Journal of Endocrinology, Tropical Medicine, and Infectious Disease (JETROMI)

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO WITH ONE-YEAR MORTALITY IN MAINTENANCE HEMODIALYSIS PATIENTS

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ARTICLE INFO

ABSTRACT

Background: Chronic kidney disease (CKD) carries a high morbidity and mortality rate, particularly among patients undergoing maintenance hemodialysis (MHD). Inflammation is a key mechanism affecting prognosis, and the neutrophil-to-lymphocyte ratio (NLR) is a simple, accessible marker of systemic inflammation.

Method: This retrospective cohort study aimed to evaluate the association between NLR and one-year mortality in MHD patients. A total of 65 adult CKD patients at Adam Malik Hospital, Medan, from January to December 2024 were included. Demographic, clinical, and laboratory data were obtained from medical records, and NLR was calculated as the neutrophil count divided by the lymphocyte count, categorized as <3.5 and ≥3.5. Associations were analyzed using Chi-square or Fisher's exact test, with odds ratios (OR) and 95% confidence intervals (CI).

Results: The mean age was 48.35 ± 13.43 years, and 66.2% were male. The median NLR was 2.93 (IQR 2.25), with 46.2% ≥3.5. One-year mortality was 30.8%. Elevated NLR (≥3.5) was significantly associated with higher mortality (46.7% vs. 17.1%; p=0.01) and a 4.23-fold higher risk of death (95% CI: 1.36–13.15).

Conclusion: Monitoring mortality in MHD patients with examination of routine NLR may help identify high-risk patients for earlier intervention.

Keywords: CKD; MHD; One-year mortality; NLR; Systemic Inflammation

ABSTRAK

Latar Belakang: Penyakit ginjal kronis (PGK) menyebabkan tingkat morbiditas dan mortalitas yang tinggi, terutama pada pasien yang menjalani hemodialisis pemeliharaan (HD). Peradangan adalah mekanisme utama yang mempengaruhi prognosis, dan rasio neutrofil-ke-limfosit (NLR) adalah penanda peradangan sistemik yang sederhana dan dapat diakses.

Metode: Studi kohort retrospektif ini bertujuan untuk mengevaluasi hubungan antara NLR dan kematian satu tahun pada pasien HD. Sebanyak 65 pasien PGK dewasa di Rumah Sakit Adam Malik, Medan, sejak Januari hingga Desember 2024 termasuk dalam penelitian. Data demografis, klinis, dan laboratorium diperoleh dari rekam medis, dan NLR dihitung sebagai jumlah neutrofil dibagi dengan jumlah limfosit, dikategorikan sebagai <3,5 dan ≥3,5. Asosiasi dianalisis menggunakan

Chi-square atau uji Fisher, dengan odds ratio (OR) dan interval kepercayaan (CI) 95%.

Hasil: *Usia rata-rata adalah 48,35 ± 13,43 tahun, dan 66,2% adalah laki-laki. NLR rata-rata adalah 2,93 (IQR 2,25), dengan 46,2% ≥3,5. Kematian satu tahun adalah 30,8%. Peningkatan NLR (≥3,5) secara signifikan dikaitkan dengan kematian yang lebih tinggi (46,7% vs. 17,1%; p=0,01) dan risiko kematian 4,23 kali lebih tinggi (95% CI: 1,36–13,15).*

Kesimpulan*: Memantau kematian pada pasien HD dengan pemeriksaan NLR rutin dapat membantu mengidentifikasi pasien berisiko tinggi untuk intervensi lebih awal.*

Kata kunci: *PGK; MHD; Kematian satu tahun; NLR; Peradangan Sistemik*

1. Introduction

Chronic kidney disease (CKD) is defined as structural or functional abnormalities of the kidney lasting for at least three months, with health implications [1]. It is a major public health problem, with global prevalence estimates ranging from 8% to 16% [2]. In 2017, approximately 697.5 million cases of CKD were reported worldwide, corresponding to a prevalence of 9.1% [3]. More than 850 million individuals suffer from various forms of kidney disease, a figure exceeding the global burden of diabetes and cancer combined [3]. In Indonesia, the 2018 Basic Health Research (RISKESDAS) survey reported a CKD prevalence of 0.38%, with approximately 60% of patients requiring dialysis [4]. The highest prevalence was recorded in North Kalimantan (0.64%), while the lowest was in West Sulawesi (0.18%). Hemodialysis remains the predominant modality for renal replacement therapy in end-stage kidney disease (ESKD) patients [4], [5]. Despite advances in technology and treatment, mortality among hemodialysis patients remains significantly higher compared to the general population, reported to be 10–30 times greater [6]. Mortality is particularly elevated within the first 90 days of initiating dialysis, with one-year crude mortality rates varying between 6.6% in Japan [7] and 21.7% in the United States [8]. Inflammation is a critical driver of adverse outcomes in CKD, arising from multiple factors including uremia, reduced clearance of inflammatory mediators, oxidative stress, and dialysis-related factors [9], [10]. Traditional inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) are valuable but costly and not routinely measured in clinical settings. The neutrophil-to-lymphocyte ratio (NLR), derived from a standard complete blood count, reflects both innate immunity (neutrophils) and adaptive immunity (lymphocytes), offering a cost-effective alternative for assessing systemic inflammation [11], [12]. Previous studies have linked elevated NLR to increased mortality in various clinical populations, including CKD and hemodialysis patients [13]–[16]. Ao et al. [14] reported that high NLR was associated with both all-cause and cardiovascular mortality in CKD, while Mayne et al. [15] found a strong correlation between NLR and mortality in hemodialysis cohorts. However, most studies have been conducted in Western or East Asian populations, with limited evidence from Southeast Asia. Given the high burden of CKD and dialysis-related mortality in Indonesia, there is a need to evaluate simple, accessible prognostic tools. This study aimed to determine the association between NLR and one-year mortality among maintenance hemodialysis patients in a tertiary referral center in Medan, Indonesia.

2. Methods

This retrospective cohort study was conducted at the Hemodialysis Unit of Adam Malik Hospital, Medan, Indonesia, from January to December 2024. The study included adult patients (aged ≥18 years) diagnosed with CKD who had undergone maintenance outpatient hemodialysis for at least three consecutive months. Patients with acute infections, active autoimmune diseases, malignancies, or incomplete medical records were excluded to reduce potential confounding factors. Ethical approval for this study was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (approval number 406/KEPK/USU/2025), and the study was conducted in accordance with the principles of the Declaration of Helsinki. As this was a retrospective study using secondary data from medical records, the requirement for

individual informed consent was waived, and all patient data were anonymized and kept confidential. A systematic sampling technique was applied to the hospital's electronic medical record system, yielding a total of 65 eligible participants. Demographic data (age, sex), clinical information (primary diagnosis and comorbidities such as hypertension and diabetes mellitus), and laboratory parameters were collected. Neutrophil and lymphocyte counts were obtained from pre-dialysis blood tests, and the neutrophil-to-lymphocyte ratio (NLR) was calculated for each patient. Based on previously published prognostic thresholds, NLR values were categorized into two groups: <3.5 and ≥3.5. The primary outcome of this study was one-year all-cause mortality, determined through hospital records and follow-up documentation. Data analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR) according to data distribution. Associations between NLR categories and mortality were evaluated using the Chi-square test or Fisher's exact test as appropriate, with odds ratios (OR) and 95% confidence intervals (CI) calculated to estimate the strength of association. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Baseline Characteristics

Based on Table 1, a total of 65 patients diagnosed with CKD undergoing maintenance hemodialysis (MHD) were included in the study. The demographic and clinical characteristics. The mean age was 48.35±13.43 years, and the majority were male (66.2%). The median duration of hemodialysis was 14 months (IQR 17). Hypertension was the most prevalent comorbidity (84.6%), followed by type 2 diabetes mellitus (12.3%). Most patients were in the normal weight category for BMI, and an arteriovenous (AV) shunt was the most frequently used vascular access (76.9%). NLR <3.5: 35 and NLR ≥3.5: 30. The majority of patients (69.2%) were survivors during one year of follow-up.

Table 1. Baseline characteristics of MHD patients

Characteristics	N (%)
Sex,	
- Male	43 (66.2)
- Female	22 (33.8)
Duration of HD (months), median (IQR)	14 (17)
Comorbidities,	
- Hypertension	55 (84.6)
- Type 2 DM	8 (12.3)
BMI (kg/m²).	
- Underweight	2 (3.1)
- Normoweight	28 (43.1)
- Overweight	8 (12.3)
- Grade 1 obesity	23 (35.4)
- Grade 2 obesity	4 (6.2)
Vascular access HD,	
- AV shunt	50 (76.9)
- CDL	10 (15.4)
- Femoral	5 (7.7)
One-year mortality,	
- Survivors	45 (69.2)
- Non-survivors	20 (30.8)

Data are presented as mean ± standard deviation (SD), median (interquartile range, IQR), or number (percentage). HD: hemodialysis; AV: arteriovenous; CDL: central double lumen catheter; BMI: body mass index; WBC: white blood count; NLR: neutrophil-to-lymphocyte ratio.

3.2. Distribution of Mortality by Comorbidity

Based on Table 2, the distribution of one-year mortality according to comorbid conditions in chronic kidney disease patients undergoing regular hemodialysis is shown. The majority of non-survivors had hypertension as the sole comorbidity, followed by those with both hypertension and type 2 diabetes mellitus. Patients without these comorbidities had the lowest proportion of non-survivors.

Table 2. Distribution of Mortality by Comorbidity

Variables	Survivors (n=20)	Non-survivors (n=40)
Type 2 DM	3	15
Hypertension	12	60
No comorbidity	5	25

3.3. Association Between NLR and One-Year Mortality

As shown in Table 3, among 35 patients with NLR < 3.5, 29 (82.9%) were survivors, and 6 (17.1%) were non-survivors. Meanwhile, among 30 patients with NLR ≥ 3.5, 16 (53.3%) were survivors, and 14 (46.7%) were non-survivors. The Pearson Chi-square test revealed a statistically significant association between NLR and one-year mortality in patients undergoing regular hemodialysis at Adam Malik Hospital, Medan ($p = 0.01$). An odds ratio (OR) of 4.229 (95% CI: 1.36–13.15) indicated that patients with NLR ≥ 3.5 had a 4.2-fold higher risk of one-year mortality compared to those with NLR < 3.5.

Table 3. Association between NLR and One-Year Mortality in Patients Undergoing Regular Hemodialysis

Variables	Mortality		*P*	OR (95% CI)
	Non-Survivors, *n* (%)	Survivors, *n* (%)		
NLR ≥ 3,5	14 (46.7)	16 (53.3)	0.01	4.23 (1.36-13.15)
< 3,5	6 (17.1)	29 (82.9)		

4. Discussion

This study included 65 patients undergoing maintenance hemodialysis (MHD) at Adam Malik General Hospital. The baseline characteristics revealed a mean age of 48.35 ± 13.43 years, with the majority being male (66.2%). These findings are consistent with previous studies reporting that most MHD patients are aged over 46 years and predominantly male [4]. A meta-analysis has confirmed that MHD patients are frequently middle-aged to elderly, with a higher prevalence in men, which is associated with an increased risk of mortality [9]. Similarly, a Nigerian study involving 280 patients reported a mean age of 47.9 ± 17.5 years and a male predominance of 65.7% [8]. In contrast, Van Biesen et al. [18] found that MHD patients in Europe were more often elderly and female, and Valga et al. [20] also reported an older median age (66.49 years) with a predominance of women. These differences indicate that the demographic characteristics of MHD patients may vary across regions due to differences in location, socioeconomic factors, and the etiology of CKD. The median duration of hemodialysis in this study was 14 months (IQR 17 months), indicating that most patients had been on long-term therapy. Hamadneh et al. [6] reported that the majority of patients had been on dialysis for 1–3 years, while Agshaeifard et al. [10] observed a longer mean duration of 4.30 ± 3.39 years, and Akram et al. found a mean duration of 5 years [5]. These variations suggest that the duration of hemodialysis therapy differs substantially between populations, and longer durations are often associated with a higher risk of complications and reduced quality of life [4]. Hypertension (84.6%) and type 2 diabetes mellitus (12.3%) were the most common comorbidities in this study. This is consistent with Ebrahimi et al., who found hypertension in 31.5% and type 2 diabetes in 24% of 135 patients [19], and with Sun et al., who reported hypertension in 74.8% and type 2 diabetes in 14.9% of MHD patients [7]. Agshaeifard et al. also noted that hypertension and diabetes are the leading causes of ESRD worldwide [10]. BMI distribution showed that most patients were in the normal-weight (43.1%) and grade 1 obesity (35.4%) categories. This indicates a relatively balanced weight distribution, though with a notable proportion of obesity. Nie et al. reported that obese MHD patients have a higher risk of sarcopenia in the presence of chronic inflammation [13]. Abdominal adiposity in MHD patients has been linked to chronic inflammation and protein-energy malnutrition (PEM), both of which are predictors

of mortality [16]. Heaf et al. reported a similar mean BMI of 25.8 kg/m² [15], while Ebrahimi et al. reported a mean BMI of 23 ± 4.6 kg/m² [19]. These differences in BMI may be influenced by variations in age, sex, socioeconomic status, dietary habits, and physical activity levels among populations. In this study, most patients (76.9%) used an arteriovenous (AV) shunt as their vascular access for hemodialysis. Weigert et al. also reported that AV shunt was the most frequently used vascular access [18]. Other studies have shown similar findings, with AV shunt usage rates of 57% [10]. Vascular access complications are common in CKD patients on MHD and contribute significantly to morbidity and mortality [6]. AV shunts are preferred because they have a lower risk of infection and thrombosis compared to central double-lumen catheters or femoral access [4]. The mean hemoglobin level in this study was 8.23 ± 1.31 g/dL, indicating that anemia remains a major concern in MHD patients. This value is lower than that reported by Sun et al., who found a mean Hb level of 11.6 ± 19.2 g/dL [7]. Anemia has been identified as a strong predictor of increased hospitalization and mortality in MHD patients [7]. Ahmed et al. reported that 45.4% of patients had Hb levels below 10 g/dL at the time of death, and both low hemoglobin and hematocrit were associated with higher infection rates, more frequent hospitalization, and poorer quality of life [8]. The median WBC was 7250/μL, and the median NLR was 2.93 (IQR 2.25). Nearly half (46.2%) of the patients had elevated NLR values (≥3.5), suggesting the presence of significant systemic inflammation. Okyay et al. reported a similar leukocyte count (7209 ± 1799/μL) but a slightly higher median NLR of 3.13 [13]. Nie et al. [13] reported an even higher mean NLR of 4.0 ± 1.9. NLR has been recognized as a marker of systemic inflammation, linked to various complications, including sarcopenia and mortality in MHD patients [13]. Variations in findings may be due to differences in population characteristics, dialysis duration and quality, concurrent infections, analysis cut-off values, and study design. In this study, 20 out of 65 patients (30.8%) were non-survivors within one year, reflecting a high mortality rate in this population. This is comparable to Ahmed et al., who reported a one-year mortality rate of 27.3% [8]. Mortality in MHD patients is reported to be 10–30 times higher than in the general population [4]. Crude one-year mortality rates are highest in the United States (21.7%) and lowest in Japan (6.6%) [7]. Heaf et al. reported that mortality among incident dialysis patients reached 33.8% in the first year, with age and comorbidities as significant risk factors [15]. The Japanese Society for Dialysis Therapy reported lower annual mortality rates of 10–15%, reflecting differences in healthcare standards and dialysis protocols [7]. This study demonstrated a significant association between NLR and one-year mortality, with patients having NLR ≥3.5 exhibiting a 4.2-fold higher risk of being non-survivors compared to those with NLR <3.5 ($p = 0.01$; OR = 4.229). Francisco et al. reported that NLR is a reliable predictor of survival in MHD patients [20], while Ao et al. found that high NLR was associated with all-cause and cardiovascular mortality in CKD patients [10]. NLR has been shown to outperform comorbidity burden and serum albumin in predicting mortality risk [9]. NLR is calculated by dividing the absolute neutrophil count by the absolute lymphocyte count and reflects both systemic inflammation and endothelial injury [11], [12]. It represents the balance between pro-inflammatory innate immune responses, mediated by neutrophils, and anti-inflammatory adaptive immune responses, mediated by lymphocytes. Neutrophils act as the first line of defense against invading pathogens through mechanisms such as chemotaxis, phagocytosis, production of reactive oxygen species (ROS), granular protein release, and cytokine secretion [17]. NLR is an emerging inflammatory index that reflects the balance between pro-inflammatory and anti-inflammatory mechanisms. It is also a prognostic indicator in a variety of diseases, including cancer, cardiovascular disease, liver disease, and surgical conditions [10]. Chronic inflammation is a key pathophysiological process in CKD and contributes to the high morbidity and mortality rates observed in MHD patients [19]. However, the findings of this study are not entirely consistent with those of Liao et al., who reported that NLR alone had limited predictive value for one-year mortality and was more effective when combined with other inflammatory markers such as MLR and PLR [14]. Similarly, Valga et al. reported that although initial NLR values were associated with mortality, the association was not significant after multivariate adjustment [20]. These discrepancies may be explained by differences in patient characteristics, analytical approaches, and unmeasured confounding factors. This study has several strengths, including the use of the neutrophil-to-lymphocyte ratio as a simple and inexpensive inflammatory marker derived from routine blood tests, an appropriate retrospective cohort design with one-year follow-up, and clearly defined inclusion and exclusion criteria that helped create a relatively homogeneous hemodialysis population.

However, the study also has important limitations, such as the relatively small sample size from a single center, the retrospective design that depends on the completeness of medical records, and the absence of multivariable adjustment for potential confounders such as age, comorbidities, nutritional status, and dialysis adequacy, which may limit the generalizability and causal interpretation of the findings.

5. Conclusion

In conclusion, this single-center retrospective study found that elevated NLR (≥3.5) was significantly associated with increased one-year mortality in MHD patients, with a more than four-fold higher likelihood of being non-survivors compared to those with lower NLR values. Given its simplicity, cost-effectiveness, and accessibility, NLR may serve as a useful early marker for identifying high-risk MHD patients. Routine monitoring of NLR should be considered as part of standard clinical evaluation, and future multicenter prospective studies with larger sample sizes are recommended to validate these findings and establish standardized cut-off values.

Conflict interest

The authors declare no conflict of interest.

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