

# 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  $\geq 18$  years and blood were taken for laboratory examination. Sepsis was diagnosed if the SOFA score was  $\geq 2$  and NAR was the ratio of neutrophil count (%) and albumin (gr/dL) based on laboratory results. Data were analyzed using a logistic regression test and Chi-square test. *Results:* 60 subjects met the study criteria with 32 female subjects and a mean age of  $54.67 \pm 14.45$  years. This study found that patients with SOFA scores  $\geq 8$  had a higher mean NAR value, which was 29.09. The logistic regression test results obtained an OR value of 29.9;  $p = 0.032$ . In addition, the cut-off value of NAR to predict SOFA score  $\geq 8$  was 33.4 with a sensitivity of 94% and specificity of 96%. *Conclusions:* This study found that there was a significant association between 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. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** 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 \*SOFA score  $\geq 2$  points (3).

Currently, several parameters support the diagnosis of sepsis and predict outcomes in sepsis patients, including leukocyte count, Erythrocyte Sedimentation Rate <sup>†</sup>ESR, and <sup>‡</sup>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, <sup>§</sup>NAR was developed to predict sepsis severity, but studies are still limited. Elevated neutrophils indicate infection, and the excess immature neutrophils in the peripheral circulation indicate <sup>\*\*</sup>SIRS is also associated with the 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.

## Methods

This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar from October 2023 until the minimum sample size was reached. Our minimum sample size was 49 patients. We included sepsis patients aged  $\geq 18$  years and blood was taken for laboratory examination. The blood was taken from the median cubital 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.

According to the Third International Consensus (Sepsis-3), organ failure resulting from the body's dysregulated response to infection constitutes sepsis. This consensus highlights the critical role that both innate and adaptive immune responses play in the clinical development of sepsis.

The Sequential Organ Failure Assessment (SOFA) score is a scoring system that assesses the performance of several organ systems in the body (neurologic, blood, liver, kidney, and blood pressure/hemodynamics) and assigns a score based on the data obtained in each category. The higher the SOFA score, the higher the likely mortality (3).

Sepsis was diagnosed if the SOFA score was  $\geq 2$  and NAR was the ratio of neutrophil count (%) and albumin (gr/dL) based on laboratory results. Our protocols have been approved by the Ethics Committee of Biomedical Research on Human, Faculty of Medicine, Universitas Hasanuddin, Makassar, South Sulawesi. Based on recommendation letter Number: 244/UN4.6.4.5.31/ PP36/ 2024, with protocol number: UH24030173.

Data were analyzed using Statistical Product and Service Solution <sup>††</sup>(SPSS) version 29 IBM with logistic regression test and Chi-square test. Statistical test results were considered significant if the p-value was  $< 0.05$ . the cut value of NAR to predict SOFA score Receiver Operating Characteristic <sup>##</sup>(ROC) curve.

## Results

60 subjects met the study criteria with 32 female subjects and a mean age of  $54.67 \pm 14.45$  years. The most common comorbidities were <sup>§§</sup>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%), and hematological infections (10%). The range of SOFA scores is 2-14 with a mean of  $8 \pm 3.13$ . 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  $2.57 \pm 0.47$ . The range of neutrophil levels was 71.65 - 95.8 with a mean of  $86.77 \pm 5.55$ . The mean neutrophil albumin ratio (NAR) value was  $33.6 \pm 8.22$ .

Our study found that patients with SOFA score  $\geq 8$  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, our study also analyzed -off the cut value of NAR to predict SOFA score  $\geq 8$  using the ROC curve. We found that the cut-off value of NAR to predict SOFA score  $\geq 8$  was 33.4 with a sensitivity of 94% and specificity of 96%.

We also analyzed the confounding variables such as age, comorbidity, and number of comorbidities. We found that there was no significant association between age ( $p = 0.146$ ), diabetes mellitus ( $p = 0.698$ ),

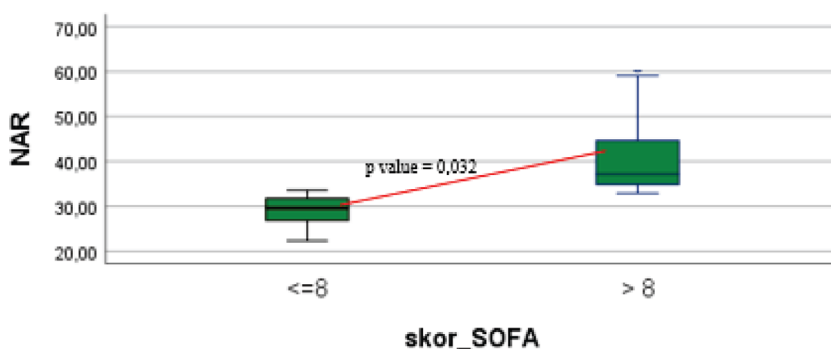
**Table 1.** Subjects' characteristics (n 60)

Variable	n (%)	Min	Max	Mean	SD
<b>Sex</b>					
Male	28 (46,7)				
Female	32 (53,3)				
<b>Age</b>					
< 60 years	37 (61,7)	18	85	54,67	14,45
≥ 60 years	23 (38,3)				
<b>Comorbidity</b>					
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)				
Immunodeficiency	2 (3,3)				
Malignancy	12 (20,0)				
<b>Number of Comorbidity</b>					
<2	23 (38,3)				
≥2	37 (61,7)				
<b>Source of Infection</b>					
Respiratory	24 (40)				
Abdominal	16 (26,7)				
Urinary tract	5 (8,3)				
Skin and soft tissue	9 (15)				
Hematology	6 (10)				
<b>Laboratory Parameter</b>					
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
<b>SOFA score</b>					
< 8	28 (46,7)				
≥ 8	32 (53,3)				

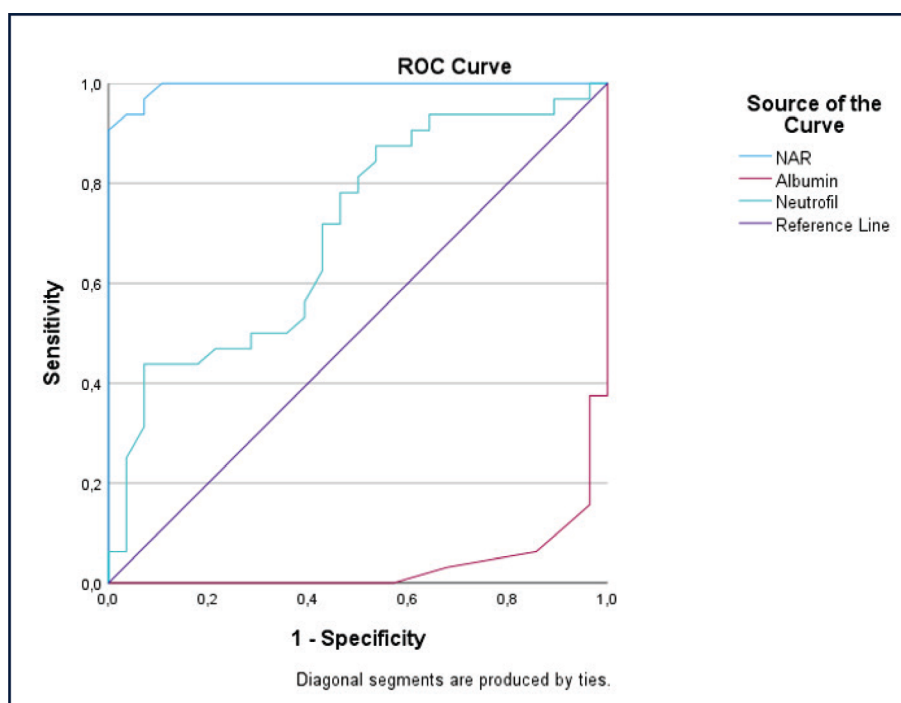
**Table 2.** The relationship between NAR value and SOFA score in sepsis patients

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

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 patients with no comorbidities or had 1 comorbidity associated with SOFA score  $\geq 8$  significantly (OR 0.21;  $p = 0.021$ ).



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



**Figure 2.** ROC curve of NAR value and SOFA score  $\geq 8$ .

## Discussion

60 subjects met the study criteria with 32 female subjects and a mean age of  $54.67 \pm 14.45$  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 the NAR value in SOFA score  $< 8$  groups was significantly lower than the mean of the NAR value in SOFA score  $\geq 8$  ( $p < 0.05$ ). It is shown that the higher

the NAR value, the higher the SOFA score. We also found that the NAR value was strongly correlated with the 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 ( $\geq$ 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  $\geq$ 8 using the ROC curve. We found that the cut-off value of NAR to predict SOFA score  $\geq$ 8 was 33.4 with a sensitivity of 94% and specificity of 96%. Wang et al found that the NAR values had high sensitivity and specificity in predicting the mortality of critical patients with acute renal impairment. However, we did not determine the cut-off of NAR value in predicting 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<sup>\*\*\*</sup> (NETs) in blood vessels or tissues, have 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 an analysis of confounding variables to SOFA score, we found that patients with no comorbidities or had 1 comorbidity significantly associated with SOFA score  $\geq$ 8 (OR 0.21;  $p = 0.021$ ). It showed that patients with two or more comorbidities would have higher SOFA scores. Innocenti et al also found that patients with comorbidities had higher mortality when compared to patients without comorbidities (13).

## Conclusion

This study found that there was a significant association between 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 the NAR value and SOFA score. We suggest the NAR value as a simple parameter to predict SOFA score in sepsis patients.

**Abbreviations:** SOFA: Sequential Organ Failure Assessment; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive protein; NAR: Neutrophil to Albumin Ratio; SIRS: Systemic Inflammatory Response Syndrome; SPSS: Statistical Product and Service Solution; ROC: Receiver Operating Characteristic; CKD: Chronic Kidney Disease; NETs: Neutrophil Extracellular traps.

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## References

1. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. *Lancet*. 2020;395:200-211. doi: 10.1016/S0140-6736(19)32989-7.

2. Hotchkiss RS, Moldawer LL, Opal SM, et al. Sepsis and septic shock. *Nat Rev Dis Prim.* 2016;2. doi: 10.1038/nrdp.2016.45.
3. Singer M, Deutschman CS, Seymour C, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA - J Am Med Assoc.* 2016;315:801-810. doi:10.1001%2Fjama.2016.0287.
4. Kaushik R, Gupta M, Sharma M, et al. Diagnostic and prognostic role of neutrophil-to-lymphocyte ratio in early and late phase of sepsis. *Indian J Crit Care Med.* 2018;22: 660-663. doi:10.4103%2Fijccm.IJCCM\_59\_18.
5. Holder AL, Gupta N, Lulaj E, et al. Predictors of early progression to severe sepsis or shock among emergency department patients with nonsevere sepsis. *Int J Emerg Med.* 2016;9:1-11. doi:10.1186%2Fs12245-016-0106-7.
6. Kendall H, Abreu E, Cheng AL. Serum Albumin Trend Is a Predictor of Mortality in ICU Patients With Sepsis. *Biol Res Nurs.* 2019;21:237-244. doi:10.1177/1099800419827600.
7. Hwang YJ, Chung SP, Park YS, et al. Newly designed delta neutrophil index-to-serum albumin ratio prognosis of early mortality in severe sepsis. *Am J Emerg Med.* 2015;33(11):1577-82. doi:10.1016/j.ajem.2015.06.012.
8. Hu C, He Y, Li J. Association between neutrophil percentage-to-albumin ratio and 28-day mortality in Chinese patients with sepsis. 2023. doi:10.1177%2F03000605231178512.
9. Gong Y, Li D, Cheng B, Ying B, Wang B. Increased neutrophil percentage-to-albumin ratio is associated with all-cause mortality in patients with severe sepsis or septic shock. *Epidemiol Infect.* 2020. doi:10.1017%2FS0950268820000771.
10. Lin Y, Lin Y, Yue J, Zou Q. The neutrophil percentage-to-albumin ratio is associated with all-cause mortality in critically ill patients with acute myocardial infarction. *BMC Cardiovasc Disord.* 2022;22(1). doi:10.1186%2Fs12872-022-02559-z.
11. Leliefeld PHC, Wessels CM, Leenen LPH, Koenderman L, Pillay J. The role of neutrophils in immune dysfunction during severe inflammation. *Crit Care.* 2016;20:1-9. doi:10.1186/s13054-016-1250-4.
12. Hu J, Lv C, Hu X, Liu J. Effect of hypoproteinemia on the mortality of sepsis patients in the ICU: a retrospective cohort study. *Sci Rep.* 2021;11:1-8. doi:10.1038/s41598-021-03865-w.
13. Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, et al. SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. *Intern Emerg Med.* 2018;13(3):405-12. doi:10.1007/s11739-017-1629-5.

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