Research Article

The correlation between the neutrophil-to-lymphocyte ratio and the stage of acute kidney injury based on akin criteria in patients hospitalized

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ABSTRACT

Background: Over the past few decades, the incidence of patients experiencing acute kidney injury (AKI) has increased, necessitating inpatient care. The prognosis of AKI patients is influenced by the management they receive, requiring swift and accurate intervention to prevent poor outcomes. Current AKI diagnostic biomarkers are considered slow, affecting the timeliness of treatment. This study aims to investigate the correlation between the neutrophil-to-lymphocyte ratio (NLR) and AKI as an early biomarker that has the potential to predict AKI. **Objective:** This study aims to determine whether there is a correlation between NLR and the stage of AKI using the AKIN criteria and the NLR cutoff for each stage of AKI. **Methods:** This study is a cross-sectional study. Subjects were selected using consecutive sampling. Data were collected using secondary data from the medical records of PKU Muhammadiyah Purbalingga Hospital. **Results:** We conducted 101 study subjects, there were 49 male and 52 female, with an average age of 62.3 years. Cardiovascular comorbidities were the most common among AKI patients, with 44 subjects affected. A significant correlation was found between NLR and the stage of AKI, as follows: a statistical analysis using ordinal logistic regression (p=0.044), odds ratio (1.03), and multivariate AUC test (77%), cut off (17.7) with specificity (71%) and sensitivity (75%). **Conclusion:** There is a correlation between NLR and the stage of AKI using AKIN criteria at PKU Muhammadiyah Purbalingga Hospital.

Keywords: acute kidney injury, neutrophil-to-lymphocyte ratio, stage of acute kidney injury

INTRODUCTION

Acute Kidney Injury (AKI) is a pathological condition characterized by a sudden decrease in kidney function, which typically occurs over a relatively short period of time. This decline in kidney function can be assessed through an increase in serum creatinine concentration, a decrease in glomerular filtration rate, or a decrease in urine output (1).

Serum creatinine (SCr) and urine output (UO) are used to determine the stage of AKI according to the AKIN criteria; however, assessing AKI based on UO depends on the patient's volemic and hemodynamic status and history of diuretic use, making it difficult to evaluate AKI from UO in patients without urinary catheters, and this assessment requires continuous monitoring, taking more time compared to SCr (2).

The Neutrophil-to-Lymphocyte Ratio (NLR) is defined as the ratio of the number of neutrophils to lymphocytes in a blood sample. NLR is calculated by dividing the number of neutrophils by the number of lymphocytes measured in routine blood tests. NLR is used as an indicator in evaluating the status of systemic inflammation in the body. An increased NLR is often associated with inflammatory responses in various disease conditions and has been proven to correlate with prognosis and clinical outcomes of a disease. Therefore, NLR has been considered a marker indicating the relationship between the immune system and disease (3).

Inflammatory conditions can cause an increase in neutrophils, whereas a decrease in lymphocyte count is due to cell damage (4). The elevated neutrophil count indicates an inflammatory response, while the decreased lymphocyte count indicates damage to the immune system (5).

Research conducted by Bi et al. (2020) found that the NLR value in patients with AKI was higher compared to non-AKI patients (6). Another study on AKI conducted by Chen et al. (2022) mentioned that NLR is a simple and effective examination; NLR can also be used to monitor the stages of AKI as well as the risks present in AKI patients and their mortality rates (7). Previous studies have not mentioned the correlation between the degree of AKI and NLR and the NLR cutoff for each stage of AKI. This study aims to determine the correlation of NLR with the stage of AKI and to establish the NLR cutoff for each stage of AKI.

METHODS

This study is a cross-sectional analysis, with data collected from laboratory results of hospitalized patients with AKI from January 1, 2022, to December 31, 2023, at RSU PKU Muhammadiyah Purbalingga. This research has received approval from the Research Ethics Commission, Faculty of Medicine, Universitas Muhammadiyah Purwokerto, with ethical letter No. KEPKK/FK/030/V/2024. The subject selection in this population was conducted using the non-probability consecutive sampling technique, which involves selecting samples according to the required research criteria. Data collection was done manually from medical records. Patients were excluded if they: were under 18 years old, had acute on chronic kidney disease, received dialysis within a month of being hospitalized, or underwent a kidney organ transplant.

The characteristics of the subjects taken include age, gender, neutrophil count, lymphocyte count, NLR, stage of AKI based on AKIN criteria, and comorbidities. The stage of AKI is determined from Serum Creatinine (SCr) and then classified according to AKIN criteria. The correlation between the NLR variable and the stage of AKI according to AKIN criteria is analyzed using an ordinal logistic regression model. The predictive cutoff value of NLR for AKI is analyzed using receiver operating characteristic (ROC).

The classification of acute kidney injury (AKI) stage using the AKIN criteria is as follows: stage 1 with a serum creatinine (SCr) of 1.5-1.9 times the normal value or $\geq$ 0.3 mg/dL; stage 2 with an increase of 2.0-2.9 times the normal value; stage 3 with criteria for an increase of $\geq$ 3.0 times the normal value or $\geq$ 4 mg/dL, as well as patients who have already undergone dialysis therapy (8).

Ordinal logistic regression is used to determine the correlation between NLR and

the degree of AKI. ROC is a type of curve that shows the relationship between sensitivity and specificity used to determine the cutoff value at each stage of AKI. The area under the curve (AUC) is below the curve and refers to the area under the ROC curve. The accuracy value is higher as the AUC value increases (9).

RESULTS

Based on the medical records obtained, the characteristics of the subjects regarding age, sex, and the presence or absence of comorbidities were identified. The results obtained were then recorded with their frequency and percentages; for laboratory results such as neutrophils, SCr, and lymphocytes, the average values obtained were documented.

Table 1. Characteristics of the Subject AKI

Subject Characteristics	Mean±SD	(n)	(%)
Gender			
Male		49	49
Female		52	51
Age			
18 – 33		4	4
34 -39		12	12
40 – 65		35	34
66 – 81		41	41
82 – 97		9	9
Comorbid			
With Comorbid		74	73
Cardiovascular Disease		44	59
Pulmonary disease		17	23
Diabetes		8	11
More than 1 comorbidity (Cardiovascular Disease and Lung Disease)		3	4
More than 2 comorbidities (Cardiovascular disease, Lung disease, and Diabetes))		2	3
No comorbidity		27	27
SCr (mg/dl)	1,788±1,06		
Neutrophil (/μL)	11.289±6.479,6		
Lymphocyte (/μL)	1.260±2.137		
Total		**101**	**100**

Based on Table 1, the characteristic of the AKI subjects with the highest percentage is the age of patients diagnosed with AKI in the age group of 66 - 81 years, reaching a value of 41%. A total of 74 subjects, or 73% of the research sample, have comorbidities along with the AKI condition, while 27 patients, or 27% of the population sample, do not have comorbidities. The majority of patients have comorbidities related to cardiovascular diseases (59%). The average laboratory results show neutrophils at

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11,289/µL, lymphocytes at 1,260/µL, and the average SCr value at 1.788 mg/dl.

Table 2. The Correlation Between NLR and Severity of AKI

Stage	AUC*	Cut Off	n(%)
1	0.327	-	86(85)
2	0.634	-	7(7)
3	0.772	17.7	8(8)

*Analysis using ordinal logistic regression

In Table 2, the results of the ordinal logistic regression statistical test are shown, indicating a significant p-value of 0.044 between NLR and the stage of AKI patients based on the AKIN criteria at PKU Muhammadiyah General Hospital in Purbalingga. An odds ratio (OR) value of 1.03 was also obtained. The distribution of patient data concerning AKI conditions based on the AKIN criteria can be observed. The majority of patients, namely 86 from the total research subjects, experienced stage 1 (85%), 7 patients had stage 2 (7%), and 8 other patients experienced stage 3 (8%).

Table 3. *NLR Cutoff in Relation to the Severity of AKI*

AKI degree	NLR (Mean±SD)	P*	OR
1 2 3	16.798±17.04	0.044	1.03

*Analysis using ROC AUC

The assessment of the accuracy of NLR for predicting the occurrence of stage 3 AKI according to AKIN criteria, measured using the AUC, is 0.772, which indicates that its accuracy falls within the good or fair discrimination category (70% - 80%). The cutoff NLR indicating stage 3 AKI according to AKIN criteria is 17.7. For stages 1 and 2, the AUC values obtained are below 70%, thus the results cannot be used (10).

DISCUSSION

From the results of the analysis of the characteristics of AKI subjects, the frequency of subjects began to increase in the age group 40 - 65 years and most were in the age group 66 - 81 years. The results of this study are in accordance with research conducted by Chang-Panesso (2021) in which the study states that elderly patients have higher risk factors for developing AKI (11). Other researchers also mention that the incidence of AKI is related to the degeneration process, causing the most age group to be at the age of 75 years and over (12).

The comorbidity of cardiovascular disease is highest in patients experiencing acute kidney injury (AKI) because cardiovascular disease can trigger ischemia in kidney tissue, leading to a decrease in Renal Blood Flow (RBF) and potentially disrupting kidney perfusion, thus increasing the risk of developing AKI (13). Research conducted by Bai et al. (2022) also noted that prerenal etiological factors, such as cardiovascular conditions, are the most significant comorbidities in patients with AKI (14). Additionally, research by Clercq et al. (2023) demonstrated that patients with AKI have a significantly increased risk of developing atrial fibrillation, acute coronary syndrome, and heart failure through their comprehensive study and meta-analysis (15).

Mean SCr value obtained was 1.788 mg/dL. The normal value is at 1.1 mg/dl for female and 1.2 mg/dl for male, the SCr value obtained in this study has increased, this is in accordance with the theory that in AKI conditions SCr will increase due to a

decrease in GFR (16). The neutrophil value obtained in the laboratory examination of patients diagnosed with AKI obtained an average value of 11,289 / µL. Based on the normal value of neutrophils in the range of 1260/µL - 8000/µL, mean neutrophil value obtained is higher than the normal value. This is in relevant with research conducted by Chen et al. (2022) in the study mentioned that an increase in neutrophils indicates inflammation, in the incidence of AKI there is damage to the kidneys that can trigger inflammation, thus activating the inflammatory response (7).

The results from Table 2 indicate that the average NLR value for all subjects is 16.796. Based on the normal range of 1 - 2, the NLR value obtained from this study shows an increase. This is consistent with previous research that reported a significant increase in NLR values in patients with AKI (6). NLR may increase due to an elevation in neutrophils, which can be caused by inflammation. In the case of AKI, there is damage to the kidneys that can trigger inflammation, thereby activating the inflammatory response (7). This study assesses the degree of AKI based on the SCr values of patients diagnosed with AKI, as UO tends to have a higher risk of bias depending on patient treatment, fluid intake, and diet (17).

Bivariate analysis in Table 2 shows that there is a significant correlation between NLR and the degree of AKI, and from the odds ratio value, it can be concluded that for every increase of 1 in NLR, there is a 3% higher risk of experiencing stage 3 AKI compared to patients who do not experience a 1-point increase in NLR.

The results of this study are somewhat different from previous research, which showed a significant positive correlation between an increase in NLR and AKI, with an OR of 1.047 ($p < 0.001$) (19).

Multivariate analysis in Table 3 utilized ROC curve analysis. A multivariate test was conducted with initial classification to determine the cutoff; classifications were assigned a value of 1 or true for the degree being evaluated for the cutoff, and false was assigned a value of 0 for other stages as a reference. In the study, a cutoff of stage 3 was found, so stage other than 3 were assigned a value of 0 or false. An AUC value is considered acceptable if the area has a value ≥ 0.7 (20).

The results of the research indicate that the accuracy of the NLR for predicting the occurrence of stage 3 AKI according to the AKIN criteria was obtained using an AUC value of 0.773 (95% CI: 0.862 – 0.882, $p < 0.011$), placing the accuracy in the category of moderate or fair discrimination (70% - 80%). The cutoff value for NLR at stage 3 was determined to be 17.7, with a sensitivity of 75% and a specificity of 71%, as determined through graphs and the Youden index. For stages 1 and 2, the AUC values were below 70%, making the results unusable; this was due to the absence of values from patients with normal conditions, thus lacking a comparison between pathological and physiological values to determine the cutoff for stages 1 and 2.

CONCLUSION

From the results of the research conducted, it was found that NLR is significantly correlated with the stage of AKI, and the cutoff value of NLR at stage 3 is 17.7. It is recommended for future research to increase the number of respondents from AKI stages 1, 2, and 3, as well as from the healthy control group, in order to determine

the normal NLR values and cutoff for each AKI stage.

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CONFLICT OF INTEREST

Researchers state that they have no conflicts of interest, and have no affiliations or connections with any organizations that could raise questions of bias in this research.

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