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Original Article

Presepsin and Mortality Risk in Sepsis: A Valuable Tool for Predicting Patient Survival

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Abstract: Background: Early identification of high-risk sepsis patients is essential for timely intervention and improved survival. Prognostic biomarkers can support clinical decision-making by stratifying mortality risk and informing treatment choices. Sepsis remains a major global health challenge due to its complex management and high mortality rate. Presepsin, a soluble CD14 subtype (sCD14-ST), has emerged as a promising biomarker for sepsis prognosis, demonstrating superior predictive value compared to conventional markers like procalcitonin (PCT). This study aims to evaluate the prognostic significance of Presepsin in predicting mortality among sepsis patients. Methods: A prospective cohort study was conducted on 110 adult sepsis patients admitted to the ICU at Dr. Saiful Anwar Hospital, Malang, from November 2018 to October 2019. Patients were diagnosed using the Sepsis-3 criteria, and Presepsin levels were measured using the chemiluminescent immunoassay (CLIA) method. Survival analysis was performed using Kaplan-Meier curves, and hazard ratios (HR) were calculated through Cox regression. Results: The ROC analysis identified 17,085 pg/mL as the optimal Presepsin threshold for predicting mortality (AUC: 0.939, 95% CI: 0.897–0.982, $p < 0.001$). Patients with Presepsin levels ≥17,085 pg/mL had a significantly lower median survival (3 days) compared to those with lower levels (9 days) (HR 3.654, 95% CI: 1.978–6.752, $p < 0.001$). Among patients with high Presepsin levels, 32 of 33 (96.9%) died, whereas only 28 of 77 (36.4%) patients with lower levels experienced mortality. Conclusion: Presepsin shows potential as a biomarker for identifying sepsis patients at increased risk of mortality. Its use may support early risk stratification and guide clinical decision-making in sepsis management.

Keywords: Presepsin; Sepsis; Survival; Mortality Risk; Prediction

1. Introduction

Sepsis remains one of the most critical global health challenges due to its complex pathophysiology, challenging difficult management, and high mortality rate. According to the World Health Organization (WHO), sepsis is a leading cause of death in intensive care units (ICUs) worldwide, with increasing incidence, particularly in developed countries. A 2017 report from WHO highlighted that sepsis accounts for a substantial proportion of ICU fatalities,

emphasizing the urgent need for early diagnosis and effective risk stratification to improve patient outcomes [1]. Despite advances in critical care, the ability to predict sepsis severity and mortality risk remains a significant clinical challenge.

According to the Sepsis-3 definition, sepsis is characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection. The Sequential Organ Failure Assessment (SOFA) score is commonly used to assess the extent of organ dysfunction in sepsis patients [2]. Singer et al. further defined septic shock as a severe subset of sepsis, in which profound circulatory and metabolic abnormalities significantly increase mortality risk [3]. However, diagnosing sepsis remains challenging, particularly in its early stages, as initial identification relies on non specific clinical signs such as fever, leukocytosis, leukopenia, tachycardia, and dyspnea. The overlap of these symptoms with other inflammatory and infectious conditions complicates early detection and timely intervention.

Currently, procalcitonin (PCT) is widely used as a biomarker for diagnosing, prognosticating, and monitoring sepsis. However, its utility in predicting mortality and distinguishing sepsis from non-infectious systemic inflammatory response syndrome (SIRS) is limited [4]. A meta-analysis by Wacker et al. concluded that procalcitonin alone is insufficient as a single biomarker for sepsis diagnosis [5]. Similarly, a meta-analysis by Tang et al. found that procalcitonin could not effectively differentiate sepsis from other non-infectious causes of SIRS [6]. These limitations highlight the need for more specific and reliable biomarkers for sepsis risk stratification and prognosis.

In 2004, a novel biomarker known as presepsin (soluble CD14 subtype, sCD14-ST) was identified as a potential alternative to procalcitonin. Presepsin is a molecular fragment produced by plasma protease activity during the immune response to infection. It has been shown to have high sensitivity and specificity for sepsis diagnosis and prognosis [7]. Unlike procalcitonin, presepsin exhibits a rapid and early rise in response to infection, making it a valuable tool for detecting sepsis at an early stage. Additionally, presepsin demonstrates a strong correlation with sepsis severity and mortality risk, further reinforcing its role as a prognostic biomarker.

Presepsin has shown superiority over procalcitonin in predicting sepsis outcomes. Studies indicate that elevated presepsin levels are associated with increased mortality, and its prognostic value may enhance clinical decision-making in sepsis management [8]. Although several studies have demonstrated the potential role of Presepsin in stratifying the risk of mortality among septic patients, few have explored its prognostic threshold in Southeast Asian ICU populations using outcome-based cutoffs. In Indonesia and other low- to middle-income countries, sepsis diagnosis and risk stratification often rely heavily on clinical judgment due to limited access to timely microbiological testing and advanced laboratory support. This situation creates a significant gap in the early identification of high-risk patients who may benefit from more intensive monitoring or intervention. Despite emerging interest in Presepsin as a prognostic biomarker, its application has not been standardized in Indonesian ICU settings, and no population-specific thresholds have been validated. Establishing a reliable, single-measure biomarker like presepsin—regardless of culture status—could greatly enhance clinical decision-making in resource-constrained environments.

Moreover, the prognostic implications of Presepsin in real-world clinical settings, where blood cultures are frequently unavailable, remain unclear. Therefore, we hypothesize that a specific threshold of serum Presepsin levels may predict 28-day mortality in ICU sepsis patients, even when microbiological confirmation is lacking.

2. Materials and Methods

This study was a prospective cohort observational study involving newly diagnosed sepsis patients at Dr. Saiful Anwar Hospital, Malang. The study was approved by the ethics committee of Saiful Anwar General Hospital (Approval No. 400/105/K.3/302/2018), ensuring compliance with ethical standards. All participants provided informed consent and met the requirements of the Declaration of Helsinki. The study, conducted from May to August 2019, included a descriptive analysis of a prospective cohort.

Participants aged 18 years and older who met the Sepsis-3 definition of sepsis were included: life-threatening organ dysfunction caused by a dysregulated host response to infection, as evidenced by a SOFA score ≥ 2. SOFA components consisted of the PaO_2/FiO_2 ratio, platelet count, bilirubin, mean arterial pressure or vasopressor use, Glasgow Coma Scale, serum creatinine, and urine output. Patients were diagnosed clinically diagnosed with sepsis by the attending physician. Inclusion criteria included age ≥ 18 years, Sepsis-3 criteria met, signs and/or symptoms

of infection, prior procalcitonin testing, and willingness to participate. Patients were excluded if they had malignancies, extensive burn trauma, cardiogenic shock, organ perfusion dysfunction, or had undergone major surgery or trauma. The study spanned from November 2018 to October 2019.

Venous blood samples were collected from eligible patients at the time of sepsis diagnosis. Follow-up blood samples were drawn at specific time points based on the half-lives of procalcitonin and presepsin to monitor biomarker dynamics. Patients were observed for 28-day survival from the date of sepsis diagnosis. A 28-day outcome was chosen based on conventions in ICU research, where 28-day mortality aligns with critical care time frames and Sepsis-3 validation studies. Presepsin levels were measured using the chemiluminescent enzyme immunoassay (CLIA) method with the PATHFAST Analyzer.

All collected data were recorded in a dedicated research logbook and digitally stored. Statistical analyses were performed using SPSS 24 for Windows. Normality testing was conducted using the Kolmogorov-Smirnov test. Diagnostic accuracy was assessed using Receiver Operating Characteristic (ROC) curve analysis, which determined the Area Under the Curve (AUC). The optimal Presepsin cut-off was calculated using the Youden Index, which maximizes the sum of sensitivity and specificity on the ROC curve. Mortality predictors were further analyzed using survival rate, median survival time, and hazard ratio (HR) calculations. Kaplan-Meier curves were generated to visualize survival outcomes. HR was chosen as it effectively evaluates risk factors over time.

3. Results

3.1. Baseline Characteristics

A total of 137 subjects met the inclusion criteria during the study period. However, 10 subjects were excluded because they were lost to follow-up after discharge within the 28-day observation period, and 17 subjects were excluded as no evidence of infection source (signs and symptoms) was recorded in their medical records. Ultimately, 110 subjects were included in the final analysis, consisting of 68 men and 42 women.

The demographic and clinical characteristics of the study population are presented in Table 1. The mean age of the patients was 55.22 ± 15.64 years. The median presepsin level was 12,374 pg/mL (interquartile range [IQR]: 4.793–18.240 pg/mL), while the median procalcitonin level was 20.41 ng/mL (IQR: 5.107–46.69 ng/mL). The median length of hospital stay was 5 days (IQR: 3–7 days). Among the study population, 50 patients (45.5%) survived, while 60 patients (54.5%) succumbed to sepsis. The most common sources of infection were multiple organ systems (35.5%), followed by the urinary tract (22.7%) and respiratory tract (18.2%).

Based on outcome, the mean age of non-survivors was higher (59.86 ± 13.81 years) compared to survivors (49.66 ± 16.00 years), but the difference was not statistically significant ($p = 0.053$). However, presepsin and procalcitonin levels were significantly higher in non-survivors compared to survivors ($p = 0.001$ for both markers). Additionally, the median length of stay was significantly shorter in non-survivors (4.5 days) compared to survivors (6 days) ($p = 0.001$).

Presepsin levels are known to be influenced by the presence and severity of bacterial infections, which are commonly confirmed through culture results. Patients with positive cultures typically exhibit higher pathogen burden, potentially leading to elevated Presepsin concentrations. Conversely, culture-negative sepsis may reflect a lower bacterial load or delayed sampling, and patients without culture data represent a clinically important subgroup often seen in resource-limited settings. By stratifying patients into three groups—positive culture, negative culture, and no culture result—we aimed to better evaluate the prognostic relevance of Presepsin across diverse real-world clinical scenarios and to minimize confounding related to microbiological confirmation status (Table 1).

3.2. Survival Analysis in Sepsis Patients

The overall survival rate of sepsis patients in the the study illustrated in Figure 1, which presents a Kaplan-Meier survival curve. The mean survival time for all sepsis patients was 7.703 days (95% CI: 6.670–8.736), and the median survival time was 7.000 days (95% CI: 6.002–7.998).

Table 1. Baseline characteristics.

Characteristics	All Patients (N = 110)	Survivor (N = 50)	Non-Survivor (N = 60)	*p* Value
Gender				
Man	68 (61.8%)	30 (60%)	38 (63.3%)	0.84
Woman	42 (38.2%)	20 (40%)	22 (36.7%)	0.053
Age (years, mean ± SD)	55.22 ± 15.64	49.66 ± 16.00	59.86 ± 13.81	
Presepsin level (pg/mL)	12,374	4331.5	17,503	0.001 *
median (Q1-Q3)	(4793–18,240)	(1961.2–9705.0)	(13,062–19,908)	
Positive culture	14,796	11,936	16,651	0.054
	(11,993–18,868)	(9967–12,003)	(11,792–20,001)	
Negative culture	13,738	13,590	14,335	NA
	(11,844–18,865)		(12,910–16,230)	
No culture results	3992	3992	17,594	0.001 *
	(1991–11,894)	(1809–6908)	(13,984–19,816)	
Procalcitonin level (ng/mL)	20.41	4.03	41.30	0.001 *
median (Q1-Q3)	(5.107–46.69)	(0.95–9.83)	(22.05–101)	
Length of stay (days)	5 (3–7)	6 (4–7)	4.5 (2–7)	0.001 *
Source of infection (suspected/proven)				
Respiratory tract	20 (18.2%)			
Skin or joints	4 (3.6%)			
GI tract	18 (16.4%)			
Urinary tract	25 (22.7%)			
Central nervous system	4 (3.6%)			
Multiple organ systems	39 (35.5%)			
Positive Culture	20 (18.2%)	4 (20%)	16 (80%)	NA
Klebsiella pneumoniae	7 (35%)			
Coagulase negative staphylococci	5 (25%)			
Escherichia coli	4 (20%)			
Acinetobacter baumannii	3 (15%)			
Candida albicans	1 (5%)			
Negative Culture	5 (4.5%)	1 (20%)	4 (80%)	NA
No culture result	85 (77.3%)	45 (52.94%)	40 (47.06%)	NA

Normally distributed continuous variables are presented as mean ± standard deviation; non-normally distributed continuous variables as median (Q1–Q3); and categorical variables as frequency (percentage). NA = not applicable.

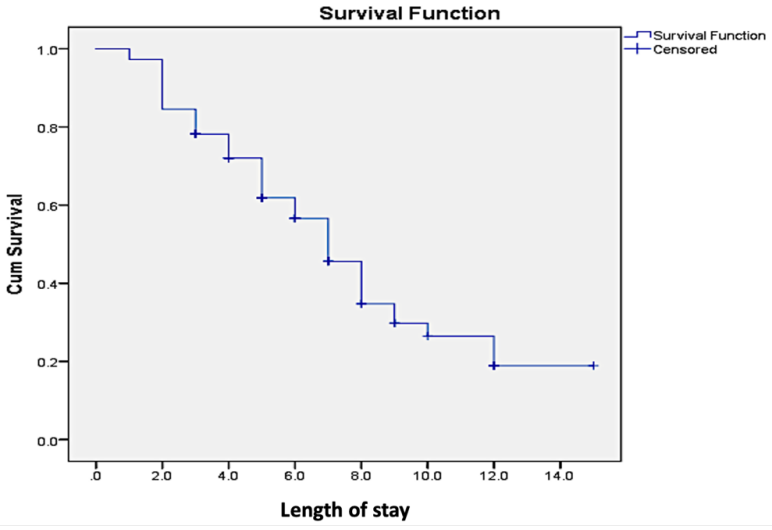

Figure 1. Kaplan-Meier curves for cumulative survival rates at 28-day.

The x-axis is time (in days), and the y-axis is the sepsis patients who have not experienced an event in the form of mortality.

3.3. Presepsin as a Mortality Predictor in Sepsis Patients

A total of 110 Presepsin measurements were analyzed to construct the ROC curve. Figure 2 depicts the ROC curve for Presepsin levels in predicting 28-day mortality. At the optimal cut-off value of 17,085 pg/mL, Presepsin demonstrated a sensitivity of 53.3%, a specificity of 98%, and an area under the curve (AUC) of 0.939 (95% CI: 0.897–0.982; $p = 0.001$), indicating excellent discriminatory performance for mortality prediction in sepsis patients.

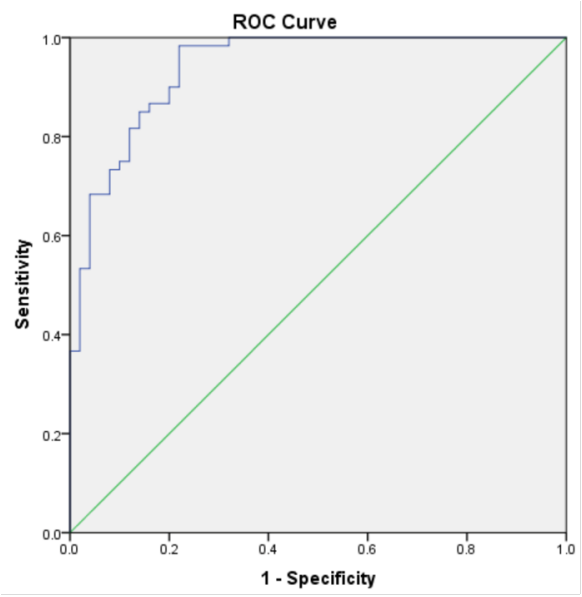

Figure 2. ROC curve of Presepsin predicting 28-day mortality.
AUC = 0.939; sensitivity = 53.3%, specificity = 98% with 95% CI 0.897–0.982 ($p = 0.001$). Diagonal green line represents the performance of a non-discriminatory test (AUC = 0.5).

Figure 3 presents the Kaplan-Meier survival curve stratified by presepsin levels (<17,085 pg/mL vs. ≥17,085 pg/mL). Patients with presepsin levels ≥17,085 pg/mL had significantly reduced survival compared to those with lower presepsin levels. The median survival time for patients with high presepsin levels was 3 days (95% CI: 2.115–3.885), whereas for those with lower presepsin levels, it was 9 days (95% CI: 6.075–11.925) ($p < 0.001$).

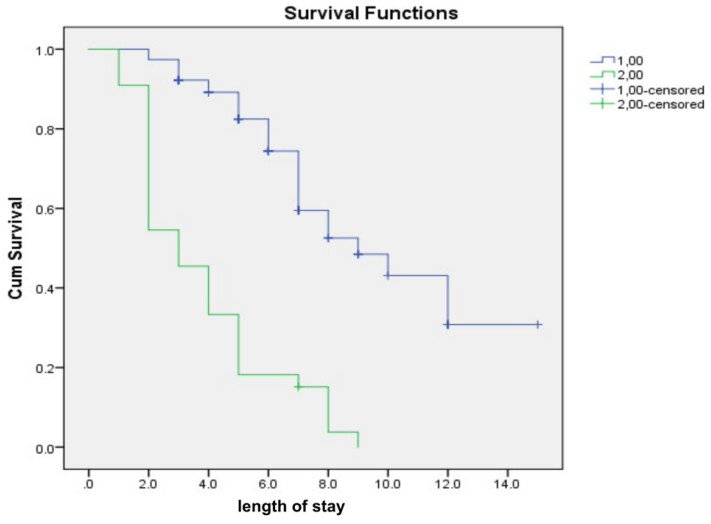

Figure 3. The Kaplan Meier Curve, based on Presepsin levels.
Description: 1.00: Presepsin < 17,085 pg/mL; 2.00: Presepsin ≥ 17,085 pg/mL. The curve shows the survival rate of sepsis patients, differentiated by the Presepsin levels. The x-axis is time (in days), and the y-axis is the percentage of sepsis patients who have not experienced an event in the form of mortality.

Subgroup analysis revealed that non-survivors had higher median Presepsin levels than survivors across all culture categories; however, statistical significance was only observed in the group without culture results ($p = 0.001$), likely due to its larger sample size. Culture-positive and culture-negative groups did not reach significance, possibly due to the limited sample sizes. Patients with renal dysfunction (eGFR < 60 mL/min/1.73 m^2) also demonstrated elevated median Presepsin levels (19,013.1 pg/mL) and increased mortality (65%) compared to those with normal renal function (8885.1 pg/mL, 47.1%). These factors were included in the multivariate Cox regression model. Using a cut-off of 17,085 pg/mL determined by the Youden Index, ROC analysis showed a sensitivity of 53.3%, specificity of 98%, and an AUC of 0.939 (95% CI: 0.897–0.982).

Table 2 details the survival time and hazard ratio analysis based on presepsin levels. The hazard ratio for mortality in patients with high presepsin levels was 3.654 (95% CI: 1.978–6.752; $p = 0.001$), indicating a significantly higher risk of mortality in this group. Among the patients with high presepsin levels, 96.9% experienced mortality events, compared to only 36.4% in the lower presepsin group.

Table 2. Event number, survival time, and Hazard Ratio analysis of survival, based on Presepsin levels.

Presepsin Level	Low (<17,085 pg/mL)	High(≥17,085 pg/mL)
Total subject	77	33
Number of events	28 (36.4%)	32 (96.9%)
Censored amount	49 (63.6%)	1 (3.1%)
Mean (95% CI)	9.747 (8.477–11.048)	3.795 (2.981–4.610)
Median (95% CI)	9.000 (6075–11,925)	3.000 (2115–3885)
p value median survival		0.000
Hazard Ratio (95% CI)		3.654 (1.978–6.752)
p value Hazard ratio		0.001

These findings highlight the potential of presepsin as a valuable biomarker for mortality prediction in sepsis patients, demonstrating strong discriminatory power and prognostic significance.

4. Discussion

4.1. Survival Outcomes and Baseline Characteristics

This study observed 110 sepsis patients over a 28-day period, with 50 patients surviving and 60 succumbing to the condition. Male patients constituted 61.8% of the cohort, while female patients accounted for 38.2%. The gender distribution between survivors (60% male, 40% female) and non-survivors (63.3% male, 36.7% female) did not significantly differ ($p = 0.84$). These findings align with previous research, such as studies by Ko et al. [9], which also reported no significant impact of gender on sepsis mortality or hospital stay duration. They found that there were no significant differences in the baseline characteristics among the three age groups, with comparable distributions of male and female patients across the entire population. Although the study reported that the overall crude in-hospital mortality rate was 27.7%, with mortality rates of 30.0% in males and 24.7% in females ($p < 0.01$), the adjusted analysis showed that the odds ratio (OR) for in-hospital mortality in males compared to females was 1.15 (95% CI: 1.02–1.29) [9]. This indicates that the risk of mortality in male and female sepsis patients is essentially the same.

Study by Luethi et al., reported that men and women had similar risk-adjusted ICU, hospital and one-year mortality implying that, although there is a male dominance among patients with sepsis and septic shock, gender might not affect short- or long-term mortality [10]. While some studies suggest that hormonal and immunological differences between genders may impact sepsis outcomes, our findings indicate that gender alone does not significantly determine survival in sepsis patients. This suggests that other factors, such as disease severity and treatment, may play a more crucial role in influencing patient survival than gender differences.

The study highlights that older age is associated with a higher risk of sepsis-related complications and mortality. While the age difference between survivors and non-survivors was not statistically significant, non-survivors had a higher mean age. This finding supports previous research by Baiq et al., emphasizing that individuals over 50 are more susceptible to sepsis and its complications, such as multi-organ failure. Age-related immune senescence

leads to a diminished immune response, making elderly patients more vulnerable to infections and poor clinical outcomes [10, 11]. Additionally, the accumulation of comorbidities, including diabetes, cardiovascular diseases, and chronic kidney disease, further exacerbates the risk of sepsis-related mortality.

A meta-analysis by Nasa et al. confirmed that older age is an independent predictor of poor sepsis outcomes, reinforcing the need for early and aggressive interventions in elderly patients. Timely administration of antibiotics, fluid resuscitation, and organ support are crucial in mitigating the heightened mortality risk in this population [12]. Future studies should explore targeted interventions and personalized treatment strategies for older sepsis patients to improve their survival rates.

One of the most striking findings in this study was the significantly higher Presepsin levels in non-survivors (median: 17,503 pg/mL; range: 13,062–19,908 pg/mL) compared to survivors (median: 4331.5 pg/mL; range: 1961–9705 pg/mL) ($p = 0.001$). Elevated Presepsin levels are indicative of a heightened immune response to severe infection, often correlating with increased systemic inflammation and organ dysfunction. The findings from this study are consistent with previous research, including the Korean study, which demonstrated a similar trend in higher Presepsin levels among non-survivors alongside elevated lactate levels and SOFA scores [13]. Beyond its diagnostic capabilities, Presepsin has been recognized for its predictive value in assessing sepsis severity and guiding clinical decision-making. Studies have shown that high Presepsin levels are associated with a greater likelihood of multi-organ failure, prolonged intensive care unit (ICU) stays, and increased mortality rates. Its role in early risk stratification makes it a valuable tool for clinicians in identifying high-risk patients who may require more intensive monitoring and aggressive interventions.

Moreover, recent literature suggests that combining Presepsin with other biomarkers, such as procalcitonin and lactate, may enhance its predictive accuracy for sepsis outcomes [8]. Future research should focus on establishing standardized Presepsin cut-off values across different populations and exploring its integration into sepsis management protocols to improve patient survival.

Notably, survivors had a significantly longer median hospital stay compared to non-survivors ($p < 0.001$). While this may seem counterintuitive, it likely reflects the rapid clinical deterioration and early in-hospital mortality among non-survivors, whereas survivors required prolonged treatment and supportive care to recover. This trend aligns with findings from Yang et al., who reported shorter hospital stays among non-survivors due to early mortality [13]. The results of this study further support previous research, highlighting the high mortality rates and significant resource utilization associated with sepsis.

Our findings reinforce that sepsis-related mortality remains a major concern, particularly in populations with high disease severity. Additionally, comorbidities and advanced age are key contributors to both hospital mortality and resource utilization. Older patients and those with underlying health conditions often require more intensive care, prolonged hospitalization, and aggressive interventions, further increasing the burden on healthcare systems. These findings emphasize the need for early identification and targeted management strategies to improve survival outcomes and optimize resource allocation in sepsis treatment.

4.2. Survival Outcomes and Baseline Characteristics

Kaplan-Meier survival analysis demonstrated a steep decline in survival rates, particularly in the early days following sepsis diagnosis. By day 5, survival had already dropped to 60%, and by day 10, it had decreased to just 30%, with a further decline to 20% by day 14. The median survival time of 7 days indicates that half of the patients in the study succumbed to sepsis within the first week. This pattern is consistent with findings from a Brazilian study, which reported variable survival rates (30% to 82% at day 15 and 20% to 72.5% at day 30) depending on disease severity and the timeliness of medical intervention [14].

The sharp decline in survival during the early phase of sepsis highlights the critical importance of immediate and aggressive management. Early goal-directed therapy (EGDT), which includes rapid hemodynamic stabilization, appropriate antibiotic administration, and timely source control, has been associated with improved patient outcomes. However, despite the well-documented benefits of early intervention, real-world implementation remains challenging due to resource constraints, delays in sepsis recognition, and variations in adherence to sepsis treatment guidelines [15].

Furthermore, the role of biomarkers such as Presepsin in identifying high-risk patients early in the disease course is gaining attention. Elevated Presepsin levels have been correlated with increased mortality, suggesting that

incorporating biomarker-based risk stratification could enhance clinical decision-making. Future research should explore strategies to integrate such biomarkers into routine sepsis management protocols, potentially improving early diagnosis and individualized treatment approaches. Additionally, optimizing intensive care resources and strengthening early warning systems in hospitals may further improve survival outcomes in sepsis patients.

4.3. Presepsin as a Predictor of Mortality

Presepsin demonstrated strong prognostic value in this study, reinforcing its potential as a biomarker for predicting sepsis-related mortality. Receiver Operating Characteristic (ROC) curve analysis identified an optimal Presepsin cut-off level of 17,085 pg/mL, yielding an area under the ROC curve (AUROC) of 93.9% (95% CI: 89.7%–98.2%, $p < 0.001$). This high AUROC value underscores its strong discriminative power in distinguishing between survivors and non-survivors. At this threshold, Presepsin exhibited a specificity of 98% and a sensitivity of 53.3%, demonstrating its ability to accurately identify patients at a higher risk of mortality. Notably, all patients with Presepsin levels above this cut-off succumbed to sepsis by day 10, whereas 50% of those with lower levels survived beyond this period.

The cut-off value of 17,085 pg/mL was determined through ROC curve analysis of the entire cohort (N = 110), without stratification by culture status. This approach was intended to mirror real-world ICU settings—particularly in resource-limited environments—where microbiological confirmation is frequently unavailable. Survival analysis further supported the prognostic value of this threshold: patients with Presepsin levels below 17,085 pg/mL had a median survival of 9 days, compared to just 3 days among those with higher levels. The marked difference in mortality rates—96.9% in the elevated Presepsin group versus 36.4% in the lower-level group—emphasizes its utility for risk stratification. Although differences within smaller subgroups were not statistically significant, Kaplan-Meier survival curves and Cox regression analysis demonstrated a strong association between elevated Presepsin levels and increased mortality risk (HR = 3.654, $p = 0.001$). These findings are consistent with previous studies that reported a significant association between elevated Presepsin levels and increased mortality risk, including a 5- to 7-fold higher risk among patients in the highest Presepsin quartile [16–18].

The study further demonstrated that Presepsin performed comparably to procalcitonin (PCT) in predicting mortality, suggesting its potential utility in guiding sepsis management. Additionally, the study highlighted that Presepsin levels remained elevated in non-survivors throughout the disease course, reinforcing its role as a biomarker not only for early risk stratification but also for monitoring disease progression. Beyond its role as a static prognostic marker, Presepsin has also been explored for its dynamic changes over time. Serial measurements have shown that persistently high or rising Presepsin levels correlate with worse outcomes, while declining levels may indicate treatment response and recovery. This concept aligns with the findings of Masson et al., who observed that non-survivors exhibited sustained elevation of Presepsin levels, whereas survivors showed a gradual decline during hospitalization [19].

These findings underscore the potential of Presepsin as a biomarker not only for early risk assessment but also for tracking therapeutic efficacy and guiding treatment decisions. Recent studies have highlighted the potential of Presepsin as part of a multi-marker approach for improving sepsis prognosis. A study by Kim et al. demonstrated that combining Presepsin with other biomarkers such as procalcitonin, galectin-3, and soluble suppression of tumorigenicity 2 (sST2) significantly improved mortality prediction in sepsis patients [20]. Similarly, Piccioni et al. emphasized the importance of Presepsin in early sepsis detection and its ability to complement traditional biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) [21]. These findings suggest that a multi-biomarker approach may offer superior prognostic value compared to relying on Presepsin alone.

The prognostic utility of Presepsin is further strengthened when combined with other clinical parameters, such as lactate levels and the Sequential Organ Failure Assessment (SOFA) score. Previous studies have demonstrated that incorporating Presepsin into predictive models enhances their accuracy in identifying high-risk sepsis patients. A study by Baik et al. validated the role of Presepsin in predicting mortality and demonstrated its effectiveness as a prognostic marker for sepsis outcomes [22]. Additionally, de Moura et al. emphasized that Presepsin serves as a unifying biomarker across different age groups, further supporting its broad applicability in clinical practice [23].

Giannakopoulos et al. conducted a systematic review highlighting the growing role of biomarkers, including Presepsin, in sepsis management. They suggested that a multi-marker approach, integrating Presepsin with other inflammatory and organ dysfunction biomarkers, could improve early diagnosis and risk stratification [24]. Sim-

ilarly, Lee et al. demonstrated that combining Presepsin with procalcitonin improved mortality prediction and distinguished sepsis from non-infectious critical illness more effectively than either biomarker alone [25]. These findings reinforce the idea that Presepsin, when used in conjunction with other established sepsis markers, enhances the accuracy of prognostic models and supports early clinical decision-making. While the overall findings support the prognostic relevance of Presepsin, this study was limited by the absence of microbiological confirmation in many patients and by the exclusion of those with certain comorbidities. Although subgroup differences by culture status were not statistically significant, likely due to small sample sizes, elevated Presepsin levels were consistently observed in non-survivors. Renal function, a potential confounder, was also considered in our interpretation to enhance the clinical relevance of the findings.

Given its strong predictive performance, Presepsin could play a crucial role in guiding early intervention strategies, such as the initiation of aggressive resuscitation and targeted organ support in critically ill patients. Future research should focus on validating these findings in larger, multicenter cohorts and exploring the potential of serial Presepsin measurements to monitor treatment response and disease progression. Additionally, further investigation into the integration of Presepsin with other emerging biomarkers and machine learning-based predictive models may enhance its clinical utility in sepsis management. The growing body of evidence suggests that personalized medicine approaches, leveraging biomarker panels and AI-driven analytics, could revolutionize sepsis diagnosis and treatment, ultimately improving patient outcomes.

4.4. Clinical Implications and Future Perspectives

Our findings underscore the potential utility of Presepsin in stratifying sepsis risk. Given its high specificity and strong association with mortality, Presepsin could be incorporated into existing sepsis scoring systems, such as SOFA or APACHE II, to enhance prognostic accuracy. Furthermore, serial Presepsin measurements may provide insights into disease progression and treatment response. Studies have suggested that declining Presepsin levels following therapy are associated with better outcomes, whereas persistently elevated levels indicate treatment failure and impending deterioration [22, 23].

Despite its promise, routine use of Presepsin in clinical practice faces challenges. The test is not yet widely available in all healthcare settings, and its cost-effectiveness compared to other biomarkers, such as procalcitonin or C-reactive protein (CRP), requires further evaluation. Additionally, the optimal timing and frequency of Presepsin measurement remain areas of active research.

Future studies should explore the role of Presepsin in guiding sepsis management decisions, such as antibiotic escalation, fluid resuscitation strategies, and early discharge planning. Large-scale, multi-center trials are needed to validate our findings and establish standardized cut-off values for different patient populations.

4.5. Limitations

This study has several limitations. It was conducted at a single tertiary referral hospital, which may limit its generalizability to other settings. Exclusion patients with malignancies, trauma, or burns was intended to reduce confounding but may have affected external validity. We also did not account for comorbidities—such as diabetes or chronic kidney disease, which could influence Presepsin levels and clinical outcomes. Although variations in Presepsin levels were observed across culture-based subgroups, the small number of cultured patients limits the strength of subgroup comparisons. Moreover, while we proposed a cut-off value for Presepsin, further validation in external populations is needed.

5. Conclusions

This study supports the role of Presepsin as a useful marker for identifying sepsis patients at higher risk of death and poor outcomes. Patients with elevated Presepsin levels showed shorter survival and a significantly higher risk of mortality. Despite some variation across subgroups, the overall findings indicate that Presepsin can serve as an early warning tool to help prioritize care, especially in settings where microbiological confirmation is limited.

Author Contributions

Conceptualization, A.I.; methodology, A.I.; software, A.I.; validation, A.I. and Y.A.P.; formal analysis, A.I. and Y.A.P.; investigation, A.I. and Y.A.P.; resources, A.I. and Y.A.P.; data curation, A.I., Y.A.P. and I.A.W.; writing—original draft preparation, A.I. and Y.A.P.; writing—review and editing, A.I., Y.A.P. and A.A.; visualization, A.I.; supervision, A.I. and M.A.; project administration, A.I. and Y.A.P.; funding acquisition, A.I. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Saiful Anwar General Hospital (Approval No. 400/105/K.3/302/2018). Ethical clearance ensured that all procedures involving human participants adhered to the highest standards of research integrity and patient safety.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The datasets generated and/or analyzed during this study are not publicly available due to institutional regulations but may be obtained from the corresponding author upon reasonable request and with appropriate institutional approvals.

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Conflicts of Interest

The authors declare no conflict of interest.

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