



NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) AND PLATELET-TO-LYMPHOCYTE RATIO (PLR) AS PREDICTORS OF MORTALITY IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS

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ABSTRACT

Chronic Kidney Disease (CKD) is associated with high mortality, especially among patients undergoing hemodialysis (HD). Inflammation markers such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) have been linked to mortality prediction. This study aims to evaluate the role of NLR and PLR as mortality predictors in CKD patients undergoing HD at H. Adam Malik Hospital, Medan. This retrospective study analyzed CKD patients receiving HD from January to December 2023, aged 18-60 years, and undergoing routine HD for at least 3 months. Excluded were those with comorbidities, immunosuppressant use, or incomplete records. Data on demographics, laboratory values (including NLR and PLR), and mortality outcomes were collected. ROC curve and logistic regression analysis were used. Out of 108 patients, 35 (32.4%) died. The median NLR was significantly higher in the mortality group (7.89 vs. 3.41, $p < 0.001$), while PLR showed no significant difference. ROC analysis revealed NLR's moderate accuracy (AUC = 73.3%, cut-off = 5). Multivariate analysis identified coronary artery disease history, age, and creatinine levels as significant mortality factors. NLR is a moderate predictor of mortality in CKD patients undergoing HD, while PLR is not.

Keywords: chronic kidney disease; hemodialysis; inflammation; mortality; NLR; PLR

How to cite (in APA style)

Silaban, R., Arto, N. S., & Lubis, M. R. (2025). Neutrophil-To-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) as Predictors of Mortality in Chronic Kidney Disease Patients Undergoing Hemodialysis. *Indonesian Journal of Global Health Research*, 7(5), 827-834. <https://doi.org/10.37287/ijghr.v7i5.6998>.

INTRODUCTION

Chronic kidney disease (CKD) remains a major contributor to hospital admissions and patient mortality. In 2017, CKD was estimated to affect approximately 843.6 million people globally (Bikbov et al., 2020). This condition is commonly observed among the elderly population. Compared to data from 1990, there has been a 29.3% increase in its incidence. A 2018 study conducted across 34 provinces in Indonesia reported an average prevalence of 0.38% in the general population, indicating that 4 out of every 1,000 individuals in Indonesia are diagnosed with CKD. The study also revealed that the highest prevalence was found in North Kalimantan, while the lowest was recorded in West Sulawesi (Hustrini, 2023; Kementerian Kesehatan RI, 2018).

Functionally, the kidneys of CKD patients gradually deteriorate until the individual reaches end-stage renal disease (ESRD) or succumbs to death (Carrero & Stenvinkel, 2010). One of the primary treatment options for ESRD is renal replacement therapy, most commonly in the form of hemodialysis (HD). Hemodialysis refers to a range of renal replacement modalities that utilize an extracorporeal circuit (external blood circulation), a device for fluid and solute exchange (hemodialyzer or filter), and a dialysate solution to facilitate the exchange between the blood and fluid compartments. Hemodialysis has evolved from a risky experimental procedure into a sophisticated and relatively safe medical technique (Flythe, 2023).

Despite technological advances, morbidity and mortality rates among ESRD patients undergoing regular hemodialysis remain high (Collins et al., 2015). The crude 1-year mortality rates among hemodialysis patients vary across countries: 6.6% in Japan, 15.6% in Europe, and 21.7% in the United States (Pippias et al., 2016). Furthermore, a study by woziwodzka et al. (Woziwodzka et al., 2019) reported that the 5-year mortality rate for hemodialysis patients reached 63.4%. However, data on mortality rates among CKD patients undergoing hemodialysis in developing countries, including Indonesia, remain scarce.

One of the key explanations for the persistently high mortality rates despite HD treatment is the presence of ongoing inflammation. In CKD patients undergoing hemodialysis, chronic inflammation may still occur, typically marked by elevated levels of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α). These elevations trigger neutrophil activation, which in turn releases enzymes and cytokines that exacerbate kidney damage. Simultaneously, lymphocytes decrease significantly due to apoptosis induced by reactive oxygen species (ROS) and the pro-inflammatory environment.⁴ Additionally, this inflammatory state promotes platelet activation. A significant increase in platelet count raises the risk of thrombosis. These processes are reflected by increased neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) (Catabay et al., 2017; Imtiaz et al., 2012).

NLR and PLR are markers that can be directly calculated from routine laboratory tests. These are considered novel, efficient, and low-cost biomarkers. Previous studies have demonstrated their utility in predicting mortality among CKD patients on hemodialysis. For instance, in a study by Zhang et al. (J. Zhang et al., 2021), elevated NLR levels were independently associated with all-cause mortality (OR 2.011, 95% CI 1.082–3.74, $P = 0.027$), while higher PLR levels were predictive of cardiovascular mortality (OR 2.768, 95% CI 1.147–6.677, $P = 0.023$). In a study by Bikbov et al. (Bikbov et al., 2020) in China involving 268 CKD patients on HD, an NLR cut-off value ≥ 3.5 was a predictor of cardiovascular-related mortality. Furthermore, a study by Kato et al. (Kato et al., 2008) involving 339 hemodialysis patients at Murayama Hospital, Japan, reported that $\text{NLR} \geq 5$ and $\text{PLR} \geq 300$ were associated with increased overall mortality over a 42-month follow-up period.

Unfortunately, while NLR and PLR have been examined in several international studies, there is a lack of research evaluating these markers in CKD patients undergoing hemodialysis in Indonesia, particularly in Medan. Moreover, previous studies have shown that NLR and PLR cut-off values differ between countries (Ahbap et al., 2016; Behairy et al., 2022; Catabay et al., 2017; Lubis, 2023; J. Zhang et al., 2021) suggesting that these markers may vary across populations. Based on this rationale, the present study aims to evaluate the role of NLR and PLR as predictors of mortality in CKD patients undergoing hemodialysis.

METHOD

This study employed a retrospective analytical design with a cross-sectional approach. The study was conducted at H. Adam Malik General Hospital in Medan from January 2023 to December 2023. The target population consisted of patients with chronic kidney disease (CKD) who underwent regular hemodialysis (HD) during the specified period. Inclusion criteria were patients aged 18–60 years, who had received regular HD for at least three months. Patients were excluded if they had comorbidities such as autoimmune diseases, malignancies, or other chronic conditions that could affect inflammatory markers; if they had a history of steroid or immunosuppressant use; or if they had incomplete medical records. Demographic data, clinical history, laboratory results, and mortality outcomes were collected from patient medical records. The laboratory parameters, including neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were recorded based on blood tests taken during the third month of HD treatment. Statistical analysis included receiver operating

characteristic (ROC) curve analysis to determine the optimal cut-off values for NLR and PLR in predicting mortality. Logistic regression was used to assess factors associated with mortality outcomes. To analyze the data, this study utilized a retrospective analytical design with a cross-sectional approach, focusing on CKD patients undergoing hemodialysis (HD) at H. Adam Malik General Hospital. Demographic data, laboratory values, and mortality outcomes were extracted from medical records. Laboratory tests, including Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), were collected at the third month of HD therapy. Statistical analyses included ROC curve analysis to determine the optimal cut-off points for NLR and PLR in predicting mortality, with logistic regression used to evaluate factors influencing mortality outcomes.

RESULT

A total of 108 patients with chronic kidney disease (CKD) undergoing hemodialysis at H. Adam Malik General Hospital, Medan, during the period of January–December 2023 were included in this study. The majority of patients were male (63.9%) with a median age of 51 years (range 21–60 years). Almost all patients had a history of hypertension (99.1%), while 54.6% had diabetes mellitus and 32.4% had a history of coronary artery disease. Among the total, 35 patients (32.4%) were found to had mortality (Table 1).

Table 1.

Demographic Characteristics of CKD Patients Undergoing Hemodialysis (n = 108)	
Demographic characteristics	f (%)
Gender, f (%)	
Male	69 (63,9)
Female	39 (36,1)
Age, years	51 (21 – 60)
Hypertension, f (%)	
Yes	107 (99,1)
No	1 (0,9)
Diabetes, f (%)	
Yes	59 (54,6)
No	49 (45,4)
Coronary artery disease, f (%)	
Yes	35 (32,4)
No	73 (67,6)
Mortality, f (%)	
Dead	35 (32,4)
Survive	73 (67,6)

Table 2.

Laboratory Characteristics of CKD Patients Undergoing Hemodialysis	
Laboratory characteristics	n = 108
Neutrophil, $10^3/\mu\text{L}$	4,99 (0,42 – 36,46)
Monocyte, $10^3/\mu\text{L}$	0,6 (0 – 2,35)
Lymphocyte, $10^3/\mu\text{L}$	$1,29 \pm 0,52$
BUN, mg/dL	70 (31,3 – 216)
Ureum, mg/dL	150 (67 – 462)
Creatinine, mg/dL	$12,09 \pm 3,87$
eGFR, ml/minute/1.73 m ²	5,13 (2,09 – 14,41)
Hb, g/dL	$8,33 \pm 1,71$
Leukocyte, / μL	7,25 (0,51 – 38,96)
Thrombocyte, $10^3/\mu\text{L}$	197 (56 – 543)
NLR	4,22 (1,06 – 55,18)
PLR	157,21 (1,43 – 703,33)

Based on the laboratory characteristics (table 2), in this study, the median neutrophil count was $4.99 \times 10^3/\mu\text{L}$, while the mean lymphocyte count was $1.29 \pm 0.52 \times 10^3/\mu\text{L}$. The median monocyte count was $0.6 \times 10^3/\mu\text{L}$. The mean serum creatinine level was 12.09 ± 3.87 mg/dL, and the median blood urea nitrogen (BUN) and urea levels were 70 mg/dL and 150 mg/dL,

respectively. The mean hemoglobin level was 8.33 ± 1.71 g/dL, indicating a prevalent anemia among the study population. The mean eGFR was 5.13 mL/min/1.73 m², reflecting advanced kidney disease. The median NLR was 4.22, with a range from 1.06 to 55.18, and the median PLR was 157.21, with a wide range from 1.43 to 703.3.

When comparing the mortality and survival groups, significant differences were observed in several variables. Patients in the mortality group had a higher median age ($p < 0.001$) and were significantly more likely to have a history of diabetes ($p < 0.001$) and coronary artery disease ($p < 0.001$). Laboratory parameters that were significantly higher in the mortality group included neutrophil count ($p < 0.001$), leukocyte count ($p < 0.001$), and NLR ($p < 0.001$). Conversely, creatinine ($p < 0.001$), eGFR ($p < 0.001$), and platelet count ($p = 0.024$) were significantly lower in the mortality group. No significant differences were found in monocyte count, hemoglobin, or PLR values.

Table 3.
Relationship Between Demographic and Laboratory Characteristics and Mortality

Demographic characteristics	Dead (n=35)	Survive (n=73)	p
Gender, f (%)			
Male	22 (31.9)	47 (68.1)	0.877 ^a
Female	13 (33.3)	26 (66.7)	
Age, years	57 (26 – 60)	48 (21 – 60)	<0.001 ^b
Hypertension, f (%)			
Yes	35 (32,7)	72 (67,3)	1.000 ^c
No	0	1 (100)	
Diabetes, f (%)			
Yes	30 (50,8)	29 (49,2)	<0.001 ^a
No	5 (10,2)	44 (89,8)	
Coronary artery disease, f (%)			
Yes	30 (85,7)	5 (14,3)	<0.001 ^a
No	5 (6,8)	68 (93,2)	
Neutrophil, 10 ³ /μL	10,1 (0,42-36,46)	4,5 (1,93-19,73)	<0.001 ^b
Monocyte, 10 ³ /μL	0,63 (0-2,35)	0,58 (0,19-1,19)	0.568 ^b
Lymphocyte, 10 ³ /μL	1,14 ± 0,68	1,37 ± 0,41	0.064 ^d
BUN, mg/dL	70,5 (32,5-216)	69,9 (31,3-155)	0.674 ^b
Ureum, mg/dL	151 (70-462)	150 (67-232)	0.677 ^b
Creatinine, mg/dL	8,34 (5,06-14,3)	13,38 ± 3,69	<0.001 ^b
eGFR, ml/minute/1.73 m ²	7,41 ± 2,74	3,99 (2,09-14,41)	<0.001 ^b
Hb, g/dL	7,97 ± 2,03	8,5 ± 1,52	0.134 ^d
Leukocyte, /μL	11,63 (0,51-38,96)	7,04 (3,85-22,16)	<0.001 ^b
Thrombocyte, 10 ³ /μL	158 (66-543)	213,14 ± 74,7	0.024 ^b
NLR	7,89 (1,46-55,18)	3,41 (1,06-18,08)	<0.001 ^b
PLR	144,73 (1,43-703,33)	158,87 (36,36-694,02)	0.916 ^b

^aChi Square, ^bMann Whitney, ^cFischer's Exact, ^dT Independent

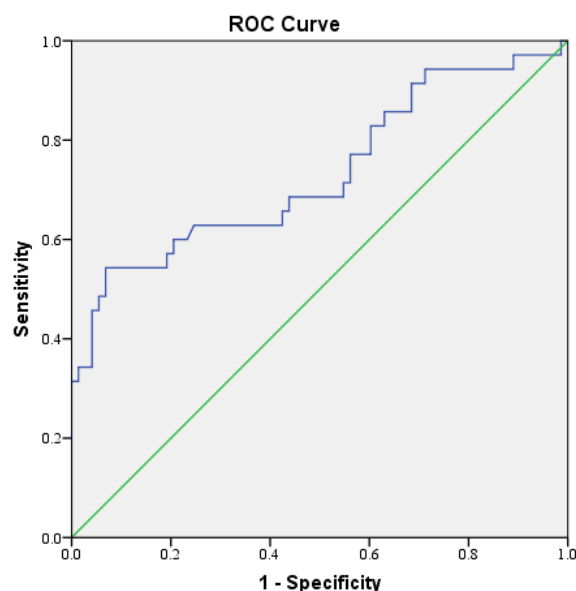
Table 4.
ROC Analysis of NLR as Predictors of Mortality

Variable	Mortality		Sensitivity	Specificity	PPV	NPV	Accuracy
	Yes	No					
NLR							
≥ 5	22	18	62.9%	75.3%	55%	80.9%	73.3%
< 5	13	55					

The ROC curve analysis showed that the area under the curve (AUC) for NLR was 71.3%, indicating moderate accuracy in predicting mortality (Table 4; Figure 1). The optimal cut-off value for NLR was 5.0, yielding a sensitivity of 62.9%, specificity of 75.3%, positive predictive value (PPV) of 55.0%, and negative predictive value (NPV) of 80.9%. In contrast, the AUC for PLR was only 50.5%, indicating poor discriminative ability and lack of predictive value for mortality in this population (Table 5; Figure 2).

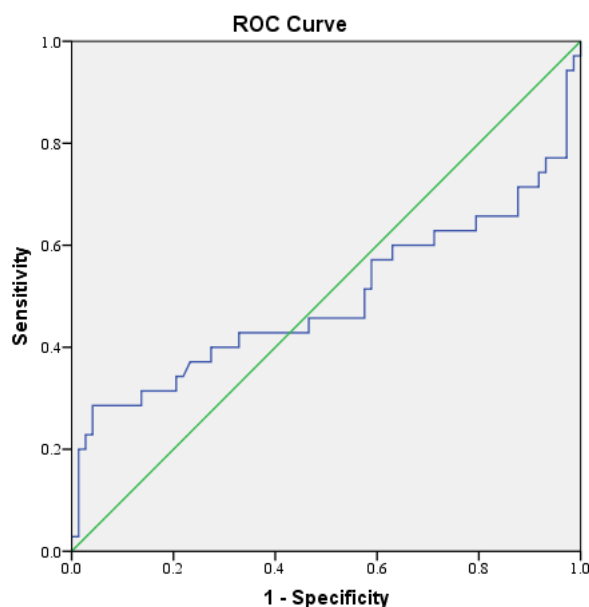
Table 5.
ROC Analysis of PLR as Predictors of Mortality

Variable	Mortality		Sensitivity	Specificity	PPV	NPV	Accuracy
	Yes	No					
PLR							
≥ 155	16	38	45.7 %	46.6%	29.6%	64.2%	49.4%
< 155	19	34					



Diagonal segments are produced by ties.

Figure 1. ROC Curve Analysis for NLR



Diagonal segments are produced by ties.

Figure 2. ROC Curve Analysis for PLR

The multivariate logistic regression revealed three independent predictors of mortality: age, history of coronary artery disease, and creatinine level. Age and coronary artery disease were positively associated with mortality, while higher creatinine levels were inversely associated with mortality, suggesting a potential protective role. Notably, neither NLR nor PLR remained significant in this multivariate model, indicating that these inflammatory markers were not independent predictors when adjusted for other clinical variables.

Table 6.
Multivariate Analysis of Independent Predictors of Mortality

Variable	B	p	OR	95% CI for OR	
				Lower	Upper
10 th selection					
Age	0.131	0.010	1.140	1,031	1,259
Coronary artery disease	5.941	0.000	380.166	26,389	5476,750
Creatinine	-0.04	0.010	0.689	0,519	0,917
Constant	-5.342	0.069	0.005		

DISCUSSION

Chronic kidney disease (CKD) remains a significant global health burden, particularly in developing countries like Indonesia, where access to early diagnosis and optimal renal replacement therapy can be limited. As the disease progresses to end-stage renal disease (ESRD), patients often require long-term hemodialysis (HD). However, mortality among HD patients remains high, especially within the first year of treatment initiation. In our study at RSUP H. Adam Malik Medan, we found a mortality rate of 32.4% among 108 patients undergoing maintenance HD, consistent with findings from previous studies, which reported mortality ranging from 10% to 45% depending on regional and clinical factors (Lukowsky et al., 2013; Mahmood et al., 2025).

The pathogenesis of mortality in HD patients is multifactorial, with systemic inflammation playing a key role. HD procedures themselves, through exposure to bioincompatible membranes, vascular access manipulation, and recurrent infections, which can trigger chronic low-grade inflammation, resulting in elevated neutrophil counts and lymphopenia (Veríssimo et al., 2022). The NLR has thus emerged as a surrogate inflammatory marker and has been investigated for its prognostic value in various conditions, including CKD. In our study, the NLR value was significantly higher in the mortality group compared to the survival group in univariate analysis. This finding aligns with prior studies. For instance, Zhang et al. and Li et al. reported that elevated NLR was associated with higher all-cause mortality in HD patients (Bae et al., 2015; Cherukuri & Bhandari, 2010). A study by L. Zhang et al. also suggested that NLR is a useful predictor of long-term outcomes in dialysis populations (L. Zhang et al., 2021).

However, upon multivariate logistic regression, our study did not identify NLR as an independent predictor of mortality. This contrasts with some previous studies and suggests that while NLR may reflect the inflammatory status of patients, it might be confounded by other clinical or biochemical factors in our cohort. Variables such as age, comorbid conditions (e.g., diabetes or cardiovascular disease), and nutritional status likely have a more dominant role in determining outcomes in HD patients. The lack of association in multivariate analysis may also be due to the relatively small sample size, limiting the statistical power to detect independent predictors.

In addition, our study assessed the PLR, another inflammatory marker. However, PLR was not significantly associated with mortality, neither in univariate nor multivariate analysis. This further supports the notion that while hematological inflammatory indices are simple and cost-effective, their clinical predictive power may be limited without integration with broader clinical assessments. Our findings suggest that NLR alone may not be sufficient for mortality risk stratification in HD patients, particularly when adjusted for other clinical factors. Clinicians should therefore interpret NLR within the broader context of each patient's condition, rather than as a standalone prognostic tool. This study has several limitations. First, the retrospective cross-sectional design limits the ability to draw causal inferences between

NLR, PLR, and mortality in patients undergoing hemodialysis. A prospective study design is recommended for future research to yield more accurate and reliable conclusions. Second, the study was conducted at a single center, which may restrict the generalizability of the findings to other populations. Including participants from multiple hemodialysis centers in future studies would allow for a larger sample size and more representative results. Third, this study focused only on the inflammatory markers NLR and PLR, without analyzing other potential biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), or procalcitonin. Incorporating these markers in future research may help identify which inflammatory parameters have stronger associations with mortality in chronic kidney disease patients undergoing hemodialysis.

CONCLUSION

NLR can be used as a predictor of mortality in CKD patients undergoing hemodialysis with moderate accuracy, based on ROC analysis, although it was not independently associated with mortality in multivariate analysis. PLR does not have predictive value for mortality. Instead, history of coronary artery disease, age, and c levels were the dominant independent predictors of mortality.

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