A HIGH PREOPERATIVE NEUTROPHIL-LYMPHOCYTE RATIO AS AN INDICATOR OF EARLY RESPONSE OF KIDNEY TRANSPLANT

¹Tanaya Ghinorawa, ¹Gilang Samudera, ¹Indrawarman Soerohardjo, ¹Ahmad Zulfan Hendri, ¹Andy Zulfiggar.

ABSTRACT

Objective: This study aims to evaluate the association of the preoperative Neutrophil-lymphocyte ratio (NLR) and postoperative creatinine levels after kidney transplantation, which is a predictor factor for determining early postoperative transplantation complications. **Material & Methods:** We conducted a retrospective study of 33 patients enrolled in Sardjito General Hospital in Yogyakarta between 2017 and 2020. In this study, we observed the preoperative NLR and compared it with the postoperative creatinine level. The data were compared and analyzed. **Results:** This study showed that preoperative NLR in these 33 patients was 4.17 + 2.82. Postoperative creatinine levels were 2.38 + 1.75 mg/dL. Postoperative creatinine levels were higher in patients with low preoperative NLR (p=0.00). Besides, the correlation is weak and had a positive correlation direction (r=0.379). **Conclusion:** This study showed preoperative NLR and the postoperative serum creatinine level is correlated even weakly. NLR could be considered a predictor factor for determining postoperative transplantation complications, and even it still needs further research.

Keywords: Neutrophil-lymphocyte ratio, creatinine levels, kidney transplantation.

ABSTRAK

Tujuan: Penelitian ini bertujuan untuk mengevaluasi hubungan rasio Neutrofil-limfosit (NLR) pra operasi dan kadar kreatinin pasca operasi setelah transplantasi ginjal, yang merupakan faktor prediktor untuk menentukan komplikasi awal transplantasi pasca operasi. **Bahan & Cara:** Kami melakukan studi retrospektif terhadap 33 pasien yang terdaftar di Rumah Sakit Umum Sardjito Yogyakarta antara tahun 2017 dan 2020. Dalam penelitian ini, kami mengamati NLR pra operasi dan membandingkannya dengan tingkat kreatinin pasca operasi. Data dibandingkan dan dianalisis. **Hasil:** Studi ini menunjukkan bahwa NLR pra operasi pada 33 pasien ini adalah 4.17 + 2.82. Kadar kreatinin pasca operasi adalah 2.38 + 1.75 mg/dL. Kadar kreatinin pascaoperasi lebih tinggi pada pasien dengan NLR praoperasi rendah (p=0.00). Selain itu, korelasinya lemah dan memiliki arah korelasi yang positif (r=0.379). **Simpulan:** Studi ini menunjukkan NLR pra operasi dan kadar kreatinin serum pasca operasi berkorelasi bahkan dengan lemah. NLR dapat dianggap sebagai faktor prediktor untuk menentukan komplikasi pasca operasi transplantasi, bahkan masih perlu penelitian lebih lanjut.

Kata kunci: Rasio neutrofil-limfosit, kadar kreatinin, transplantasi ginjal.

Correspondence: Andy Zulfiqqar; c/o: Division of Urology, Department of Surgery, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital. Jl. Kesehatan No.1, Senolowo, Sinduadi, Mlati, Sleman, Daerah Istimewa Yogyakarta 55281, Indonesia. Email: andyzulfiqqar@gmail.com.

INTRODUCTION

The neutrophil-lymphocyte ratio (NLR) is a simple method to assess a systemic inflammation response. NLR is the measurement of the ratio of number of neutrophil count reflected as inflammatory condition, and the Lymphocytes count that reflected patient adaptive immunity. NLR has been validated to predict patient survival in several systemic diseases such as major cardiac diseases,

and several cancer.²⁻³ The inflammatory response played a significant role in the reaction of ischemic injury and reperfusion to kidney grafts. That is an initial sign of failure after a kidney transplant.⁴

Acute kidney rejection is an increase of serum creatinine within 48 hours of an inciting event. Delayed graft function would need a patient for dialysis within the first week after transplantation unless performed in hyperkalemia. Delayed graft function is a common complication after kidney

¹ Department of Urology, Faculty of Medicine, Public Health, and Nursing/University of Gadjah Mada, Sardjito General Hospital, Yogyakarta.

transplantation. Incidence rates of DFG were varying from 4% to 10% in a living donor. Serum creatinine is a standard parameter used to evaluate it.

OBJECTIVE

In this retrospective study, we aimed to evaluate the association of preoperative NLR and postoperative creatinine levels after kidney transplantation, which is a predictor factor for determining early postoperative transplantation complications.

MATERIAL & METHODS

We retrospectively investigated 33 kidney transplant patients in our center who were under follow-up treatment from 2017 to 2020 at the Sardjito General Hospital in Yogyakarta. The Medical and Health Research Ethics Committee Faculty of Medicine and Nursing Gadjah Mada University (KE/FK/1070/EC/2020) has approved this study. Inclusion criteria were patients who underwent a first-time kidney transplant. Exclusion criteria were receiving a second kidney transplant, a proven history of cardiovascular disease or cancer, and not using steroids to eliminate steroids' effect on neutrophil and lymphocyte distribution. We reviewed the medical record to find data for the patient's age, gender, preoperative white blood cell count, and serum creatinine level 3 days postoperatively.

NLR was counted by Relative % Neutrophils / Relative % Lymphocytes. Serum creatinine was drawn 3cc blood sample from a vein in the arm, using EDTA tube, and blood serum was analyzed by the clinical pathology laboratory in Sardjito General Hospital Yogyakarta. Data were analyzed using the IBM SPSS 23.00 statistics. Nonparametric tests were performed for correlation analyses due to the restricted sample size. We are using the Spearman correlation test to know the strength of the correlation. P < 0.05 was considered statistically significant.

RESULTS

We have collected 33 samples that fulfilled our inclusion and exclusion criteria. The characteristic of our patients was served in Table 1. The age of the patient was 40.39 + 13.65 years. Males are more than females, with a male percentage of 72.7% and 37.3% females; with a male to female ratio is 2.7:1.

Table 1. Sample characteristics.

Characteristics	Total	
Age (mean \pm SD)	40.39 <u>+</u> 13.65	
Gender		
Male	24 (72.7%)	
Female	9 (37.3%)	
Male-female ratio	2.7:1	

From the Wilcoxon and Spearman test, a significance value of 0.000 was obtained. A significant relationship was shown between the NLR and the serum creatinine levels after kidney transplant. The correlation coefficient at 0.379 indicates that the correlation coefficient is positive with weak strength correlation, so it means that the preoperative NLR and the postoperative creatinine level in a linear form.

DISCUSSION

Kidney transplant is the best therapy for end-stage renal disease compared to other kidney replacement therapies, due to better quality of life. Acute rejection is defined as acute rejection that may occur within days to weeks after the surgery. This can occurs due to antibody-mediated rejection or acute T-cell mediated rejection. An elevated NLR is indication that the count of neutrophils is increased and the count of lymphocyte is otherwise; our study demonstrated there's medium correlation between NLR value and Post-operative Cr level.

Previous studies have shown elevated NLR as the marker of systemic inflammation. Preoperative NLR value has been used as a

Table 2. Comparative and correlative test using Wilcoxon and Spearman.

	Mean + SD	p-Value	R
Preoperative NLR	4.17+2.82	0.00	0.379
Postoperative creatinine levels	2.38 + 1.75 mg/dL		

^{*} Spearman correlation

prognostic factor in many surgeries.⁸⁻¹⁰ In our observation, the NLR preoperatively is significantly associated with serum creatinine in post-kidney transplant patients.¹¹ Compared to the previous study by Halazun et al. from 295 patients with primary graft function, 26% of patients developed DGF, where 65% had NLRs > 3.5, and 15% of patients elevated NLR.¹²

The prediction risk of Acute rejection has a vital role in preventing its short-term and long-term consequences.¹³ This study has important clinical implications and can form science in predicting postoperative kidney function in ESRD patients after kidney transplant procedure in the future. For further research, because of the limitation of this study, the next study needs to use more samples and variables.

CONCLUSION

There is a significant correlation between preoperative NLR and postoperative serum creatinine levels in the transplant kidney recipient. It showed preoperative NLR and the postoperative serum creatinine level is correlated even weakly. This study demonstrated that the NLR could be considered a predicting factor for determining postoperative transplantation complications.

REFERENCES

- Song M., Graubard B.I., Rabkin C.S., Engels E.A. Neutrophil-to-lymphocyte ratio and mortality in the United States general population. Sci. Rep. 2021; 11:464.
- 17. Tamhane U.U., Aneja S., Montgomery D., Rogers E.K., Eagle K.A., Gurm H.S. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am. J. Cardiol. 2008; 102: 653-657.
- Templeton A.J., McNamara M.G., Šeruga B., Vera-Badillo F.E., Aneja P., Ocaña A., Leibowitz-Amit R., Sonpavde G., Knox J.J., Tran B., et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: A systematic review and meta-analysis. J. Natl. Cancer Inst. 2014; 106: dju124.
- 4. Hogendorf P, Suska A, Skulimowski A, Rut J, Grochowska M, Wencel A, et al. Neutrophil-

- lymphocyte ratio and creatinine reduction ratio predict good early graft function among adult cadaveric donor renal transplant recipients. Single institution series. Pol Przegl Chir. 2018 Apr; 90(2): 28-33.
- Baral D, Yang Y, Katwal G, Li S, Wang S, Fan X, et al. Recipient Pre-Operative Neutrophil Lymphocyte Ratio Better Predicts Delayed Graft Function than Platelet Lymphocyte Ratio in Donation after Brain Death Kidney Transplantation. Med J Pokhara Acad Heal Sci. 2019; 2(2): 209-16.
- Ergin G, De?er SM, Köprü B, Derici Ü, Arinsoy T. High neutrophil-to-lymphocyte ratio predicts acute allograft rejection in kidney transplantation: A retrospective study. Turkish J Med Sci. 2019; 49(2): 525-30.
- 7. Garg AX. Helping more patients receive a living donor kidney transplant. Clin J Am Soc Nephrol. 2018; 13(12): 1918-23.
- 8. Hayashi H, Takamura H, Ohbatake Y, Nakanuma S, Tajima H, Fushida S, et al. Postoperative changes in neutrophil-to-lymphocyte ratio and platelet count: A simple prognostic predictor for adult-to-adult living donor liver transplantation. Asian J Surg. 2018 Jul; 41(4): 341-8.
- 9. Walker PA, Kunjuraman B, Bartolo DCC. Neutrophil-to-lymphocyte ratio predicts anastomotic dehiscence. ANZ J Surg. 2018 Jan; 7-8: E573-E577.
- 10. Giakoumidakis K, Fotos N, Patelarou A, Theologou S, Argiriou M, Chatziefstratiou A, et al. Perioperative neutrophil to lymphocyte ratio as a predictor of poor cardiac surgery patient outcomes. Pragmatic Obs Res. 2017; 8: 9-14.
- 11. Kahramanca S, Ozgehan G, Seker D, Gökce EI, Seker G, Tunç G, et al. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. Ulus travma ve acil cerrahi Derg = Turkish J trauma Emerg Surg TJTES. 2014 Jan; 20(1): 19-22.
- 12. Halazun KJ, Marangoni G, Hakeem A, Fraser SM, Farid SG, Ahmad N. Elevated preoperative recipient neutrophil-lymphocyte ratio is associated with delayed graft function following kidney transplantation. Transplant Proc. 2013 Nov; 45(9): 3254-7
- Decruyenaere A, Decruyenaere P, Peeters P, Vermassen F, Dhaene T, Couckuyt I. Prediction of delayed graft function after kidney transplantation: Comparison between logistic regression and machine learning methods Standards, technology, and modeling. BMC Med Inform Decis Mak. 2015; 15(1): 1-10.