Annals of Clinical and Analytical Medicine
Original Research

Comparison of risk factors for systemic inflammation in patients using different vascular access routes for hemodialysis treatment

Systemic inflammation and hemodialysis treatment

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Abstract

Aim: Chronic renal failure is a disease with increased inflammation. In this study, we aimed to evaluate the neutrophil-to-lymphocyte ratio (NLR), platelet-tolymphocyte ratio (PLR) and systemic immune-inflammation index (SII), which have recently been considered as predictive factors for systemic inflammation in patients receiving hemodialysis treatment for chronic renal failure, and also to investigate whether there is a difference between the inflammation markers when the use of hemodialysis catheter as vascular access is compared with the use of arteriovenous fistula.

Methods: A total of 42 patients (15 females, 27 males) receiving hemodialysis treatment for chronic renal failure were included in the study. The ratios of absolute neutrophil, lymphocyte, and platelet count to CRP and hemogram values were analyzed among patients who used hemodialysis catheters or arteriovenous fistula as vascular access routes for hemodialysis treatment.

Results: An NLR threshold of 2.30 was accepted as an indicator of systemic inflammation. The mean NLR value of all patients was 3.87, which was much higher than the accepted value. A moderate positive correlation was found between CRP and SII. Additionally, a strong positive correlation was observed between SII and NLR, as well as SII and PLR. No difference was found between patients with hemodialysis catheter or arteriovenous fistula.

Conclusion: NLR, PLR, and SII have been evaluated as indicators of systemic inflammation in recent years. With these indicators, it is possible to say that systemic inflammation is significantly higher in chronic renal failure patients receiving hemodialysis treatment compared to the normal population.

Keywords

systemic inflammation, hemodialysis treatment, systemic immune-inflammation index, neutrophil-lymphocyte ratio

DOI: 10.4328/ACAM.22382 Ann Clin Anal Med 2025;16(2):109-112
Received: 27.08.2024 Accepted: 21.10.2024 Published Online: 05.11.2024 Printed: 01.02.2025
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Introduction

Chronic renal failure (CRF), like many other chronic diseases, is a disease in which inflammation and atherosclerosis develop with high morbidity and mortality. CRF develops for various reasons, and when it progresses to the end stage, hemodialysis is frequently preferred as a treatment option. In hemodialysis patients, arteriovenous fistulas and peripheral venous catheters are often used as vascular access routes. Catheters are of vital importance as therapeutic support in hemodialysis. The first thought is that peripheral venous catheters may increase inflammation because they are a foreign body. The association of catheters with inflammation is mostly related to local infection but not to systemic inflammation.

In addition to etiologic factors, including diabetes mellitus and hypertension, factors including anemia, inflammation, and endothelial dysfunction have been reported as cardiovascular risk factors in end-stage renal failure (ESRD) patients receiving hemodialysis treatment.[1] It has been emphasized that there is an increase in inflammatory mediators in ESRD patients due to oxidative stress and increased extracellular fluid volume.[2] Chronic inflammation is also a part of malnutrition inflammation atherosclerosis (MIA) syndrome in ESRD patients.[3]

Neutrophils are involved in both innate and acquired immune regulation.[4] It is also mentioned that dendritic cells, B cells, NK cells, CD4, CD8, T cells, and mesenchymal stromal cells are also involved in immune regulation by interacting with neutrophils.[5] The neutrophil-to-lymphocyte ratio (NLR), platelet-tolymphocyte ratio (PLR), and systemic immune/inflammation ratio (SII) have gained more importance in recent years as markers used to predict inflammation and atherosclerosis. NLR is a test used to evaluate systemic inflammation in diabetes mellitus, hypertension, cirrhosis, malignancies, and cardiovascular diseases, as well as in ESRD, because it is costeffective and easily calculable.[6-9] NLR is also emphasized as one of the biomarkers that may indicate that CRF may progress.[10]

PLR measurement shows both inflammatory and thrombotic pathways because it is both affordable and easily measurable. It has more significant meaning than platelet or lymphocyte counts alone.[11] PLR can, therefore, be used to assess cardiovascular risk and mortality.[12]

The systemic immune/inflammation index has also been shown to have prognostic significance in cardiovascular diseases, cancers, and chronic renal failure.[13,14] The presence of high levels of albuminuria has been shown to be associated with high systemic immune inflammation index (SII) values.[15] NLR, PLR, and SII are calculated by proportioning the absolute values of neutrophils, lymphocytes, and platelets in the hemogram obtained by the venous route.[16] These three ratios calculated with hemogram values have facilitated approaches to inflammation.

Materials and Methods

Patients

Forty-two patients (15 females and 27 males) who were receiving hemodialysis treatment two or three times a week for at least three months due to ESRD and who were being treated at Gebze Fatih State Hospital Nephrology Clinic Hemodialysis Center were retrospectively included in the study. The age range was 27-81 years. Patients with active infection, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), acute renal failure, and chronic liver disease were excluded. The ratios of absolute neutrophil, lymphocyte, and platelet counts in CRP and hemogram values obtained in the absence of active infection were analyzed.

Ethical Approval

This study was approved by the Ethics Committee of Kocaeli City Hospital (Date: 15.08.2024, Decision No: 2024-65).

Statistical Analysis

GraphPadPrism 9.5.0 and IBM SPSS Statistics for Windows. Version 25.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA) statistical package programs were used. Descriptive statistics of the variables belonging to the patient group participating in the study are presented as frequency and % for categorical variables and as Mean ± SD and median (IQR) for continuous variables. The data of the study were examined in terms of normality assumptions: One-Sample t-test was used to test whether the N/L ratio was different from 2.30, Spearman Correlation analysis was used for the relationships between two continuous variables, Independent Sample t test or Mann Whitney U test was used for two independent group comparisons, One-Way Analysis of Variance (ANOVA) was used for three independent group comparisons. A value of $p<0.05$ was considered statistically significant.

Reporting Guidelines

The study was reported in accordance with STROBE guidelines.

Results

Results A total of 42 patients, 15 females (35.7%) and 27 males (64.3%) were included in the study. The age range was 27 to 81 years, with a mean age of 62.26 years. Patients had been receiving hemodialysis treatment for 1 to 11 years, with a mean of 3.64 years. The mean CRP was 15.95, mean hemoglobin 10.81 g/dL, mean NLR 3.87, mean PLR 168.4, and mean SII 793.11 (Table 1). In all patients, NLR was found to be statistically significantly different from the value of 2.30, which is considered normal in the community (p=0.000) (Figure 1). The mean NLR in patients with a hemoglobin value ≤10 (5.40) was higher than the mean NLR in patients with a Hb value>10 (3.26) (p=0.001). The NLR was not statistically different between the group of patients who used a hemodialysis catheter as the vascular Access route for hemodialysis treatment and the group who used an arteriovenous fistula (p=0.174). There was no statistically significant relationship between gender, duration of dialysis, vascular Access route used,

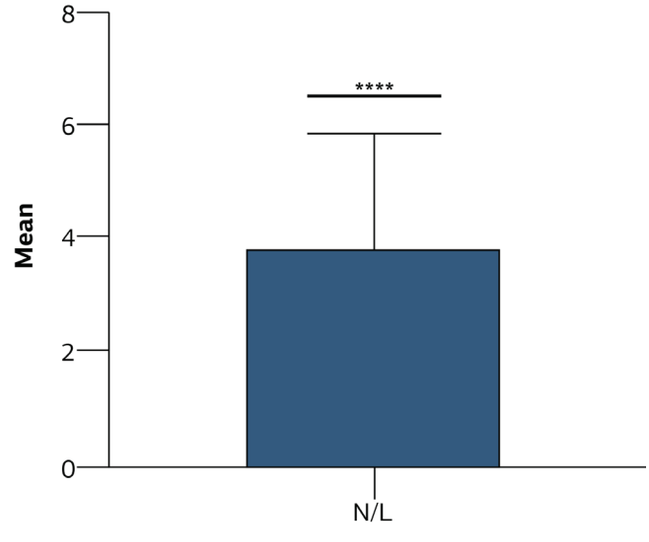

Figure 1. *N/L Ratio variable, ****p<0.0001*

Table 1. *Descriptive statistics of patient variables*

Variables	Mean ± SD	Median (IQR)
Age	62.26 ± 13.57	66.00 (18.00)
Duration of dialysis	3.64 ± 2.40	3.00 (2.50)
CRP	15.95 ± 21.64	6.90 (15.15)
Albumin	3.71 ± 0.43	3.70 (0.53)
Hemoglobin	10.81 ± 1.50	10.85 (1.71)
PLR	168.40 ± 61.84	164.25 (73.1)
NLR	3.87 ± 1.92	3.69 (2.01)
SII	793.11 ± 458.83	687.68 (662.96)

CRP: C-reactive protein, PLR: platelet-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, SII: Systemic immune-inflammation index

Table 2. *Comparison of NLR Measurements of patients according to groups*

Variables	Group	Mean ± SD	*P* value
Gender	Female	3.90 ± 2.14	.943[a]
	Male	3.85 ± 1.83	
Duration of dialysis, y	≤ 5	3.89 ± 1.98	.888[a]
	> 5	3.76 ± 1.62	
Hemoglobin	≤ 10	5.40 ± 2.31	.001*
	>10	3.26 ± 1.35	
ESA use	Yes	4.22 ± 1.98	.045[a]
	No	2.88 ± 1.37	
Vascular access	AVF	3.64 ± 1.84	.174[a]
	Indwelling hemodialysis catheter	4.60 ± 2.10	
Etiology	DM	4.07 ± 2.07	.354[a]
	HT	3.46 ± 1.94	
	Other	3.87 ± 1.62	

AVF: Arteriovenous fistula, ESA: Erythrocyte stimulating agent
DM: Diabetes Mellitus, HT: Hypertension

Table 3. *Correlation analysis results between variables*

	SII	CRP	N/L Ratio	PLT/L Ratio
SII	1			
CRP	r = 0.544**	1		
	p = 0.000			
NLR	r = 0.825**	r = 0.501**	1	
	p = 0.000	p = 0.000		
PLR	r = 0.820**	r = 0.407**	r = 0.789**	1
	p = 0.000	p = 0.007	p = 0.000	

SII: Systemic immune-inflammation index, CRP: C-reactive protein, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio

etiology of CRF, and mean NLR (p>0.05) (Table 2). There was a moderate positive correlation between SII and CRP variables (r = 0.544, p=0.000), a high positive correlation between SII and NLR (r = 0.825, p=0.000), and a high positive correlation between SII and PLR (r = 0.820, p=0.000). Furthermore, positive correlations were found between CRP and NLR (r = 0.501, p=0.000), CRP and PLR (r = 0.407, p=0.007), and NLR and PLR (r = 0.789, p=0.000), respectively (Table 3).

Discussion

In this study, systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), and platelet-tolymphocyte ratio (PLR), which are considered predictive factors of systemic inflammation, were evaluated in end-stage renal failure patients receiving hemodialysis treatment. SII = platelet count x neutrophil count/lymphocyte count ratio, NLR = neutrophil count/lymphocyte count ratio, and PLR = platelet count/ lymphocyte count ratio were calculated with the formulas. The results indicated that SII, NLR, and PLR were strong indicators of inflammation in correlation with CRP in ESRD patients receiving hemodialysis treatment. Yesilaltay A. mentioned that the mean NLR was accepted as 2.30 in the normal population.[17] It is possible to say that the mean NLR in the patients we included in the study was considerably higher than 2.30 (3.87 ± 1.92) (Figure 1). In many studies, it has been emphasized that NLR is increased in CRF.[18] Akbaş et al. mentioned in their study that elevated NLR accelerated the progression to dialysis.[19] It was also emphasized by Türkmen et al. that NLR is an important marker of inflammation in CRF patients.[20]

In our study, patients undergoing hemodialysis treatment were found to have a significantly elevated NLR. Ercan et al. showed in their study that immune/inflammation and SII were associated with all-cause mortality.[2] According to the results of our study, SII was found to be significantly higher in ESRD patients receiving dialysis treatment. Similarly, it can be said that the depth of anemia (Hb<10) is also associated with higher inflammation in this study. The high rate of erythropoietinstimulating agent use is associated with the presence of anemia. In addition, in our study, whatever the etiologic factor in the development of CRF, there was no difference in terms of the development of inflammation. In other words, inflammation indices were found to be high in dialysis patients regardless of etiology. The phlebitis, infection, and inflammatory effects of peripheral venous catheters have been emphasized in many studies.[21,22] In their study, Tudurachi et al. Associated high inflammatory hematologic ratios, including PLR and NLR, with major cardiovascular events, especially in young myocardial infarction patients.[11] Kaya B. et al. mentioned that PLR may be helpful in predicting mortality in hemodialysis patients.[23] In our study, PLR was found to be significantly higher in ESRD patients receiving hemodialysis treatment. Aygün et al. mentioned that catheters were mostly associated with local inflammation in their examination of peripheral venous catheters in terms of inflammation/infection in the intensive care unit.[24] In our study, there was no statistical data showing that the use of hemodialysis catheters as vascular Access increased systemic inflammation. There was no significant difference in inflammatory indicators between the use of arteriovenous fistula as a vascular Access route and catheter use.

Limitations

The small sample size, single-center and retrospective design, lack of a control group, and limited control of confounding factors restrict the generalizability and causal interpretation of the findings.

Conclusion

Inflammation is associated with all-cause mortality in patients receiving hemodialysis treatment for ESRD. Elevated SII, NLR, and PLR in patients undergoing hemodialysis for ESRD may be used to indicate a more severe increase in inflammation. SII, NLR, and PLR values, which are calculated by the ratio of hemoglobin, neutrophil, lymphocyte, and platelet counts in hemogram values routinely measured in venous blood, are statistically significantly higher. It is seen that inflammation is significantly higher in ESRD patients receiving hemodialysis treatment compared to the normal population. The depth of anemia is also associated with inflammation. There is no statistical evidence that the use of hemodialysis catheters as vascular Access increases systemic inflammation.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was waived due to the retrospective design of the study.

Data Availability

The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there is no conflict of interest.

Funding

None.

Abbreviations

ANOVA: Analysis of variance
CRF: Chronic renal failure
CRP: C-reactive protein
ESRD: End-stage renal disease
HBV: Hepatitis b virus
HCV: Hepatitis c virus
HIV: Human immunodeficiency virus
IQR: Interquartile range
NLR: Neutrophil-to-lymphocyte ratio
PLR: Platelet-to-lymphocyte ratio
SII: Systemic immune-inflammation index

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How to Cite

Kemal Mağden. Comparison of risk factors for systemic inflammation in patients usingdifferent vascular access routes for hemodialysis treatment. Ann Clin Anal Med 2025;16(2):109-112. doi:10.4328/ACAM.22382