.99 (Day 3), indicating its strong ability to discriminate between different degrees of organ dysfunction. Procalcitonin showed moderate-to-good discrimination (AUC range 0.77–0.91), reflecting its usefulness but somewhat delayed kinetics compared to presepsin. CRP had lower performance (AUC range 0.58–0.73), which aligns with its less specific role in sepsis. These ROC results reinforce the role of presepsin as the most reliable biomarker in predicting organ dysfunction severity in sepsis, aligning with its very strong correlation with SOFA scores across all three days. The high AUC values of presepsin emphasize its potential utility as a front-line biomarker for risk stratification and timely intervention in ICU patients with sepsis

However, the limited sample size of our study, while sufficient to demonstrate significant correlations, may affect the generalizability of our findings. Larger, multicenter studies are needed to validate these results across diverse patient populations and clinical settings.

5. Conclusion

The levels of presepsin, procalcitonin, and CRP show positive correlations with the SOFA score. Among these biomarkers, presepsin demonstrates the strongest positive correlation with the SOFA score compared to procalcitonin and CRP. This highlights presepsin's more significant role in assessing sepsis severity and organ dysfunction, positioning it as a more effective biomarker for monitoring and evaluating the condition of sepsis patients in the intensive care unit.

6. Ethical Committee Approval

Research permit were obtained from the University of Riau Ethical Review Board for Medicine & Health Research Committee (No. B/045/UN19.5.1.1.8/UEPKK/2024).

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflicts of interest.

9. Acknowledgement

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