

Research Article

Association between Neutrophil-lymphocyte Ratio and Incidence of Acute Kidney Injury (AKI) Related Drug in Post-surgical ICU Patients at Haji Adam Malik Hospital Medan

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Abstract

Background: Postoperative AKI is a common complication of surgery. The incidence of postoperative AKI varies according to the type of surgery and most studies are limited to cardiac surgery. Blood Neutrophil-lymphocyte Ratio (RNL) is one of the good systemic inflammatory markers to predict AKI. The Neutrophil-lymphocyte Ratio (RNL) has been studied as a predictor of postoperative AKI in various surgical contexts. A higher NLR was found to be associated with an increased risk of postoperative AKI after major abdominal surgery. Another study found that a high NLR was associated with an increased risk of developing AKI in patients undergoing cardiac surgery. These findings suggest that NLR may be a useful biomarker for predicting postoperative AKI, but further studies are needed to establish its clinical utility and to determine the optimal cut-off for risk stratification.

Method: This study used a retrospective analytic method with the aim of knowing the relationship between the value of the neutrophil-lymphocyte ratio and the incidence of AKI in post-surgical ICU patients at H. Adam Malik Hospital Medan. The total sample in this study was 188 patients taken in the period January 2023-December 2023. The samples were then analyzed using the Independent T test to see the relationship between the 2 research groups.

Research result: The value of neutrophil lymphocyte ratio to the incidence of AKI, in Non AKI patients obtained neutrophil lymphocyte ratio 18.62 ± 7.91 , in AKI patients obtained neutrophil lymphocyte ratio 47.57 ± 29.85 , with a P Value of 0.01. The NLR cut off value was found to be 23.14 with a large AUC value of 86.3% with a sensitivity of 86% and a specificity of 62% where there was a relationship between the NLR value and the incidence of AKI.

Conclusion: There is a relationship between the value of neutrophil lymphocytes and the incidence of AKI.

Keywords: AKI; Neutrophils; Lymphocytes; NLR

Introduction

Surgery is one of the main causes of Acute Kidney Injury (AKI) in hospitalised patients due to insensitive early detection. Sensitive AKI marker tests have the disadvantage of being expensive and not all health facilities have them. The existing test in most health facilities to detect post-surgical AKI is Serum Creatinine (SCr), which is known to be often delayed. Acute Kidney Injury (AKI) is a sudden decline in kidney function characterised by a decrease in glomerular filtration rate, an increase in serum creatinine and a decrease in urine production caused by prerenal, intrarenal and post renal factors [1].

Based on current consensus, the diagnosis of AKI is based on elevated serum creatinine and decreased urine output. However, creatinine levels are not an early marker as they do not always reflect the actual decline in Glomerular Filtration Rate (LFG). When creatinine is elevated, kidney damage has already reached about 50%. In addition, serum creatinine can also be influenced by several non-renal factors such as age, gender, muscle mass and metabolism, dietary pattern, medication, and hydration status [2,3].

A recent systematic review involving 47 studies reported that the incidence of AKI in ICU patients ranged from 2.5% to 92.2% [4]. The Beijing Acute Kidney Injury Trial (BAKIT) reported an incidence of AKI among 3107 patients admitted to ICUs from various medical centres of

51% [5]. Among the various types of postoperative organ injury, AKI is the biggest complication that occurs in 20%-40% of high-risk patients. Patients with critical illnesses are prone to AKI and almost a 3rd of them require Renal Replacement Therapy (RRT) [6]. Studies in Asia show that AKI in East Asia is 19.4%; in South Asia it is 7.5%; in Southeast Asia it reaches 31.0%; Central Asia 9.0% and 16.7% in West Asia with patient mortality due to AKI of 36.9% in East Asia, 13.8% in South Asia and 23.6%. Based on the 2018 Riskesdas data, the prevalence of AKI was 3.8% [7,8].

Postoperative AKI is a common complication of surgery. The incidence of postoperative AKI varies by type of surgery and most studies are limited to cardiac surgery. Studies using the current agreed definition of AKI in non-cardiac surgery are lacking. Using KDIGO criteria, the incidence of AKI ranged from 4.1% after ear, nose and throat surgery to 13.2% after general surgery in a large cohort of more than 16,000 US patients. Results from a Scottish cohort of 12,482 patients ranged from 4% after gynaecological surgery to 25% after vascular surgery also using KDIGO criteria. A recent systematic review of 19 studies including 82,514 patients undergoing major abdominal surgery reported an incidence of AKI of 13.4% (95% CI 10.9%-16.4%) [9].

Blood Neutrophil Lymphocyte (RNL) ratio is one of the good systemic inflammatory markers to predict AKI. A study conducted by Kim WH, et al, showed an increase in RNL in patients undergoing cardiac surgery and was associated with an increased risk of post-surgical AKI and mortality with an odds ratio of 5.9. One retrospective study by Bu X et al. (2019) proved an increase in RNL as a predictor of AKI in sepsis patients in the ICU. Neutrophils migrate rapidly from the peripheral circulation to the kidneys due to the influence of chemokines resulting in renal vascular disorders, secretion of oxygen free radicals and proteases resulting in AKI [10-13].

Methods

This study was a retrospective analytical study with the aim of knowing the relationship between the value of neutrophil-lymphocyte ratio with the incidence of AKI in post-surgical ICU patients at the Hajj Adam Malik Hospital Medan. The study was conducted since the issuance of Ethical clearance by the Health Research Ethics Committee of the Universitas Sumatera Utara and Central General Hospital Haji Adam Malik Medan from 1st January, 2023 to 31st December, 2023.

Inclusion criteria in this study were patients aged 18 years-65 years, elective patients undergoing general surgery and undergoing treatment in the post-surgical ICU and complete patient medical record data. Patients with impaired renal function or undergoing haemodialysis before surgery and ICU patients before surgery were included as

exclusion criteria. After obtaining approval from the Ethics Committee of the Faculty of Medicine, University of North Sumatra and the Central General Hospital Haji Adam Malik Medan (RSUP HAM). Researchers recapitulated data on patients who underwent post-surgical ICU treatment at H. Adam Malik Hospital Medan. Patient medical record data was searched and searched for data. Data on serum creatinine values, and complete blood before and after surgery were taken as primary research data, and calculated the value of the neutrophil lymphocyte ratio and assessed the incidence of AKI based on RIFLE criteria.

Descriptive analysis was conducted to see the characteristics and frequency distribution of the subjects. After the Shappiro Wilk normality test. Numerical data were displayed as mean, SD (Standard Deviation) and median (minimum-maximum). While categorical data is displayed in number (percentage). For categorical data analysis using the Chi-Square test. The confidence interval used in this study is 95% with a p value of <0.05 which is considered significantly meaningful.

Results

A study was conducted on the relationship between neutrophil-lymphocyte ratio and the incidence of Acute Kidney Injury (AKI) in post-surgical ICU patients at RSUP. Haji Adam Malik Medan, medical record data collection was carried out on all ICU patients who had undergone general surgery in the period 1st January, 2023 to 31st December, 2023 and managed to collect 188 people.

This study was followed by 188 subjects who were reviewed from the medical record data of postoperative patients and admitted to the Intensive Critical Care Unit (ICU). The characteristics of the study sample are displayed in the form of a frequency distribution and normality test is performed as shown in Table 1.

Table 1: Distribution and characteristics of the study subject population

Variable	Not AKI	AKI	P value
Sex			
Man	59 (60.8%)	59 (64.8%)	0.338 ^a
Woman	38 (39.2%)	32 (35.2%)	-
PS ASA			
2	47 (48.5%)	24 (26.4%)	0.053 ^a
3	50 (51.5%)	67 (73.6%)	-
Age	48.37 ± 15.38	53.62 ± 15.09	0.136 ^b
Preoperative neutrophils	39.81 ± 8.61	42.82 ± 6.84	0.056 ^b
Preoperative lymphocytes	3.75 ± 1.66	3.52 ± 1, 09	0.531 ^b
Neutrophils post operation	86.45 ± 14.52	92.53 ± 2, 56	0.007 ^b
Lymphocytes post operation	5.70 ± 3.03	2.90 ± 2, 06	0.001 ^b
Duration Operation	130.20 ± 28.68	184.28 ± 52.45	0.001 ^b
Type surgery			

Surgery nerve	39 (40.2%)	41 (45.1%)	0.342 ^a
Surgery digestive	13 (13.4%)	8 (8.8%)	
Surgery obgyn/ gynecology	9 (9.3%)	3 (3.3%)	
Surgery thorax	15 (15.5%)	13 (14.3%)	
Surgical oncology	5 (5.2%)	9 (9.9%)	
Surgery extremities	2 (2.1%)	5 (5.5%)	
Burns	14 (14.4%)	12 (13.2%)	

For the frequency distribution of the incidence of AKI, it can be seen in Table 2 from a total of 188 samples, the total number of AKI patients was 91 patients (48.3%), there were 51 patients in the Risk category (27.1%), there were 36 patients in the Injury category (19.1%), there were 4 patients in the Failure category (2.1%), and 97 patients were not AKI (51.6%).

Table 2: Distribution frequency incidence of AKI and Not AKI

AKI incidence	Amount	Percentage (%)
AKI		
Risk	51	27.1
Injury	36	19.1
Failure	4	2.1
Not AKI	97	51.6

In this study, the mean preoperative creatinine level of patients without AKI was 1.04 ± 0.35 , the mean preoperative creatinine level of AKI patients was 0.98 ± 0.18 , with a P value of 0.486. In this study, the mean postoperative creatinine level of patients without AKI was 1.30 ± 0.37 , the mean postoperative creatinine level in AKI patients was 1.91 ± 0.31 , with a P Value of 0.001 (Table 3).

Table 3: Rate Creatinine before and after operation on AKI incidence

Mark Creatinine	Not AKI	AKI	P Value
Preoperative creatinine	1.04 ± 0.35	0.98 ± 0.18	0.486c
Creatinine post operation	1.30 ± 0.37	1.91 ± 0.31	0.001c
c: Mann-whitney test			

Table 4 shows a comparison of preoperative neutrophil lymphocyte ratio values against the incidence of AKI, in Non AKI patients obtained a neutrophil lymphocyte ratio of 12.30 ± 3.09 , in AKI patients obtained a neutrophil lymphocyte ratio of 12.97 ± 3.23 , with a P Value of 0.502. in this table it is found that there is no significant difference between NLR values in AKI patients and Non AKI patients.

Table 4: Comparison preoperative NLR value to AKI incidence

Variable	Non AKI	AKI	P Value
NLR	12.30 ± 3.09	12.97 ± 3.23	0.502c
c: Mann-whitney test			

Table 5 shows a comparison of postoperative neutrophil lymphocyte ratio values against the incidence of AKI, in Non AKI patients obtained neutrophil lymphocyte ratio levels 18.62 ± 7.91 , in AKI patients obtained neutrophil lymphocyte ratio levels 47.57 ± 29.85 , with a P Value of 0.01.

Table 5: Comparison post NLR value operation to AKI incidence

Variable	Non AKI	AKI	P Value
NLR	18.62 ± 7.91	47.57 ± 29.85	0.01c
c: Mann-whitney test			

Figure 1 and Table 6 shows the ROC curve regarding the comparison of NLR levels with the incidence of AKI, obtained the comparison of neutrophil lymphocyte ratio levels with the incidence of AKI, AUC 86.6%, obtained P Value 0.001, obtained cut off 23.14, obtained sensitivity of 86% and specificity of 62%. in the postoperative assessment found a p value <0.005 so that postoperative NLR assessment provides a significant value to the incidence of postoperative AKI.

Table 6: The comparison of neutrophil lymphocyte ratio levels with the incidence of AKI

Variable	AUC	P value	Cut off	Sensitivity	Specificity
NLR	86.60%	0.001	23.14	86%	62%
*AUC Curve Test					

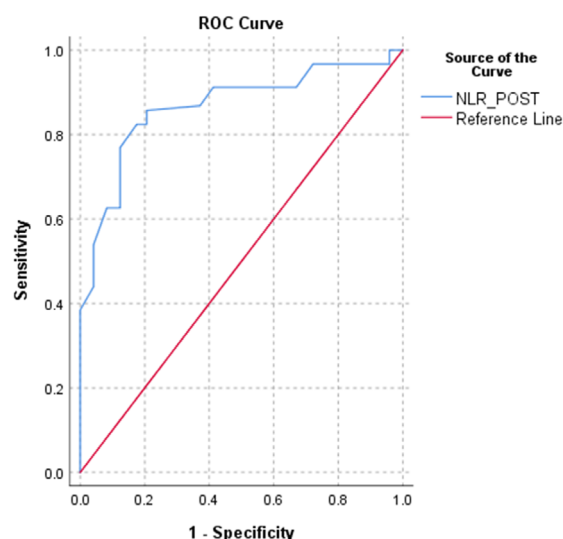


Figure 1: ROC curve at comparison NLR levels with AKI incidence

After obtaining the cut-off value of the NLR value that can affect the incidence of AKI in post-surgical patients, a cross-validation of the cut-off value with the incidence of AKI that occurred in the study subjects was carried out. In Table 7, it was found that at the NLR value ≤ 23.14 , 61 research subjects did not experience AKI and 12 patients experienced AKI. Whereas at the cut off value of NLR >23.14 there were 79 patients who experienced AKI and 36 research subjects did not experience AKI, the chi-square test found a p value of 0.001 which indicates that there is a significant difference in the incidence of AKI and not AKI based on the cut off value.

Table 7: AKI incidence based on mark limit (Cut off) Post NLR operation of 23.14

NLR criteria	Non AKI	AKI	P Value
NLR ≤ 23.14	61(32.4%)	12(6.4%)	0.001 ^a
NLR>23.14	36(19.1%)	79(42%)	
a: Chi Square Test			

Discussion

In this study obtained the frequency distribution of the incidence of AKI, obtained a total of 188 samples who before surgery were admitted to the regular ward and obtained a total number of AKI patients 91 patients (48.3%), there were 51 patients with the Risk category (27.1%), there were 36 patients with the Injury category (19.1%), there were 4 patients with the Failure category (2.1%), and 97 patients were not AKI (51.6%). The most common category obtained in patients with acute kidney injury is the RISK category. Several large cohort studies have focused on describing the incidence of AKI in the intensive care unit. In a large multinational study, the incidence of AKI among patients admitted to the Intensive Care Unit (ICU) was only 5.7%. However, Bhagsaw and Rewa's 2014 study used a definition of AKI (i.e., urine output <200 ml in 12 hours; serum urea >30 mmol/l or initiation of RRT) that was intended to identify only the most severely affected patients (of whom approximately 70% required RRT). Subsequent cohort studies integrating the consensus definition of AKI and using administrative databases reported an ICU incidence of AKI of 16%-39% [14,15].

In response to physiological stress including infection or inflammation, endogenous cortical catecholamines increase, thereby increasing the number of neutrophils and resulting lymphopenia. Therefore, physiological stress can increase NLR, which can thus serve as an indicator of systemic stress response. NLR increases rapidly within 6 hours after physiological stress. NLR can also be used as a prognostic marker in various diseases [16]. So it is in accordance with this study that patients with AKI have a greater mean NLR of 92.21 ± 2.82 . Bu X et al. (2019) stated that AKI developed in 59% of patients admitted to the intensive care unit and diagnosed with sepsis, the average NLR was 17 ± 4 , and there was a significant correlation between AKI and NLR. Various studies have reported the relationship between AKI and NLR [11,17].

A study of patients undergoing coronary artery bypass grafts found that those in the Contrast Induced-AKI group had a higher NLR than those in the non-contrast induced-AKI group. The patients were also sorted into 3 groups based on their NLR, and showed that the group with higher NLR had a higher risk of developing postoperative AKI compared to the group with lower NLR (30% vs 25% vs 55.8%, $p=0.003$). In addition, multivariable logistic regression analysis showed that patients with high preoperative NLR had a higher risk of developing postoperative AKI [Odds Ratio (OR)=4.91, 95% Confidence Interval (CI): 1.45-16.58, $p=0.0104$], thus confirming that NLR has predictive utility independent of other known risk factors [18].

Conclusion

There is a relationship between the value of neutrophil lymphocytes and the incidence of AKI.

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Conflicting Interests

The authors declare that there is no conflict of interest in this report.

Authors' Contribution

All authors are responsible for conceptualization, manuscript preparation, manuscript editing, and manuscript assurance.

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References

1. N. Boyer, J. Eldridge, J.R. Prowle, L.G. Forni, Postoperative acute kidney injury, *Clin J Am Soc Nephrol*, 17(2022):1535-45.
2. S. Khawaja, L. Jafri, I. Siddiqui, M. Hashmi, F. Ghani, The utility of Neutrophil Gelatinase Associated Lipocalin (NGAL) as a marker of Acute Kidney Injury (AKI) in critically ill patients, *Biomark Res*, 7(2019):4.
3. R. Matsa, E. Ashley, V. Sharma, A.P. Walden, L. Keating, Plasma and urine Neutrophil gelatinase-associated lipocalin in the diagnosis of new onset acute kidney injury in critically ill patients, *Crit Care*, 18(2014):R137.
4. R.P. Santos, A.R.S. Carvalho, L.A.B. Peres, C. Ronco, E. Macedo, An epidemiologic overview of acute kidney injury in intensive care units, *Rev Assoc Med Bras*, 65(2019):1094-01.
5. L. Jiang, Y. Zhu, X. Luo, Y. Wen, B. Du, et al. Epidemiology of acute kidney injury in intensive care units in Beijing: The multi-center BAKIT study, *BMC Nephrol*, 20(2019):468.
6. L. Yang, Acute kidney injury in Asia, *Kidney Diseases*, 2(2016):95-102.
7. The committee of medical research ethics of medical faculty, Nutritional status and physical activity of people with Diabetes Mellitus terhadap nilai handgrip strenght test, *Lambung Mangkurat University*, 4(2020):212-21.
8. I. Puspitawati, A.Y. Jufan, V. Cahyaningrum, C.T. Dewi, I. Chasanah, et al. Urine Neutrophil Gelatinase-associated Lipocalin (NGAL) as an initial biomarker of Acute Kidney Injury (AKI) in an Intensive Care Unit (ICU) patients: A preliminary study, *Bali Med J*, 8(2019):297-301.
9. J. Gameiro, J.A. Fonseca, M. Neves, S. Jorge, J.A. Lopes, Acute kidney injury in major abdominal surgery: Incidence, risk factors, pathogenesis and outcomes, *Ann Intensive Care*, 3(2018):114-21.
10. W.H. Kim, J.Y. Park, S.H. Ok, I.W. Shin, J.T. Sohn, Association between the neutrophil/lymphocyte ratio and acute kidney injury after cardiovascular surgery: A retrospective observational study, *Medicine (United States of America)*, 99(2020):e20200.

- States), 94(2015):1–10.
11. X. Bu, L. Zhang, P. Chen, X. Wu, Relation of neutrophil to lymphocyte ratio to acute kidney injury in patients with sepsis and septic shock: A retrospective study, *Int Immunopharmacol*, 70(2019):372–377.
 12. Y. Li, Z. Zou, Y. Zhang, B. Zhu, Y. Ning, et al. Dynamics in perioperative neutrophil to lymphocyte*platelet ratio as a predictor of early acute kidney injury following cardiovascular surgery, *Ren Fail*, 43(2021):1012–19.
 13. M. Wu, Y.Y. Luan, J.F. Lu, H. Li, H.C. Zhan, et al. Platelet count as a new biomarker for acute kidney injury induced by hemorrhagic shock, *Platelets*, 31(2020):94–102.
 14. E.A.J. Hoste, S.M. Bagshaw, R. Bellomo, C.M. Cely, Epidemiology of acute kidney injury in critically ill patients: The multinational AKI-EPI study, *Intensive Care Med*, 41(2015):1411–23.
 15. O. Rewa, S.M. Bagshaw, Acute kidney injury-epidemiology, outcomes and economics, *Nature reviews nephrology*, 10(2014):193-207.
 16. J.J. Chen, G. Kuo, P.C. Fan, T.H. Lee, C.L. Yen, et al. Neutrophil-to-lymphocyte ratio is a marker for acute kidney injury progression and mortality in critically ill populations: A population-based, multi-institutional study, *J Nephrol*, 35(2022):911-20.
 17. F. Jiang, J. Lei, J. Xiang, Y. Chen, J. Feng, et al. Monocyte-to-lymphocyte ratio: A potential novel predictor for acute kidney injury in the intensive care unit, *Ren Fail* 44(2022):1004-11.
 18. Z. Guangqing, C. Liwei, L. Fei, Z. Jianshe, Predictive value of neutrophil to lymphocyte ratio on acute kidney injury after on-pump coronary artery bypass: A retrospective, single-center study, *Gen Thorac Cardiovasc Surg*, 70(2022):624–33.