

Relationship between Neutrophil Albumin Ratio and SOFA score in sepsis patients at Wahidin Sudirohusodo Hospital

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ORIGINAL ARTICLES

1 Relationship between Neutrophil Albumin Ratio and SOFA score in sepsis patients at Wahidin Sudirohusodo Hospital

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ABSTRACT

Background and aim. Sepsis is organ dysfunction due to dysregulation of the body's response to infection. Currently, there are several parameters to predict outcomes in sepsis patients. Recently, neutrophil to albumin ratio (NAR) was developed to predict sepsis severity, but studies are still limited. This study was conducted to determine the relationship between NAR and sepsis severity.

Methods. This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Hospital, Makassar. We included sepsis patients aged ≥ 18 years and blood were taken for laboratory examination. Sepsis was diagnosed if the SOFA score was ≥ 2 and NAR was the ratio of neutrophil count (%) and albumin (gr/dL) based on laboratory results. Data were analyzed using logistic regression test and Chi-square test.

Results. There were 60 subjects who met the study criteria with 32 female subjects and a mean age of 54.67 ± 14.45 years. In this study, it was found that patients with SOFA score ≥ 8 had a higher mean NAR value, which was 29.09. The logistic regression test results also obtained an OR value of 29.9; $p = 0.032$. In addition, the cut-off value of NAR to predict SOFA score ≥ 8 was 33.4 with sensitivity of 94% and specificity of 96%.

Conclusions. This study found that there was a significant association of increased NAR with SOFA scores. A higher neutrophil count was proportional to a higher SOFA score, while lower albumin was proportional to a higher SOFA score.

Keywords: sepsis, SOFA score, neutrophil-to-albumin ratio, NAR

INTRODUCTION

Sepsis is organ dysfunction due to dysregulation of the body's response to infection. The global prevalence of sepsis is high with an estimated 49 million new cases of sepsis with 11 million deaths annually, accounting for 19.7% of deaths worldwide.⁽¹⁾ Despite medical advances in the diagnosis and management of sepsis, sepsis remains one of the leading causes of morbidity and mortality in critically ill patients.⁽²⁾ Based on the Sepsis-3 consensus, the diagnosis of sepsis is made in patients with suspected or historical infection who show an acute increase in the sequential organ failure assessment (SOFA) score ≥ 2 points.⁽³⁾

Currently, there are several parameters that support the diagnosis of sepsis and predict outcomes in sepsis patients, including leukocyte count, ESR, and C-reactive protein (CRP).⁽⁴⁾ Hypoalbuminemia (albumin < 3.5 grams/dL) and diastolic blood pressure < 52 mmHg have been identified as predictors of severe sepsis. However, these parameters have poor sensitivity and specificity.⁽⁵⁾

Recently, neutrophil to albumin ratio (NAR) was developed to predict sepsis severity, but studies are still limited. Elevated neutrophils indicate infection, the excess immature neutrophils in the peripheral circulation indicate systemic inflammatory response syndrome (SIRS) which is also associated with worsening of the patient's condition in sepsis. In addition, albumin is the most abundant protein in plasma which has an anti-inflammatory effect on sepsis patients. It is supported that hypoalbuminemia in sepsis patients decreases the survival rate by 70.6%.⁽⁶⁾ Therefore, we conducted this study to determine the association between NAR and sepsis severity, so that it can be an effective and efficient biomarker in predicting the severity and outcome of sepsis patients.

MATERIALS AND METHODS

This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar from October 2023 until the minimum sample size reached. Our minimum sample size was 49 patients. We included sepsis patients aged ≥ 18 years and blood were taken for laboratory examination. The blood was taken from median cubiti vein in 3 ml amounts and put into a citrate tube. Blood samples were examined by counting the number of neutrophils and albumin levels using the chemical method.

Sepsis was diagnosed if the SOFA score was ≥ 2 and NAR was the ratio of neutrophil count (%) and albumin (gr/dL) based on laboratory results. Our protocols has been approved by Ethics Committee of Biomedical Research on Human, Faculty of Medicine, Universitas Hasanuddin, Makassar, South Sulawesi. Data were analyzed using logistic regression test and Chi-square test. Statistical test results were considered significant if the p value was < 0.05 .

RESULTS

There were 60 subjects who met the study criteria with 32 female subjects and a mean age of 54.67 ± 14.45 years. The most common comorbidities were CKD with 22 subjects (36.7%) followed by liver and biliary disease with 21 subjects (35%), diabetes mellitus and malignancy with 12 subjects (20.0%) each, cardiovascular disease with 9 subjects (15%), cerebrovascular disease with 5 subjects (8.3%) and immunodeficiency with 2 subjects (3.3%). Most of the patient (61.7%) has two or more comorbidities.

The most common source of infection from the respiratory system is (40%), followed by abdominal infection (26.7%), urinary tract infections (8.3%), skin and soft tissue infections (15%), hematological infections (10%). The range of SOFA scores is 2-14 with the mean of 8 ± 3.13 . The number of subjects with SOFA scores < 8 was 28 subjects (46.7%) and subjects with SOFA scores > 8 were 32 subjects (53.3%). The range of albumin levels in the study was 1.5- 4 gr/dl with a mean of 2.57 ± 0.47 . The range of neutrophil levels was 71.65 - 95.8 with a mean of 86.77 ± 5.55 . The mean of neutrophil albumin ratio (NAR) value was 33.6 ± 8.22 .

Table 1. Subjects' characteristics.

Variable	n (%)	Min	Max	Mean	SD
Sex					
Male	28 (46,7)				
Female	32 (53,3)				
Age					
< 60 years	37 (61,7)	18	85	54,67	14,45
≥ 60 years	23 (38,3)				
Comorbidity					
Diabetes melitus	12 (20,0)				
Chronic kidney disease	22 (36,7)				
Hepatobiliary disease	21 (35,0)				
Cardiovascular disease	9 (15,0)				
Cerebrovascular disease	5 (8,3)				



Variable	n (%)	Min	Max	Mean	SD
Immunodeficiency	2 (3,3)				
Malignancy	12 (20,0)				
Number of Comorbidity					
<2	23 (38,3)				
≥2	37 (61,7)				
Source of Infection					
Respiratory	24 (40)				
Abdominal	16 (26,7)				
Urinary tract	5 (8,3)				
Skin and soft tissue	9 (15)				
Hematology	6 (10)				
Laboratory Parameter					
Neutrophil Count		71,60	95,8	86,77	5,55
Albumin		1,5	4	2,57	0,47
NAR		22,30	61,20	33,6	8,22
SOFA score					
< 8	28 (46,7)				
≥ 8	32 (53,3)				

Our study found that patients with SOFA score ≥ 8 had a higher mean NAR value, which was 29.09. The logistic regression test results also obtained an OR value of 29.9; $p = 0.032$.

Table 2. The relationship between NAR value and SOFA score in sepsis patients

SOFA score	NAR value					
	N	Mean	SD	R	OR	p
< 8	28	29,09	3,18			
≥ 8	32	39,96	7,85	0,695	29,9	0,032

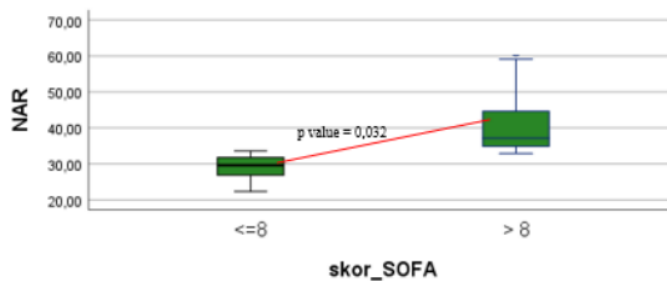


Figure 1. The relationship between NAR value and SOFA score in sepsis patients



In addition, our study also analyzed the cut-off value of NAR to predict SOFA score ≥ 8 using Receiver Operating Characteristic (ROC) curve. We found that the cut-off value of NAR to predict SOFA score ≥ 8 was 33.4 with sensitivity of 94% and specificity of 96%.

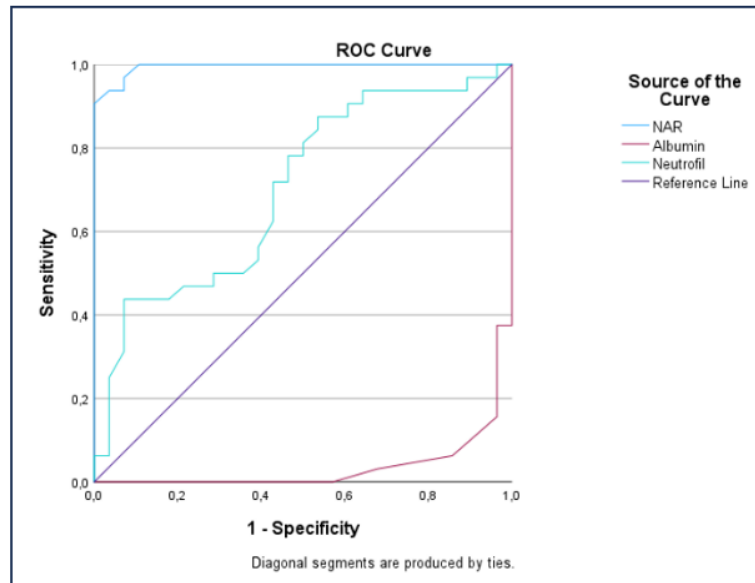


Figure 2. ROC curve of NAR value and SOFA score ≥ 8

We also analyzed the confounding variable such as, age, comorbidity, and number of comorbidities. We found that there were no significant association between age ($p = 0.146$), diabetes mellitus ($p = 0.698$), chronic kidney disease ($p = 0.079$), hepatobiliary disease ($p = 0.914$), cardiovascular disease ($p = 0.111$), cerebrovascular disease ($p = 0.755$), immunodeficiency ($p = 0.124$), and malignancy ($p = 0.301$). However, we found that patient with no comorbidities or had 1 comorbidity associated with SOFA score ≥ 8 significantly (OR 0.21; $p = 0.021$).

DISCUSSION

There were 60 subjects who met the study criteria with 32 female subjects and a mean age of 54.67 ± 14.45 years. The most common comorbidities were CKD with 22 subjects (36.7%). The most common source of infection from the respiratory system is (40%). We found that the mean of NAR value in SOFA score < 8 groups was significantly lower than the mean of NAR value in SOFA score ≥ 8 ($p < 0.05$). It is showed that the higher the NAR value, the higher the SOFA score. We also found that the NAR value was



strongly correlated with SOFA score ($r = 0.695$). Hwang et al found that the NAR value was an independent risk factor and could be used as a promising prognostic marker of mortality in sepsis patients.⁽⁷⁾ Hu et al also found that there was an association between increased NAR values and a high risk of mortality in sepsis patients. However, multivariate analysis in that study found no significant association between NAR value and SOFA score.⁽⁸⁾

Gong et al. analyzed the prognostic value of NAR on overall mortality in patients with severe sepsis or sepsis shock. Patients were categorized by NAR value into three groups, namely group 1 (<24.4), group 2 ($24.5-31.3$), and group 3 (≥ 31.4). After adjustment for confounding variables, including age, ethnicity, and gender, NAR remained significantly associated with 30-day, 90-day, and 365-day mortality risk in critically ill patients with severe sepsis or sepsis shock.⁽⁹⁾

In this study, we also determined the cut-off of NAR value to predict SOFA score ≥ 8 using ROC curve. We found that the cut-off value of NAR to predict SOFA score ≥ 8 was 33.4 with sensitivity of 94% and specificity of 96%. Wang et al found that the NAR values had high sensitivity and specificity in predict mortality of critical patients with acute renal impairment. However, we did not determine the cut-off of NAR value in predict patient mortality.⁽¹⁰⁾ The increased number of immature neutrophils in the peripheral circulation is a hallmark of systemic inflammatory response syndrome, also associated with clinical worsening in sepsis patients. Impaired neutrophil migration to the site of infection, dysregulation of neutrophil function, as well as the prolonged presence of neutrophil extracellular traps (NETs) in blood vessels or tissues had been identified during the sepsis process and play a role in sepsis progression.⁽¹¹⁾ In addition, the condition of hypoalbuminemia occurs due to impaired vascular endothelial function caused by systemic inflammatory factors. Hypoalbuminemia associated with poor prognosis in sepsis patients.⁽¹²⁾

In analysis of confounding variables to SOFA score, we found that patient with no comorbidities or had 1 comorbidity significantly associated with SOFA score ≥ 8 (OR 0.21; $p = 0.021$). It showed that patient with two or more comorbidities would have higher SOFA score. Innocenti et al also found that patient with comorbidities had higher mortality when compared to patients without comorbidities.⁽¹³⁾

CONCLUSION

This study found that there was a significant association of increased NAR with SOFA scores. A higher neutrophil count was proportional to a higher SOFA score, while lower

albumin was proportional to a higher SOFA score. However, we did not assess the hospital stay and history of antibiotic use. We also did not perform the serial laboratory examination of NAR value and SOFA score. We suggest the NAR value as simple parameter to predict SOFA score in sepsis patients.

Conflict of interest:

With regard to the submitted article, each author certifies that he or she has no financial relationships (such as stock ownership, equity holdings, consulting contracts, patent/licensing agreements, etc.) that could create a conflict of interest.

Ethics committee approval:

The ethics committee of Hasanuddin University's ³ Faculty of Medicine in Makassar, South Sulawesi, Indonesia, accepted ²⁷ this study. in accordance with recommendation letter 244/UN4.6.4.5.31/PP36/ 2024, protocol number UH24030173

Author's contributions:

AIS (Concept, Design, Sources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Manuscript Writing). RH (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). SA (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). SB (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). SK (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). AAZ (Concept, Design, Analysis and Interpretation, Critical Review). All authors were involved in drafting the manuscript, revising it, and evaluating its content. They have all read and approved the manuscript, confirming the accuracy and integrity of the research details.

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