



BLOOD UREA NITROGEN/ALBUMIN RATIO AS A PREDICTOR OF CLINICAL OUTCOME IN SEPSIS

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ABSTRACT

Sepsis is a life-threatening condition characterized by organ dysfunction resulting from a dysregulated immune response to infection. Sepsis is the leading cause of death from infection globally. Blood Urea Nitrogen (BUN) serves as a marker of kidney damage, and albumin is an indicator of fluid homeostasis. The BUN/albumin ratio can be used to predict mortality in infectious diseases, making it a widely studied and effective prognostic marker for mortality in sepsis patients. Analyzing the Blood Urea Nitrogen (BUN)/albumin ratio as a predictor of clinical outcome in sepsis patients. This retrospective cohort study used secondary data from laboratory results and electronic medical records of adult sepsis patients treated in intensive care units at RSUP Dr. Hasan Sadikin Bandung from January 2022 to December 2023. Patients were identified using ICD-10 code A41.9 and a Sequential Organ Failure Assessment (SOFA) score ≥ 2 . Blood urea nitrogen and serum albumin levels were obtained from the first laboratory examination within 48 hours after ICU admission. A total of 139 patients who met the inclusion criteria were included. Statistical analysis was performed, with significance set at $p < 0.05$. The subjects of this study included 139 sepsis patients, with a significant difference in the BUN/Albumin ratio between those who died and those who survived. The median BUN/albumin ratio was significantly higher in sepsis patients who died (16.58) compared to those who survived (9.16), $p < 0.001$. The analysis of the Receiver Operating Characteristic (ROC) curve showed an Area Under the Curve (AUC) of 0.814, indicating good predictive ability for mortality. The BUN/Albumin ratio with a cutoff of ≥ 10.1617 had a sensitivity and specificity of 73 and 71.8%, respectively. The Relative Risk in this study was 1.77, indicating that sepsis patients with a BUN/albumin ratio of ≥ 10.1617 had a 1.77 times higher risk of death compared to those with a BUN/albumin ratio of < 10.1617 . The BUN/albumin ratio is a significant predictor of mortality for determining clinical outcomes in sepsis patients. A higher BUN/albumin ratio is associated with increased mortality in sepsis patients, therefore the BUN/albumin ratio is useful as a prognostic marker of mortality in sepsis patients in clinical practice.

Keywords: albumin; blood urea nitrogen; clinical outcome; prognostic marker; sepsis

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INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated immune response to infection (Singer et al., 2016). Sepsis remains a major global health problem and is the leading cause of death due to infection worldwide (Knoop et al., 2017). The global incidence of sepsis reached approximately 49 million cases in 2017, with 11 million deaths, accounting for 19.7% of total global mortality (Rudd et al., 2020). Septic shock has an annual incidence rate of approximately 10–30%. Its occurrence is influenced by factors such as pathogen type, source of infection, use of immunosuppressive drugs, and the presence of comorbidities. When these factors are present, sepsis-related mortality can increase to 30%–50% or higher (Jarczak et al., 2021). In Indonesia, the incidence of sepsis was reported to be 30.29%, with mortality rates ranging from 11.56% to 49% in 2018 (Sya'bani et al., 2021). A study by Wicaksono et al. (2022) reported that

among 110 patients with sepsis and septic shock treated in the intensive care unit (ICU) of a Type B hospital, 49% died while 51% showed clinical improvement.

Bacterial infection is one of the main causes of sepsis. Bacterial components activate monocytes and macrophages, leading to the release of pro-inflammatory cytokines and chemokines and resulting in an excessive inflammatory response. In addition, bacterial infections can activate neutrophil extracellular traps (NETs), which contribute to hypercoagulation and endothelial damage. These processes cause hypoperfusion, tissue hypoxia, plasma leakage, and ultimately organ, tissue, and cellular dysfunction. Cardiovascular dysfunction reduces oxygen delivery to tissues, while decreased renal perfusion, acute tubular necrosis, and microvascular defects may lead to acute kidney failure of varying severity (Gyawali et al., 2019; Jarczak et al., 2021). Blood urea nitrogen (BUN) is a final product of protein metabolism that is primarily excreted by the kidneys. BUN levels increase in conditions of excessive protein catabolism or reduced glomerular filtration rate. Decreased renal filtration enhances urea reabsorption and reflects impaired kidney function. Sepsis patients frequently develop multi-organ dysfunction, including acute kidney injury, which can significantly elevate BUN levels. BUN values can be calculated by dividing serum urea levels by 2.14 as a correction factor (Li et al., 2021; Min et al., 2022).

Albumin is a major plasma protein that serves as an indicator of nutritional status and fluid homeostasis. In kidney failure, albuminuria occurs due to increased glomerular membrane permeability, leading to reduced serum albumin levels (hypoalbuminemia). In sepsis, hypoalbuminemia is further exacerbated by capillary leakage, tissue ischemia, reperfusion injury, and systemic inflammation. Decreased serum albumin levels have been shown to be associated with poor clinical outcomes and increased mortality in sepsis and septic shock (Figuroa et al., 2021; Gong et al., 2020). Several studies have demonstrated that the blood urea nitrogen-to-albumin (BUN/albumin) ratio can serve as a prognostic biomarker for mortality in infectious diseases, including pneumonia, *Escherichia coli* bacteremia, and acute pulmonary embolism (Fang & Xu, 2021; Feng et al., 2019; Zou et al., 2021). The BUN/albumin ratio has also been identified as an independent predictor of mortality in sepsis patients treated in the ICU (Min et al., 2022). However, data regarding the prognostic value of the BUN/albumin ratio in sepsis patients in Indonesia remain limited. Therefore, this study aimed to analyze the blood urea nitrogen-to-albumin ratio as a predictor of clinical outcomes in sepsis patients treated in intensive care units.

METHOD

This research method is an observational analytic study using a retrospective cohort design to analyze the blood urea nitrogen (BUN)/albumin ratio as a predictor of clinical outcomes in sepsis patients. This study used secondary data of sepsis patients from the clinical pathology laboratory information system and electronic medical records of Dr. Hasan Sadikin General Hospital, Bandung, from January 2022 to December 2023. The subjects of this study were sepsis patients treated in the intensive care unit, namely General Intensive Care Unit (GICU), Cardiac Intensive Care Unit (CICU), Kemuning Special Infection Isolation Room (RIKK) and Medical Intermediate Care (MIC). This study required a minimum sample size of 132, calculated using the estimated sample size approach for a matched case-control study. The sampling method used was total sampling, which included the entire population of sepsis patients who met the inclusion criteria. The inclusion criteria for the subjects of this study were all patients diagnosed with sepsis aged ≥ 18 years with a Sequential Organ Failure Assessment (SOFA) score of ≥ 2 and code A41.9 based on the International Classification of Diseases 10th Revision (ICD-10) who were treated in the intensive care unit between January 2022 and December 2023. The exclusion criteria for the subjects of this study were patients who died within the first 24 hours of treatment and incomplete laboratory data (no BUN and/or albumin laboratory data available within the first 48 hours after admission to the intensive care unit). Descriptive statistical analysis was performed to describe the characteristics of the study subjects, including age, sex, comorbidities, length of stay, blood urea nitrogen (BUN) levels, albumin levels, and the BUN/albumin ratio. Normality of numerical data was assessed

before analysis. Categorical variables were analyzed using the chi-square test, while non-normally distributed numerical variables were analyzed using the Mann–Whitney U test. Statistical significance was defined as a p-value <0.05. The optimal cut-off value and predictive ability of the BUN/albumin ratio for clinical outcomes (survival and mortality) were determined using the area under the receiver operating characteristic (AUROC) curve. Prediction of clinical outcomes was assessed by calculating relative risk. This study received ethical approval from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung (No. DP.04.03/D.XIV.6.5/226/2024).

RESULT

Sepsis patient data was obtained from the laboratory information system and electronic medical records for 139 people who met the inclusion criteria from a total of 1,643 sepsis patients in the period January 2022 to December 2023.

Table 1.
Characteristics of Research Subjects

Subject Characteristics	OutcomeClinical		p-value
	Die (n=100)	Life (n=39)	
Age			0.795
18-44 years, n (%)	28 (28.0)	9 (23.1)	
45-59 years, n (%)	24 (24.0)	9 (23.1)	
≥60 years, n (%)	48 (48.0)	21 (53.8)	
Gender			0.808
Male, f (%)	60 (60.0)	24 (61.5)	
Female, f (%)	40 (40.0)	15 (38.5)	
Comorbidities			
Diabetes Mellitus, f (%)	30 (30.0)	12 (30.8)	0.929
Hypertension, f (%)	42 (42.0)	15 (38.5)	0.703
COPD, f (%)	4 (4.0)	5 (12.8)	0.058
Malignancy, f (%)	16 (16.0)	3 (7.7)	0.200
Length of Treatment (days), Median (Min-Max)	8.00 (1.00-70.00)	10.00 (1.00-69.00)	0.403
BUN (mg/dL), Median (Min-Max)	40.93 (8.36-202.99)	24.67 (2.99-45.98)	<0.001
Albumin (mg/dL), Median (Min-Max)	2.53 (1.00-4.40)	2.90 (1.60-4.30)	0.002
BUN/Albumin Ratio, Median (Min-Max)	16.58 (6.26-114.72)	9.16 (0.76-14.93)	<0.001

Description: Min (minimum), Max (Maximum), COPD (Chronic Obstructive Pulmonary Disease), BUN (Blood Urea Nitrogen)

Table 1 shows the characteristics of the study subjects based on clinical outcomes, namely patients who died and those who survived. The number of sepsis patients who died was higher, namely 100 people compared to patients who survived, namely 39 people. Comparison of subjects by age group, gender, comorbidities (diabetes, hypertension, COPD, malignancy), and length of stay showed that there was no significant difference between sepsis patients who died compared to those who survived. Most sepsis patients who died were aged ≥60 years with a total of 48 people (48%). 60% more male sepsis patients died compared to females, namely 40%. The most common comorbidity in sepsis patients was hypertension, with 42 people (42%) in the deceased group and 15 people (38.5%) in the surviving group. Table 1 shows that the BUN, albumin, and BUN/albumin ratio results differed significantly between the group of sepsis patients who died and the group who survived. Analysis of the difference test on BUN, albumin, and BUN/albumin ratio levels used the Mann-Whitney test because the data were not normally distributed. The BUN/albumin ratio results of sepsis patients differed significantly with a median of 16.58 (6.26-114.72) in the group who died and 9.16 (0.76-14.93) in the group who survived with a p value <0.001.

Figure 1 above shows Receiver Operating Characteristic (ROC) curve for the BUN/albumin ratio index in differentiating between sepsis patients with clinical outcomes of death or survival. The Area Under the Curve (AUC) value obtained was 0.814, indicating that the BUN/albumin ratio had good ability to detect differences between the two groups in sepsis patients who died and who survived. The determination of the cut-off value of the BUN/albumin ratio was carried out by

considering balanced sensitivity and specificity and was good enough to predict mortality in sepsis patients, namely 10.1617 as seen in Table 2 below.

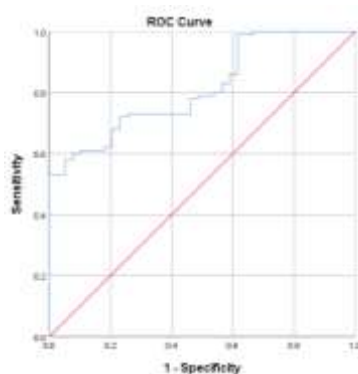


Figure 1. Receiver Operating Characteristic Curve for BUN/Albumin Ratio Index on Clinical Outcomes in Sepsis Patients

Table 2.

Comparison of BUN/Albumin Ratio with Clinical Outcomes in Sepsis Patients

BUN/Albumin Ratio	Outcome Clinical		Sensitivity	Specificity	p-value	RR
	Die	Life				
Died (≥ 10.1617)	73	11	73.0%	71.8%	<0.001	1.77
Life (< 10.1617)	27	28				

Description: Relative Risk (RR)

Table 2 above shows that the BUN/albumin ratio of sepsis patients with a value of ≥ 10.1617 is significantly different from the BUN/albumin ratio < 10.1617 in the deceased and surviving groups with a p value of < 0.001 . The results of this study showed that 73% of sepsis patients who died had a BUN/Albumin ratio ≥ 10.1617 with a sensitivity of 73% and a specificity of 71.8%. The relative risk (RR) value of 1.77 indicates that sepsis patients with a BUN/Albumin ratio ≥ 10.1617 had a 1.77 times greater risk of death compared to sepsis patients with a BUN/Albumin ratio < 10.1617 .

DISCUSSION

Sepsis is one of the most common critical illnesses treated in intensive care units (ICUs). Despite advances in facilities and clinical guidelines for sepsis management, morbidity and mortality rates remain high, making sepsis a major concern in critical care practice. In this study, the number of sepsis patients who died was higher than those who survived. This finding is consistent with the World Health Organization report, which stated that approximately one in three patients with sepsis treated in the ICU died (World Health Organization, 2020). Similarly, a study by Liu et al. (2022) reported a higher number of non-survivors (435 patients) compared to survivors (335 patients) among hospitalized sepsis patients. This study also showed that mortality among male sepsis patients (60%) was higher than among females (40%). This finding aligns with the WHO report indicating that sepsis-related mortality is higher in men than women, with rates of 164 versus 134 per 100,000 population, respectively (World Health Organization, 2020). In addition, sepsis in this study predominantly occurred in patients aged ≥ 60 years, both in the deceased (48%) and surviving (53%) groups. This result is consistent with the study by Min et al. (2022), which reported a mean age of 64.70 ± 16.79 years among sepsis patients.

Comorbidities, including diabetes mellitus, hypertension, and malignancy, were not significantly different between deceased and surviving sepsis patients in this study. This finding is consistent with previous studies by Min et al. (2022) and Mellhammar et al. (2023), which also found no significant differences in these comorbidities between outcome groups. Similarly, the length of hospital stay did not differ significantly between deceased and surviving patients, supporting findings from Liu et al. (2022) that reported no significant difference in ICU length of stay among sepsis patients. The blood urea nitrogen-to-albumin (BUN/albumin) ratio was significantly higher in deceased sepsis patients than in survivors. This result is consistent with previous studies by Li et al. (2021) and Cai et al. (2022), which demonstrated that the BUN/albumin ratio could predict

clinical outcomes during hospitalization and at 30 days. In the present study, sepsis patients with a BUN/albumin ratio ≥ 10.1617 had a 1.77-fold higher risk of death compared to those with lower ratios. This finding is in line with the study by Wang et al. (2023), which reported an increased mortality risk in patients with a BUN/albumin ratio ≥ 8 .

According to the Sepsis-3 definition, sepsis is characterized by life-threatening organ dysfunction resulting from dysregulated host responses to infection (Singer et al., 2016). The pathophysiology of sepsis involves complex immune responses aimed at controlling infection and repairing tissue damage. Excessive release of pro-inflammatory mediators relative to anti-inflammatory mediators, known as a cytokine storm, contributes to multiple organ dysfunction, including acute kidney injury. Kidney dysfunction in sepsis can be reflected by elevated BUN levels (Jarczak et al., 2021; Napolitano, 2018). In sepsis, increased microvascular permeability during systemic inflammation alters intravascular and extravascular albumin distribution. Albumin, a negative acute-phase reactant, decreases in concentration due to inhibited hepatic synthesis mediated by inflammatory cytokines such as tumor necrosis factor- α and interleukin-1. Low serum albumin levels have been associated with poor clinical outcomes and increased mortality in sepsis patients, as demonstrated by Kendall et al. (2019). Sepsis is also characterized by hypercatabolic states and renal microcirculatory dysfunction, leading to increased protein breakdown and elevated BUN synthesis. Inflammatory mediator release, immune cell infiltration, and dysregulated nitric oxide synthesis contribute to impaired renal function and increased urea reabsorption, particularly in dehydrated patients. Recent studies by Min et al. (2022), Cai et al. (2022), and Wang et al. (2023) have highlighted the potential utility of the BUN/albumin ratio as a prognostic marker for mortality in sepsis patients. The limitations of this study include the absence of body mass index data, such as obesity status, which may influence kidney function, and the lack of adjustment for other diseases that can independently increase BUN levels or decrease serum albumin levels. These factors may affect the BUN/albumin ratio and should be considered in future studies (Chen et al., 2021).

CONCLUSION

Sepsis patients who died had a significantly higher BUN/albumin ratio compared to sepsis patients who survived. Sepsis patients with a BUN/albumin ratio ≥ 10.1617 have a 1.77 times greater risk of death than sepsis patients who have BUN/albumin ratio < 10.1617 .

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