

Examining the correlation of CRP, MPV, and NLR levels with the severity of stroke in ischemic stroke patients

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ABSTRACT

Aims: The severity of ischemic stroke may vary depending on the levels of certain biochemical markers. We aimed to investigate the relationship between C-reactive protein (CRP), mean platelet volume (MPV), and neutrophil-to-lymphocyte ratio (NLR) levels and stroke severity in patients presenting to the emergency department with ischemic stroke.

Methods: A total of 159 patients diagnosed with ischemic stroke and 160 healthy volunteers were included in the study. CRP, NLR, and MPV levels were measured in venous blood samples obtained in the emergency department. The relationship between National Institutes of Health Stroke Scale (NIHSS) scores and CRP, MPV, and NLR levels measured at the time of admission to the emergency department was examined.

Results: The mean CRP value of individuals in the control group was 6.19 ± 6.48 , and the mean CRP value of individuals in the patient group was 16.79 ± 18.14 . Patients had higher CRP values. CRP values showed statistically significant differences between the patient and control groups ($p < 0.001$). The mean NLR value of individuals in the control group was 2.50 ± 1.18 , and the mean NLR value of individuals in the patient group was 5.74 ± 5.40 . NLR values were higher in patients. NLR values showed statistically significant differences between the patient and control groups ($p < 0.001$). The mean MPV value of individuals in the control group was 8.15 ± 0.84 , and the mean MPV value of individuals in the patient group was 8.57 ± 1.40 . MPV values were higher in patients. MPV values showed statistically significant differences between the patient and control groups ($p = 0.002$).

Conclusion: The severity of ischemic stroke may vary depending on biochemical markers. Further research is needed to evaluate changes related to multiple biochemical parameters.

Keywords: Ischemic stroke, National Institutes of Health Stroke Scale, C-reactive protein, mean platelet volume, neutrophil-to-lymphocyte ratio

INTRODUCTION

Acute ischemic stroke (AIS) causes irreversible damage to brain tissue due to impaired cerebral blood flow. The incidence of AIS is relatively high; approximately 15 million people experience stroke worldwide each year.¹

It is also the main cause of permanent acquired disability, causing a heavy economic burden on society. AIS is the most common cerebrovascular disease and accounts for about 85% of all strokes.² Stroke risk prediction based on conventional risk factors such as hypertension (HT), diabetes mellitus (DM), and dyslipidemia remains inadequate. Identification of novel predictive biomarkers would contribute to risk prediction in subjects at risk of developing stroke. Inflammation plays an important role in the development of atherosclerosis.^{3,4}

C-reactive protein (CRP), an acute-phase reactant produced by hepatocytes, is considered a biomarker of inflammation. Meanwhile, hs-CRP accurately detects low-grade inflammation.⁵ A high CRP level, measured by hs-CRP, has been proposed as a risk factor for ischemic stroke or total stroke.⁶ A previous meta-analysis conducted by the Emerging Risk Factors Collaboration suggested that a 1-SD increment in CRP was associated with 46% and 39% greater risk of ischemic stroke and all strokes, respectively.⁷

Numerous studies have demonstrated that the neuroinflammatory response plays an essential role in the pathophysiology of ischemic stroke.⁸ Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) have recently



been reported as potential novel biomarkers of the baseline inflammatory process and could serve as predictors in patients with ischemic stroke.⁹

MPV is an important parameter reflecting platelet size and is considered a marker of platelet activity.¹⁰ Findings have shown that MPV is positively correlated with platelet activity.¹¹ Compared with cerebral infarction, the association between MPV and coronary disease has been more frequently reported. A meta-analysis of MPV in cardiovascular events found that patients with higher MPV had a 12% higher risk of death from cardiovascular events than those with lower MPV.¹² MPV also predicts the risk of ischemic stroke in patients with atrial fibrillation (AF).¹³

Previous studies have evaluated these parameters separately; however, this study is unique in simultaneously evaluating all three parameters. In our study, we aimed to examine the effects of CRP, NLR, and MPV on the severity of ischemic stroke.

METHODS

Ethics

This study was conducted with the approval of the Scientific and Evaluation Ethics Committee for Medical Researches at Ankara Bilkent City Hospital (Date: 05.11.2025, Decision No: TABED 1/1835/2025). Written informed consent was obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The research was conducted as a prospective case-control study.

A total of 159 ischemic stroke patients who were admitted to the emergency department and subsequently hospitalized in the neurology inpatient clinic or neurology intensive care unit were included in the study. Additionally, 160 healthy volunteers aged between 18 and 80 years, with no history of stroke, malignancy, dementia, demyelinating disease, infectious disease, or inflammatory disease, participated. Detailed clinical, laboratory, and radiological characteristics of stroke patients were recorded. The presence of DM, HT, coronary artery disease, and AF was assessed.

National Institutes of Health Stroke Scale (NIHSS) was calculated at the time of the patients' admission to the emergency department. Blood samples were obtained from the patients at their initial presentation to the emergency department. CRP, NLR, and MPV values, which were routinely measured in the blood samples collected at admission, were recorded. CRP, MPV, and NLR values of healthy volunteers who applied to the neurology outpatient clinic were also measured, and the results were recorded.

Statistical Analysis

Demographic information, numbers, and percentage values of the individuals participating in the study were calculated. The Shapiro-Wilk test was used to check whether the continuous variables were normally distributed.

There were no differences between the patient and control groups regardless of age and gender. Independent sample t-test and chi-square comparison tests were used. The independent sample t-test was used to determine whether CRP, NLR, and MPV values showed significant differences between patients and controls.

Analysis was performed to determine whether there was a significant relationship between CRP, NLR, and MPV values and NIHSS values based on the patients' data. Pearson correlation coefficients were calculated. The corresponding numbers and percentage values were also calculated.

IBM SPSS Statistics 21.0 (IBM Corp., Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used for statistical analyses. G*Power 3.1 software was used for sample size calculation.

Results were considered statistically significant for $p < 0.05$.

RESULTS

The mean age of the individuals in the control group was calculated as 72.41 ± 8.47 , and the mean age of the individuals in the patient group was 71.60 ± 12.53 . No statistically significant difference was found in age values between the patient and control groups (Table 1).

61.3% of the individuals in the control group are female and 38.7% are male. In the patient group, 64.2% of the individuals are female and 35.8% are male. No difference was detected between the patient and control groups in terms of gender (Table 1).

Table 1. Patient and control group demographic information

Demographic information	Control n (%) mean \pm SD	Patient n (%) mean \pm SD	p
Age	72.41 \pm 8.47	71.60 \pm 12.53	0.425
Gender			
Women	92 (61.3)	102(64.2)	0.256
Men	58 (38.7)	57 (35.8)	

SD: Standard deviation

The mean CRP value of individuals in the control group was 6.19 ± 6.48 , and the mean CRP value of individuals in the patient group was 16.79 ± 18.14 . Patient individuals have higher CRP values. CRP values show statistically significant differences between patient and control groups ($p < 0.001$) (Table 2).

Table 2. Comparison of variables based on patient and control groups

Variables	Control mean \pm SD	Patient mean \pm SD	p
CRP	6.19 \pm 6.48	16.79 \pm 18.14	<0.001
NLR	2.50 \pm 1.18	5.74 \pm 5.40	<0.001
MPV	8.15 \pm 0.84	8.57 \pm 1.40	0.002

SD: Standard deviation, CRP: C-reactive protein, NLR: Neutrophil-to-lymphocyte ratio, MPV: Mean platelet volume

The mean NLR value of individuals in the control group was determined as 2.50 ± 1.18 , and the mean NLR value of individuals in the patient group was determined as 5.74 ± 5.40 .

NLR values of patient individuals are higher. NLR values show statistically significant differences between patient and control groups ($p < 0.001$) (Table 2).

The mean MPV value of individuals in the control group was 8.15 ± 0.84 , and the mean MPV value of individuals in the patient group was 8.57 ± 1.40 . MPV values of patient individuals are higher. MPV values show statistically significant differences between patient and control groups ($p = 0.002$) (Table 2).

A strong, positive, linear and statistically significant relationship was found between the CRP-NIHSS values of the patients included in the study ($p < 0.001$). As CRP value increase, NIHSS values increase (Table 3, Figure 1).

Table 3. Correlation analysis between variables and NIHSS values in patient individuals (n=159)

Variables	Group: patient	Test statistics
	Correlation coefficient	p
CRP-NIHSS	0.722	<0.001
NLR-NIHSS	0.263	0.001
MPV-NIHSS	0.625	<0.001

CRP: C-reactive protein, NIHSS: National Institutes of Health Stroke Scale, NLR: Neutrophil-to-lymphocyte ratio, MPV: Mean platelet volume

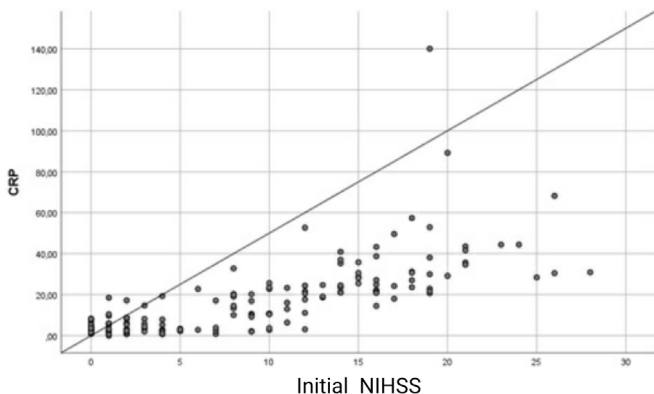


Figure 1. Relationship distribution between C-reactive protein-National Institutes of Health Stroke Scale

A weak, positive, linear and statistically significant relationship was found between the NLR-NIHSS values of the patients included in the study ($p = 0.001$). As NLR value increase, NIHSS values increase (Table 3, Figure 3).

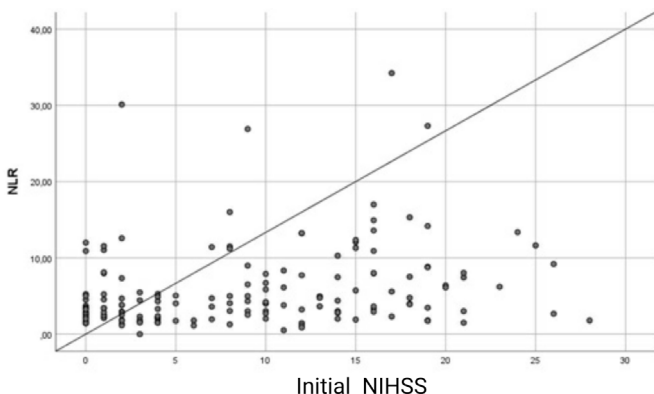


Figure 2. Relationship distribution between neutrophil-to-lymphocyte ratio-National Institutes of Health Stroke Scale

A medium-strength, positive, linear and statistically significant relationship was found between the MPV-NIHSS values of the patients included in the study ($p < 0.001$). As the MPV value increase, NIHSS values increase (Table 3, Figure 2).

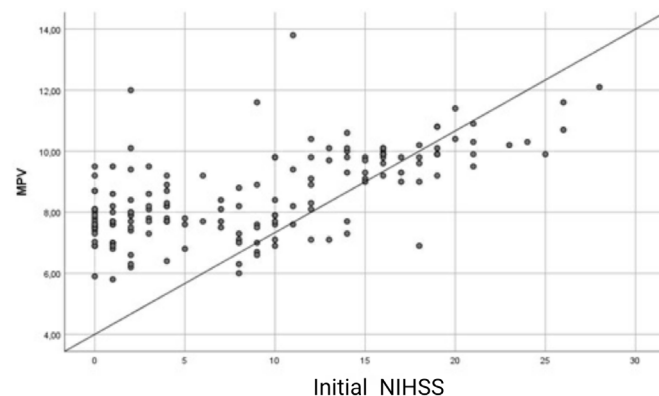


Figure 3. Relationship distribution between mean platelet volume-National Institutes of Health Stroke Scale

We examined the patient and control groups in terms of additional diseases. No significant difference was found between the two groups in terms of the presence of DM, HT, CAD and AF (Table 4).

Table 4. Distribution of additional diseases

Additional diseases	Control n (%)	Patient n (%)	p
HT	50 (31.25)	59 (37.11)	0.75
DM	40 (25)	44 (27.68)	0.155
CAD	45 (28.125)	51(32.08)	0.96
AF	20 (12.5)	26 (16.35)	0.125

HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, AF: Atrial fibrillation

There were no statistically significant differences in CRP, MPV, and NLR parameters based on whether individuals had hypertension or not (Table 5).

Table 5. Comparison of CRP, MPV, and NLR based on hypertension

Variables	Additional medical conditions		Test statistics	
	HT (-) mean±SD	HT (+) mean±SD	t	p
CRP	18.76±32.23	14.21±34.46	0.806	0.421
MPV	7.82±1.13	8.04±1.15	1.122	0.264
NLR	5.48±5.34	5.83±5.44	0.393	0.695

CRP: C-reactive protein, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, HT: Hypertension, SD: Standard deviation

There were no statistically significant differences in CRP, MPV, and NLR parameters based on whether individuals had diabetes mellitus or not (Table 6).

Table 6. Comparison of CRP, MPV, and NLR based on DM

Variables	Additional medical conditions		Test statistics	
	DM (-) mean±SD	DM (+) mean±SD	t	p
CRP	17.02±37.08	13.42±26.47	0.644	0.521
MPV	7.90±1.12	8.10±1.19	1.058	0.292
NLR	6.03±5.34	5.12±5.49	1.013	0.313

CRP: C-reactive protein, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, DM: Diabetes mellitus, SD: Standard deviation

There were no statistically significant differences in CRP, MPV, and NLR parameters based on whether individuals had CAD or not (Table 7).

Variables	Additional medical conditions		Test statistics	
	CAD (-) mean±SD	CAD (+) mean±SD	t	p
CRP	17.34±38.65	13.79±25.26	0.642	0.522
MPV	7.94±1.15	8.03±1.15	0.460	0.646
NLR	5.72±5.49	5.84±5.31	0.129	0.897

CRP: C-reactive protein, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, CAD: Coronary artery disease, SD: Standard deviation

CRP, MPV, and NLR parameters did not show statistically significant differences based on whether individuals had AF or not (Table 8).

Variables	Additional medical conditions		Test statistics	
	AF (-) mean±SD	AF (+) mean±SD	t	p
CRP	14.77±27.89	19.11 ± 48.22	0.689	0.492
MPV	7.91±1.15	8.16 ± 1.14	1.175	0.242
NLR	5.26±4.90	6.35 ± 6.54	1.511	0.186

CRP: C-reactive protein, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, AF: Atrial fibrillation, SD: Standard deviation

When analyzed according to TOAST classification, the mean CRP level was 14.14±24.29 in the extensive arterial atherosclerosis group, 10.20±15.68 in the cardioembolism group, 27.76 ± 56.07 in the small vessel occlusion group, 13.90±31.05 in the ischemic stroke due to other identified causes group, and 3.60±1.45 in the ischemic stroke of unknown cause group. No statistically significant difference was observed in CRP levels across TOAST subtypes (p=0.236) (Table 9).

Similarly, the mean MPV values were 7.87±1.08 in the extensive arterial atherosclerosis group, 8.01±1.03 in the cardioembolism group, 8.15±1.34 in the small vessel occlusion group, 8.00±1.19 in the ischemic stroke due to other identified causes group, and 7.38±0.84 in the ischemic stroke of unknown cause group. MPV levels did not differ significantly among TOAST subtypes (p=0.636) (Table 9).

The mean NLR values were 5.81±5.26 in the extensive arterial atherosclerosis group, 5.05±4.16 in the cardioembolism group, 6.52±6.50 in the small vessel occlusion group, 5.50±5.60 in the ischemic stroke due to other identified causes group, and 5.06±4.07 in the ischemic stroke of unknown cause group. No

statistically significant differences were detected in NLR levels across TOAST etiological categories (p=0.874) (Table 9).

DISCUSSION

Although the relationship between ischemic stroke and acute-phase reactants (APR) has been reported in previous publications, some studies suggest that APR levels may be normal in stroke patients and may not be determinants of prognosis.¹⁴ CRP, as an APR, may reflect inflammation associated with the etiopathogenesis of ischemic stroke and is a plasma marker for atherothrombotic diseases. CRP most likely recognizes phospholipid components of damaged cells and foreign pathogens and affects the inflammatory process by binding to phosphocholine.¹⁵ CRP may contribute to pathogenesis and a procoagulant state. High CRP levels have been associated with a two-fold increase in AIS in men, a five-fold increase in any vascular event in women, and a seven-fold increase in myocardial infarction or stroke.¹⁶

In the study conducted by Beamer et al.,¹⁷ CRP levels were found to increase in the early period in patients with ischemic stroke. In the study of 151 patients conducted by Montaner et al.,¹⁸ the relationship between CRP levels and mortality in stroke patients treated with tissue plasminogen activator (TPA) was evaluated, and mortality was found to be higher in patients with elevated CRP levels. In the same study, no correlation was found between stroke severity and CRP. In the study conducted by Muir et al.,¹⁹ including 283 patients, CRP levels were found to be higher in patients with ischemic stroke and in those with higher NIHSS values, indicating a relationship between stroke severity and CRP. Similarly, Di Napoli et al.²⁰ demonstrated that CRP levels were elevated in ischemic stroke patients and were positively associated with stroke severity.

In our study, which included 319 individuals, CRP levels were significantly higher in ischemic stroke patients compared with the control group. A positive correlation was observed between admission NIHSS scores and CRP levels, indicating an association between stroke severity and CRP. Based on existing literature and our findings, CRP appears to be an important biochemical marker in ischemic stroke. However, further comprehensive studies are needed.

In recent years, neuroinflammation has attracted increasing attention, and numerous studies have confirmed that inflammatory mechanisms play crucial roles in the pathogenesis and progression of ischemic stroke.²¹ Peripheral leukocytes are recruited by inflammatory cytokines and chemokines released from ischemic tissue. Conversely,

Variables	Toast classification					Test statistics	
	Extensive arterial atherosclerosis (n=52) mean±SD	Cardioembolism (n=26) mean±SD	Small vessel occlusion (n=31) mean±SD	Ischemic stroke due to other identified causes (n=45) mean±SD	Ischemic stroke of unknown cause (n=5) mean±SD	F	p
CRP	14.14±24.29	10.20±15.68	27.76±56.07	13.90±31.05	3.60±1.45	1.401	0.236
MPV	7.87±1.08	8.01±1.03	8.15±1.34	8.00±1.19	7.38±0.84	0.638	0.636
NLR	5.81±5.26	5.05±4.16	6.52±6.50	5.50±5.60	5.06±4.07	0.306	0.874

One-way ANOVA, CRP: C-reactive protein, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, SD: Standard deviation

peripheral leukocytes may also influence ischemic tissue. Lymphocyte counts have been suggested to exert neuroprotective effects and contribute to neurological recovery.²² Peripheral monocytes and neutrophils may serve as sources of matrix metalloproteinase-9, contributing to hemorrhagic transformation and symptomatic deterioration.^{23,24} Neutrophils may also induce free oxygen radicals, leading to brain injury.²⁵ Furthermore, AIS may result in platelet dysfunction, and excessive platelet activation and aggregation may impair stroke recovery.²⁶

Goyal et al.²⁷ reported that admission NLR may serve as a prognostic biomarker in patients with large vessel occlusion stroke. In a study by Gong et al.²⁸ including 1,060 patients, NLR was found to be higher in patients with early neurological deterioration, and a positive relationship was observed between stroke severity and NLR. Similarly, Zhu et al.²⁹ reported that NLR was elevated in patients with higher NIHSS scores and was positively associated with stroke severity. In our study, NLR levels were significantly higher in ischemic stroke patients, and a positive correlation was found between NLR and NIHSS scores.

In a study conducted by Bath et al.³⁰ involving 3,134 patients with cerebrovascular disease, MPV was identified as an independent determinant of stroke risk. Sadeghi et al.³¹ reported higher MPV levels in ischemic stroke patients, and Sarkar et al.³² demonstrated that platelet indices could predict stroke severity. A meta-analysis by Zheng et al.³³ showed that elevated MPV was associated with unfavorable clinical outcomes in ischemic stroke. Ludhiadch et al.³⁴ also reported increased MPV levels in ischemic stroke patients and suggested its potential use as a biomarker.

Inflammation plays a central role in ischemic stroke pathophysiology beyond the initial vascular occlusion. Increasing evidence characterizes AIS as a thromboinflammatory syndrome rather than a purely hemodynamic event.³⁵⁻³⁷ Following arterial occlusion, damage-associated molecular patterns (DAMPs) released from ischemic tissue activate microglia and endothelial cells, triggering proinflammatory cytokine release (IL-6, TNF- α , IL-1 β), leukocyte recruitment, endothelial dysfunction, blood-brain barrier disruption, and secondary neuronal injury.^{36,37}

CRP should therefore be regarded not only as an acute-phase marker but also as a mediator of vascular inflammation. It contributes to complement activation and procoagulant signaling,^{38,39} and elevated levels have been associated with infarct volume and unfavorable outcomes.⁴⁰ The strong correlation between CRP and NIHSS in our study likely reflects the magnitude of systemic thromboinflammatory activation accompanying more extensive cerebral injury.

NLR integrates innate immune activation and relative adaptive immune suppression. Neutrophils exacerbate ischemic damage through reactive oxygen species and neutrophil extracellular traps (NETs), key mediators of immunothrombosis linking inflammation to thrombus formation.^{41,42} Conversely, post-stroke lymphopenia has been associated with worse outcomes.⁴³ Recent meta-analyses confirm that elevated admission NLR independently predicts

stroke severity,⁴⁴ supporting the biological plausibility of our findings.

Platelets are active mediators of immune-thrombotic crosstalk. Mean platelet volume (MPV) reflects platelet reactivity; larger platelets exhibit enhanced prothrombotic potential and adhesion molecule expression.⁴⁵ Platelet-leukocyte interactions amplify thromboinflammatory responses,^{44,46} and elevated MPV has been linked to greater stroke severity and poorer outcomes.^{34,47} The moderate-to-strong association between MPV and NIHSS in our cohort aligns with this concept.

In this prospective case-control study, we demonstrated that serum CRP, NLR, and MPV levels were significantly higher in patients with AIS compared with healthy controls. All three biomarkers showed positive correlations with stroke severity as assessed by the NIHSS at admission. CRP and MPV exhibited strong correlations, whereas NLR showed a weaker but statistically significant association.

Importantly, the associations between CRP, NLR, and MPV and stroke severity were independent of common vascular comorbidities such as hypertension, diabetes mellitus, coronary artery disease, and atrial fibrillation. Furthermore, no statistically significant differences were detected across TOAST etiological subtypes. These findings suggest that systemic inflammatory and platelet activation responses may represent a shared downstream pathway in AIS, regardless of stroke etiology.

Several methodological strengths reinforce the validity of our findings. The prospective design enhances data reliability and reduces potential bias. The inclusion of a well-matched healthy control group enabled direct comparison of inflammatory biomarker levels. Stroke severity was assessed using the NIHSS, an internationally validated and objective neurological scoring system. Additionally, the total sample size (n=319) provides reasonable statistical power to detect clinically meaningful associations. The performance of TOAST-based subtype analyses further increases the comprehensiveness of the study.

Limitations

Nevertheless, several limitations should be acknowledged. The study was conducted in a single center with a relatively modest sample size. Biomarkers were measured only at admission, precluding evaluation of dynamic temporal changes. Longitudinal measurements and multicenter validation studies are needed to confirm the prognostic value of these parameters and to determine whether modulation of thromboinflammatory pathways translates into improved clinical outcomes.

In conclusion, our findings support the hypothesis that CRP, NLR, and MPV are significantly associated with stroke severity in acute ischemic stroke. These biomarkers likely reflect underlying immune activation and immunothrombotic mechanisms contributing to neurological deficit. Future large-scale, prospective studies are warranted to further clarify their mechanistic role and therapeutic implications in AIS.

CONCLUSION

Ischemic stroke can occur suddenly and may cause physical disability or even death. There is a need for reliable biomarkers to predict ischemic stroke and determine its severity, thereby potentially reducing disability associated with the disease. For this purpose, we examined the relationship between CRP, NLR, and MPV levels and stroke and found positive associations.

The limitations of our study include the relatively small sample size and the lack of serial measurements of biomarkers at regular intervals. We also demonstrated a relationship between CRP, NLR, and MPV levels and stroke severity. Therefore, we suggest that CRP, NLR, and MPV may be useful in predicting ischemic stroke and assessing its severity. However, randomized, double-blind, placebo-controlled clinical trials on this topic are still lacking and are needed to further clarify their predictive value in ischemic stroke and stroke severity.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Scientific and Evaluation Ethics Committee for Medical Researches at Ankara Bilkent City Hospital (Date: 05.11.2025, Decision No: TABED 1/1835/2025).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights-including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Conceptualization: EV, SB; Study Design: EV, SB, SAM; Supervision: EV, SB, HB; Data Collection and/or Processing: EV, SAM; Data Analysis and/or Interpretation: EV, SB, SAM, HB; Literature Review: EV, SB; Manuscript Writing: EV, SB; Critical Review: All Authors.

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