

Diagnostic and Potentially Prognostic Value of Novel Inflammatory Indices in Non-Arteritic Anterior Ischemic Optic Neuropathy

Sensoy Eyupcan, Uke Uzun Saniye, Inac Kivanc

University of Health Sciences, Ankara Etlik City Hospital, Department of Ophthalmology, Ankara, Turkey



Eyupcan Sensoy, MD, FEBO

Submitted to the editorial board: November 21, 2025

Accepted for publication: January 10, 2026

Available on-line: February 20, 2026

The author(s) reported that there is no funding associated with the work featured in this article. The work is original, has not been published elsewhere, and is not under consideration by any other journal.

Committee Approval: AEŞH-BADEK1-2025-475, Ankara Etlik City Hospital
Diagnostic and Potentially Prognostic Value of Novel Inflammatory Indices in Non-Arteritic Anterior Ischemic Optic Neuropathy

Correspondence address:
Department of Ophthalmology - University of Health Sciences
Ankara Etlik City Hospital, General Hospital T1 Building
Varlık Mahallesi, Halil Sezai Erkut Caddesi
06170 Yenimahalle
Ankara
Turkey
E-mail: dreyupcansensoy@yahoo.com

SUMMARY

Aim: The aim of this study was to investigate the potential contribution of systemic inflammation to the pathogenesis of non-arteritic anterior ischemic optic neuropathy (NAION), to evaluate the diagnostic and potentially prognostic value of relatively novel inflammatory indices, and to assess their associations with visual function and structural optic nerve findings at presentation.

Materials and Methods: The medical records of 26 patients diagnosed with NAION and 28 age-, sex-, and comorbidity-matched controls were retrospectively reviewed. From complete blood count results obtained at diagnosis, platelet, neutrophil, lymphocyte, monocyte, and immature granulocyte counts were recorded, and the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), pan-immune inflammation value (PIV), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI) were calculated. Baseline best-corrected visual acuity (BCVA), retinal nerve fiber layer (RNFL) thicknesses, and visual field parameters were also evaluated.

Results: In the NAION group, platelet and neutrophil counts, as well as NLR, PLR, PIV, SII, and SIRI values, were significantly higher than in controls ($p < 0.05$). ROC analysis revealed that PIV (AUC = 0.830) and SII (AUC = 0.812) demonstrated the highest discriminatory power. PIV, SII, SIRI, and NLR showed significant negative correlations with mean, superior, and nasal RNFL thickness ($p < 0.05$), whereas PLR did not correlate ($p > 0.05$).

Conclusion: Elevated inflammatory markers, including NLR, PLR, PIV, SII, and SIRI, indicate the potential role of systemic inflammation in NAION pathogenesis. PIV and SII, in particular, demonstrated strong predictive potential for diagnosis and were associated with baseline optic nerve damage.

Key words: inflammatory indices; non-arteritic anterior ischemic optic neuropathy; pan-immune inflammation value; retinal nerve fiber layer; systemic immune-inflammation index

Čes. a slov. Oftal., 82, 2026, No. x, p.

INTRODUCTION

Non-arteritic anterior ischemic optic neuropathy (NAION) is one of the leading causes of sudden, painless, unilateral vision loss in middle-aged and older individuals. It typically presents with optic disc edema and peripapillary hemorrhages. The annual incidence is estimated at approximately 2 to 10 cases per 100,000 population, and its pathogenesis remains incompletely understood [1]. Current evidence suggests that hypoperfusion at the optic nerve head initiates a cascade of ischemia and edema, ultimately leading to progressive retinal nerve fiber

layer (RNFL) loss. A small, crowded optic disc configuration is recognized as an important local risk factor, while systemic conditions such as diabetes mellitus, hypertension, and cardiovascular disease also play significant roles in disease development [1–3]. This multifactorial profile supports the notion that NAION may involve not only vascular compromise, but also inflammatory mechanisms in its pathophysiology [4–7].

In recent years, hematological markers derived from complete blood count data and the inflammatory parameters calculated from them have emerged as simple, rapid, and low-cost indicators of systemic inflammation

and have become a frequently investigated topic in many ocular and systemic diseases. Among these, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), pan-immune inflammation value (PIV), systemic immune-inflammation index (SII), and systemic inflammatory response index (SIRI) are the most commonly studied parameters [4–13]. In the literature, these markers have generally been evaluated separately in NAION patients. Nevertheless, comprehensive studies investigating all these parameters together in the same patient group and examining their relationship with clinical presentation findings (visual acuity, RNFL thickness, visual field loss) are very limited.

The aim of this study is to determine the diagnostic and potentially prognostic value of basic hematological parameters and derived inflammatory indices such as NLR, PLR, MLR, PIV, SII, and SIRI in patients with NAION, and to comprehensively evaluate their associations with initial visual functions and structural optic nerve measurements.

MATERIAL AND METHODS

This study retrospectively reviewed patients diagnosed with NAION who were referred to the Neuro-Ophthalmology unit of a tertiary eye clinic between January 2024 and May 2025. The research was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Local Ethics Committee of Ankara Etilik City Hospital (AEŞH-BADEK1-2025-475).

Participant Selection and Diagnostic Criteria

The diagnosis of NAION was established based on the presence of symptoms consistent with the disease, such as sudden-onset visual loss, together with optic disc edema and/or peripapillary hemorrhage observed on fundus examination, localized or diffuse swelling of the RNFL, and visual field defects characteristic of the condition. Fundus fluorescein angiography was performed when required for differential diagnosis. The control group included individuals matched for age, sex, and systemic disease profile, all of whom had normal ophthalmological findings without additional ocular pathology. Hematological parameters for the control subjects were derived from routine preoperative evaluations or health check-up, with complete blood counts obtained within one week prior to the ophthalmic examination. The study included measurements from 26 patients with NAION (affected eyes) and 28 control subjects (right eyes) who fulfilled these criteria.

Clinical and Visual Function Assessment

Detailed medical history, comorbid systemic conditions, and demographic data, such as age and sex, were retrieved from patient records. Best-corrected visual acuity (BCVA), intraocular pressure, and results of comprehensive anterior and posterior segment examinations

were documented. RNFL thickness measurements were obtained, using optical coherence tomography (OCT; Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA). Average RNFL values and quadrant-specific measurements (temporal, nasal, superior, and inferior) were recorded. Visual field testing was performed with the Humphrey Field Analyzer 30-2 (Carl Zeiss Meditec, Dublin, CA, USA), using the Swedish Interactive Threshold Algorithm (SITA) FAST 30-2 protocol. For a test to be considered reliable, fixation losses had to be below 20% and false-positive and false-negative responses below 33%. Mean deviation (MD) and pattern standard deviation (PSD) values from reliable tests were included in the analysis. Snellen visual acuities were converted into LogMAR format for statistical evaluation.

Laboratory Evaluation

At presentation, fasting venous blood samples were collected from the antecubital vein for complete blood count analysis. Hematological parameters, including platelet, neutrophil, lymphocyte, monocyte, and immature granulocyte counts, were recorded. Based on these values, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), pan-immune-inflammation value (PIV: monocytes \times platelets \times neutrophils / lymphocytes), systemic immune-inflammation index (SII: platelets \times neutrophils / lymphocytes), and systemic inflammation response index (SIRI: monocytes \times neutrophils / lymphocytes) were calculated and documented.

Exclusion Criteria

Patients were excluded if their medical records showed missing data, if RNFL scan quality was below 7/10, if imaging artifacts, such as segmentation errors or motion artifacts, were detected, if visual field tests did not meet reliability criteria, if spherical equivalent exceeded ± 2 diopters, or if optic nerve pathologies, such as tilted disc or optic disc drusen, were present.

Statistical Analysis

All data were analyzed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was administered to assess the normality of distribution for continuous variables. Results were presented as mean \pm standard deviation, median, and minimum-maximum values. Between-group comparisons were performed, using an independent samples t-test for normally distributed variables and a Mann-Whitney U test for non-normally distributed variables. Categorical variables were analyzed with Yates' chi-square test. Correlations between clinical and laboratory parameters were examined using Spearman's correlation analysis. The diagnostic performance of inflammatory indices was evaluated by receiver operating characteristic (ROC) curve analysis, reporting the area under the curve (AUC), cut-off values, sensitivity, and specificity. A p-value < 0.05 was considered statistically significant.

A post-hoc power analysis was conducted, based on the differences in PIV and SII between the NAION and control groups. The achieved power ($1-\beta$) was 0.98 for PIV (Cohen's $d = 1.12$) and 0.77 for SII (Cohen's $d = 0.75$) at a significance level of 0.05, indicating adequate statistical power for the primary outcomes, despite the limited sample size.

RESULTS

A total of 26 patients diagnosed with NAION (22 males, 4 females) and 28 control subjects (19 males, 9 females) were included in the study. The mean age was 60.23 ± 11.49 years in the NAION group and 59.71 ± 6.89 years in the control group, with no significant difference between them ($p = 0.84$). Similarly, no significant differences were observed between groups regarding sex distribution or the presence of systemic comorbidities ($p > 0.05$) (Table 1).

The mean platelet count was significantly higher in the NAION group compared to controls (282.58 ± 60.09 vs. $230.89 \pm 53.35 \times 10^3/\mu\text{L}$; $p = 0.002$). The median neutrophil count was also significantly elevated in the NAION group [5.37 ($3.55-22.84$) $\times 10^3/\mu\text{L}$ vs. 4.79 ($2.14-7.50$) $\times 10^3/\mu\text{L}$; $p = 0.034$]. Inflammatory indices including NLR [2.61 ($1.30-11.80$) vs. 2.07 ($1.14-3.20$); $p = 0.033$], PLR [116.03 ($66.67-826.67$) vs. 93.12 ($47.22-233.83$); $p = 0.013$], PIV [457.25 ($236.35-1614.03$) vs. 276.30 ($141.61-497.36$); $p < 0.001$], SII [655.05 ($317.53-4389.60$) vs. 453.79

($279.55-668.62$); $p < 0.001$], and SIRI [1.50 ($0.93-5.98$) vs. 1.22 ($0.47-2.00$); $p = 0.004$] were all significantly higher in the NAION group compared to controls. No significant differences were found in lymphocyte, monocyte, or immature granulocyte counts between groups (all $p > 0.05$) (Table 2).

ROC curve analysis demonstrated that PIV (AUC = 0.830, $p < 0.001$) and SII (AUC = 0.812, $p < 0.001$) had the highest diagnostic accuracy in distinguishing NAION from controls. For PIV, a cut-off value of 332.52 yielded 77% sensitivity and 75% specificity, while for SII, a cut-off of 525.19 provided 77% sensitivity and 71% specificity. Although SIRI (AUC = 0.728, $p = 0.004$), PLR (AUC = 0.698, $p = 0.013$), and NLR (AUC = 0.669, $p = 0.033$) also demonstrated significant discriminative ability, their AUC values were lower compared to PIV and SII (Table 3 and Graph 1).

In the NAION group, the mean baseline BCVA was 1.25 ± 1.00 logMAR. The mean RNFL thickness was $214.62 \pm 106.42 \mu\text{m}$, with quadrant-specific measurements of $145.35 \pm 87.80 \mu\text{m}$ (temporal), $253.92 \pm 138.49 \mu\text{m}$ (superior), $183.00 \pm 104.63 \mu\text{m}$ (nasal), and $276.57 \pm 159.84 \mu\text{m}$ (inferior). Visual field testing revealed a mean MD of -18.86 ± 9.62 dB and a mean PSD of 8.49 ± 4.46 dB. Spearman's correlation analysis showed that PIV, SII, SIRI, and NLR were significantly negatively correlated with average, superior, and nasal RNFL thickness ($p < 0.05$). No significant correlation was found between PLR and RNFL measurements ($p > 0.05$) (Table 4). No statistically significant correlation was found between MD and PSD values and inflammatory indices ($p > 0.05$).

Table 1. Demographic and Systemic Characteristics of Patients with Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) and Controls

Parameters	NAION (n:26)	Control Group (n:28)	P* value
Age (years)	60.23 ± 11.49 Median: 59 Min-max: 45–90	59.71 ± 6.89 Median: 59 Min-max: 47–76	0.84 ^T
Gender			0.26 ^Y
Female	4 (15.4%)	9 (32.1%)	
Male	22 (84.6%)	19 (67.9%)	
Additional Systemic Disease			
Diabetes Mellitus			1.00 ^Y
Yes	12 (46.2%)	12 (42.9%)	
No	14 (53.8%)	16 (57.1%)	
Hypertension			0.58 ^Y
Yes	15 (57.7%)	13 (46.4%)	
No	11 (42.3%)	15 (53.6%)	
Cardiovascular Disease			0.44 ^Y
Yes	5 (19.2%)	9 (32.1%)	
No	21 (80.8%)	19 (67.9%)	

M – Mann-Whitney U test, T – Independent Samples t Test, Y – Yates chi square test

Table 2. Hematological and Inflammatory Parameters in NAION and Control Groups

Parameters	NAION (n:26)	Control Group (n:28)	P* value
Platelet (10 ³ /μL)	282.58 ±60.09 Median: 276 Min-max: 172–449	230.89 ±53.35 Median: 231 Min-max: 141–353	0.002^T
Neutrophil (10 ³ /μL)	6.26 ±3.68 Median: 5.37 Min-max: 3.55–22.84	4.85 ±1.33 Median: 4.79 Min-max: 2.14–7.50	0.034^M
Lymphocyte (10 ³ /μL)	2.38 ±0.91 Median: 2.58 Min-max: 0.45–4.05	2.48 ±0.95 Median: 2.28 Min-max: 1.32–5.57	0.965 ^M
Monocyte (10 ³ /μL)	0.68 ±0.21 Median: 0.66 Min-max: 0.11–1.12	0.62 ±0.14 Median: 0.60 Min-max: 0.29–0.92	0.186 ^T
Immature granulocyte (10 ³ /μL)	0.11 ±0.36 Median: 0.03 Min-max: 0.01–1.86	0.03 ±0.01 Median: 0.03 Min-max: 0.01–0.07	0.476 ^M
NLR	3.07 ±2.14 Median: 2.61 Min-max: 1.30–11.80	2.07 ±0.57 Median: 2.07 Min-max: 1.14–3.20	0.033^M
PLR	152.34 ±143.68 Median: 116.03 Min-max: 66.67–826.67	101.60 ±36.85 Median: 93.12 Min-max: 47.22–233.83	0.013^M
MLR	0.31 ±0.11 Median: 0.27 Min-max: 0.19–0.66	0.27 ±0.07 Median: 0.25 Min-max: 0.17–0.41	0.156 ^M
PIV	521.39 ±287.47 Median: 457.25 Min-max: 236.35–1614.03	283.21 ±89.24 Median: 276.30 Min-max: 141.61–497.36	0.000^M
SII	881.37 ±780.46 Median: 655.05 Min-max: 317.53–4389.60	465.00 ±122.78 Median: 453.79 Min-max: 279.55–668.62	0.000^M
SIRI	1.88 ±1.05 Median: 1.50 Min-max: 0.93–5.98	1.26 ±0.37 Median: 1.22 Min-max: 0.47–2.00	0.004^M

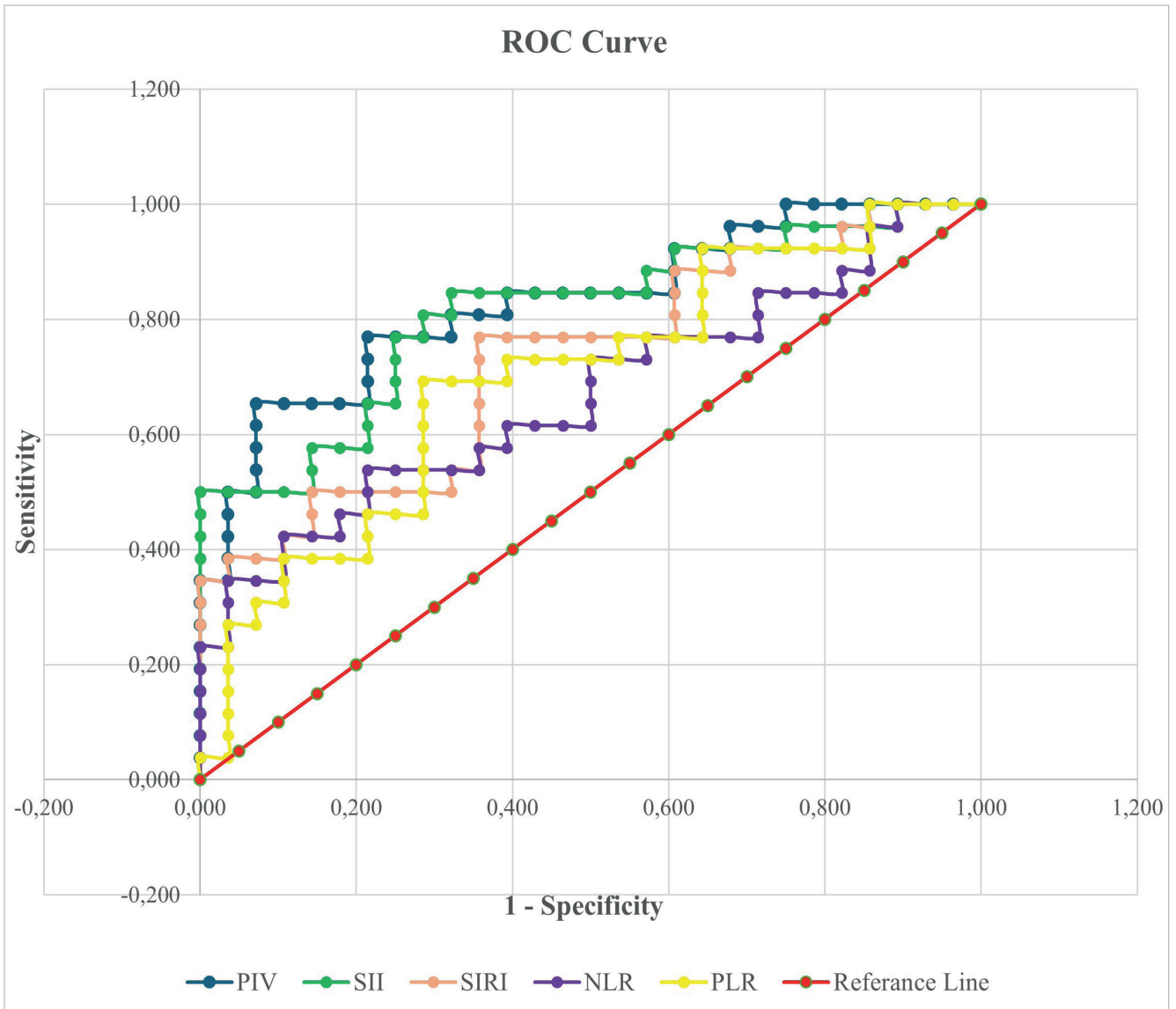
NAION – Non-Arteritic Anterior Ischemic Optic Neuropathy, NLR – Neutrophil-to-lymphocyte ratio, MLR – Monocyte-to-lymphocyte ratio, MPV – Mean Platelet Volume, PDW – Platelet Distribution Width, PLR – Platelet-to-lymphocyte ratio, PIV – Pan-immune Inflammation Value, RDWSD – Red Cell Distribution Width – Standard Deviation, SII – Systemic immune-inflammation index, SIRI – Systemic inflammatory response index

M – Mann-Whitney U test, T – Independent samples t test

Table 3. Diagnostic performance of inflammatory markers in patients with NAION based on ROC curve analysis

Parameters	AUC (95%)	P value	Cutt off	Sensitivity (%)	Specificity (%)
PIV	0.830 (0.720–0.939)	0.000	332.52	77.0	75.0
SII	0.812 (0.696–0.928)	0.000	525.19	77.0	71.0
SIRI	0.728 (0.593–0.863)	0.004	1.29	77.0	64.0
PLR	0.698 (0.557–0.839)	0.013	103.42	69.2	71.0
NLR	0.669 (0.523–0.815)	0.033	2.16	62.0	61.0

NAION – Non-Arteritic Anterior Ischemic Optic Neuropathy, AUC – Area under the ROC curve, NLR – Neutrophil-to-lymphocyte ratio, PLR – Platelet-to-lymphocyte ratio, PIV – Pan-immune Inflammation Value, SII – Systemic immune-inflammation index, SIRI – Systemic inflammatory response index



Graph 1. ROC curves of inflammatory markers (PIV, SII, SIRI, NLR, and PLR) in predicting non-arteritic anterior ischemic optic neuropathy
PIV – pan-immune-inflammation value, SII – systemic immune-inflammation index, SIRI – systemic inflammation response index, NLR – neutrophil-to-lymphocyte ratio, PLR – platelet-to-lymphocyte ratio

Table 4. Correlation Between Inflammatory Indices and Retinal Nerve Fiber Layer Thickness in NAION

Parameters	Retinal Nerve Fiber Layer Thickness (µm)				
	Average	Temporal	Superior	Nasal	Inferior
PIV	ρ : -0.56 P: 0.003	ρ : -0.36 P: 0.07	ρ : -0.65 P < 0.001	ρ : -0.52 P: 0.007	ρ : -0.43 P: 0.030
SII	ρ : -0.46 P: 0.017	ρ : -0.20 P: 0.32	ρ : -0.46 P: 0.019	ρ : -0.42 P: 0.03	ρ : -0.38 P: 0.05
SIRI	ρ : -0.61 P: 0.001	ρ : -0.48 P: 0.013	ρ : -0.66 P < 0.001	ρ : -0.55 P: 0.003	ρ : -0.41 P: 0.040
NLR	ρ : -0.48 P: 0.013	ρ : -0.32 P: 0.11	ρ : -0.46 P: 0.017	ρ : -0.41 P: 0.036	ρ : -0.37 P: 0.06
PLR	ρ : -0.16 P: 0.45	ρ : 0.03 P: 0.89	ρ : -0.07 P: 0.73	ρ : -0.09 P: 0.68	ρ : -0.27 P: 0.18

NAION – Non-Arteritic Anterior Ischemic Optic Neuropathy, ρ – Correlation coefficient (Spearman's correlation test), P – Significance level, NLR – Neutrophil-to-lymphocyte ratio, PLR – Platelet-to-lymphocyte ratio, PIV – Pan-immune Inflammation Value, SII – Systemic immune-inflammation index, SIRI – Systemic inflammatory response index

DISCUSSION

The pathogenesis of NAION remains incompletely understood. In recent years, the potential contribution of inflammation to its multifactorial pathophysiology has been increasingly investigated, and the predictive value of inflammatory markers has become a major focus of interest. In our study, the levels of inflammatory indices, including PIV, SII, SIRI, NLR, and PLR were found to be significantly higher in patients with NAION, compared to controls with a similar systemic comorbidity burden, with PIV and SII demonstrating particularly strong discriminatory power for diagnosis. Moreover, PIV, SII, SIRI, and NLR showed significant negative correlations with average RNFL thickness and certain quadrant measurements, suggesting that these inflammatory indices may be associated not only with diagnosis, but also with structural nerve fiber damage. In contrast, although PLR was diagnostically significant, it showed no relationship with RNFL parameters. These findings indicate that systemic inflammation may represent an important component in the pathogenesis of NAION, and that indices derived from peripheral blood parameters could provide predictive insight into both clinical diagnosis and the severity of initial presentation.

The most widely accepted hypothesis for the development of NAION is that insufficient perfusion of the optic nerve leads to ischemia, stasis, and optic disc edema. This, in turn, compresses the existing laminar structures of the optic nerve head, exacerbating ischemia and resulting in RNFL loss through a self-perpetuating cycle. Coexisting systemic diseases and inflammatory processes may further aggravate this pathology and facilitate the permanence of optic nerve damage [14–16]. Experimental animal studies have also demonstrated that various immunological mechanisms play a role in the pathogenesis of the disease and contribute to the development of neural injury [15,17]. Collectively, these findings support the notion that inflammatory markers may serve as important biomarkers in both the development and detection of the disease.

The role of inflammatory parameters in pathogenesis and their predictive properties have recently been investigated in a wide range of systemic and ocular diseases. Among these, NLR, PLR, and MLR are the most frequently studied indices, while the use of SII and SIRI has been steadily increasing. PIV, a relatively novel parameter, has been less extensively studied, but is considered a potential bio-inflammatory marker [4–13,18]. These indices have been examined not only in systemic diseases, such as systemic lupus erythematosus and Takayasu arteritis, but also in ocular pathologies including glaucoma, keratoconus, and retinal artery or vein occlusions, with research focusing on their potential roles in disease mechanisms [11,19–23]. With regard to NAION, previous studies have mostly focused on NLR, SII, PLR, and MLR. However, studies assessing all these parameters collectively and in relation to structural optic nerve findings remain limited

[4–7,16]. Our study aimed to address this gap in the literature by additionally evaluating SIRI and PIV – parameters investigated for the first time in cases of NAION, to our knowledge – and by examining their associations with ocular parameters.

Kocak et al. evaluated NLR, PLR, MLR, and SII parameters in patients with NAION and also compared neutrophil, monocyte, lymphocyte, and platelet counts with those of a control group. Although no significant differences were observed in hematological parameters, NLR and SII levels were reported to be markedly higher in the NAION group [6]. Similarly, Chen et al. assessed a broad range of hematological parameters, including SII, MLR, PLR, and NLR. They demonstrated that these values were significantly elevated in patients with NAION, compared to controls [5]. Uzakgider et al. [7] reported higher MPV, RDW, and NLR levels in NAION patients, while Polat et al. [4] found elevated leukocyte, platelet, monocyte, and NLR levels compared to controls. In addition to these findings in the literature, our study demonstrated that both SIRI and PIV were also significantly increased in NAION cases. Notably, PIV stood out diagnostically, with a high AUC value obtained from ROC analysis (0.830; 95% CI: 0.720–0.939; $p < 0.001$), highlighting its potential as a biomarker for the diagnosis of NAION.

Another distinction of our study from previous reports is the evaluation of the relationship between inflammatory indices and ocular findings at the time of diagnosis. In our analysis, we found that PIV, SII, SIRI, and NLR showed a negative correlation with average RNFL thickness, as well as superior and nasal quadrant values. We believe two possible mechanisms may explain this association. The first is that heightened inflammation and platelet activity impair microvascular perfusion at the optic nerve head, thereby aggravating ischemia and leading to axonal disruption even in the acute stage. In this scenario, an enhanced inflammatory response and platelet-mediated microthrombosis could restrict edema, resulting in lower RNFL thickness measurements. The second possibility is that inflammatory activity and platelet-derived mediators may limit vascular permeability, thereby suppressing the development of edema. Although RNFL thickness typically increases in the early phase of NAION due to edema, in patients with elevated inflammatory activity and platelet activation, restriction of edema may cause RNFL values to appear relatively lower. The observation of significantly increased platelet counts in NAION patients supports the biological plausibility of this correlation. However, whether reduced RNFL values at presentation reflect true axonal loss or merely decreased edema requires clarification through long-term follow-up studies.

Although inflammatory indices demonstrated statistically significant differences and acceptable diagnostic performance, their clinical relevance should be interpreted cautiously. These biomarkers are not intended to serve as standalone diagnostic tools or to replace established clinical examination and imaging findings in NAION. Specifically, the diagnostic specificity of these

markers is challenged by their elevation in other ocular and neurological pathologies. For instance, in retinal vein occlusion, markers such as NLR and SII are significantly elevated, particularly in patients with serous retinal detachment, where they serve as indicators of increased inflammatory burden [24]. Similarly, in neuroinflammatory conditions, such as optic neuritis, the NLR is significantly higher than in healthy controls and correlates with disease activity and acute relapses [25]. This suggests that, rather than being disease-specific, these indices may reflect a common systemic response to various ischemic and inflammatory triggers. Given their low cost, wide availability, and non-invasive nature, these parameters may have practical value as adjunctive tools, particularly in patients with atypical presentations, or in situations where the clinical diagnosis is uncertain. However, the nonspecific elevation of inflammatory markers in various ischemic conditions underscores the need for cautious interpretation and limits their use to a complementary role, rather than direct clinical decision-making.

Despite all these novel findings, our study also has some limitations. The limitations of the study include the small sample size, which reduces statistical power and reliability; the retrospective, single-center design; the evaluation of hematological and ocular findings only at the time of diagnosis; and the lack of assessment of prospective changes in blood parameters and final ocular outcomes. Despite the limited sample size due to the rarity of NAION, post-hoc power analysis confirmed that the study had sufficient power for the primary outcomes. Moreover, due to the retrospective nature of the study and the fact that not all tests were performed on every patient, commonly used inflammatory markers such as CRP and erythrocyte sedimentation rate were not evaluated, representing another important limitation. In addition, it should be acknowledged that, despite the increasing investigation of inflammatory indices in NAION,

a substantial proportion of the available literature originates from studies published approximately a decade ago, with only a limited number of reports emerging after 2022. This relative scarcity of recent data indicates that the current evidence represents an evolving field, rather than a consistently validated body of knowledge. Furthermore, many existing studies have been conducted within a limited geographic context, particularly in a single region, which may restrict the generalizability of the findings across different populations and healthcare settings.

CONCLUSION

In conclusion, to the best of our knowledge, our study is the first to evaluate the predictive value of multiple inflammatory parameters, including novel markers, such as systemic inflammatory response index and the pan-immune inflammation value, and their associations with baseline ocular findings in patients with non-arteritic anterior ischemic optic neuropathy. In these patients, levels of the pan-immune inflammation value, systemic immune-inflammation index, systemic inflammatory response index, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio were significantly elevated, with the pan-immune inflammation value and the systemic immune-inflammation index demonstrating particularly high diagnostic performance. The observed negative correlation between these inflammatory markers and retinal nerve fiber layer thickness highlights an important area for future research to explore their impact on long-term ocular outcomes and visual prognosis. Being easily applicable, low-cost, and non-invasive, these biomarkers may provide valuable support to clinicians in the diagnosis and potentially prognostic assessment of non-arteritic anterior ischemic optic neuropathy.

REFERENCES

- Katz DM, Trobe JD. Is there treatment for nonarteritic anterior ischemic optic neuropathy. *Curr Opin Ophthalmol*. 2015;26(6):458-463.
- Arnold A. Vascular supply of the optic nerve head: implications for optic disc ischaemia. *Brit J Ophthalmol*. 2023;107(5):595-599.
- Hayreh SS. Ischemic optic neuropathies - Where are we now? *Graefes Arch Clin Exp Ophthalmol*. 2013;251(8):1873-1884.
- Polat O, Yavaş GF, Inan S, Inan ÜÜ. Neutrophil-to-Lymphocyte Ratio as a Marker in Patients with Non-arteritic Anterior Ischemic Optic Neuropathy. *Balkan Med J*. 2015;32(4):382.
- Chen X, Liu H, Yue Y, Wang H. Hematological indicators and ocular parameters in patients with non-arteritic anterior ischemic optic neuropathy. *Inter Ophthalmol*. 2025 45:1. 2025;45(1):1-8.
- Koçak N, Eraydın B, Turun M, Yeter V, Güngör I. Serum Inflammatory Biomarkers in Patients with Nonarteritic Anterior Ischemic Optic Neuropathy. *Korean J Ophthalmol*. 2020;34(6):478.
- Uzakgider NK, Karaca Adıyeke S, Aytogan H. Understanding the Etiopathogenesis of Non-Arteritic Anterior Ischemic Optic Neuropathy with Laboratory Findings. *Beyoglu Eye J*. 2024;9(1):8-13.
- Imtiaz F, Shafique K, Mirza S, Ayoob Z, Vart P, Rao S. Neutrophil Lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *Int Arch Med*. 2012;5(1):2
- Zhang C, Wang H, Ning Z, et al. Prognostic value of systemic inflammatory response markers in patients with intrahepatic cholangiocarcinoma. *Int J Clin Exp Med*. 2016;9(6):11502-11509.
- Qin B, Ma N, Tang Q, et al. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol*. 2016;26(3):372-376.
- Pan L, Du J, Li T, Liao H. Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio associated with disease activity in patients with Takayasu's arteritis: a case-control study. *BMJ Open*. 2017;7(4):e014451.
- Canlı D. Evaluation of systemic immune-inflammation index, systemic inflammatory response index and hematologic inflammatory parameters in generalized anxiety disorder: a controlled study. *Anatolian Current Medical Journal*. 2024;6(2):161-167.
- Tarım B. The role of serum biomarkers in determining systemic inflammation and cardiovascular risk in pseudoexfoliation syndrome. *Int Ophthalmol*. 2025;45(1).
- Kates MM, Isen DR, Vaphiades MS, Kline LB. Pallid Optic Disc Edema in Nonarteritic Anterior Ischemic Optic Neuropathy. *Journal of Neuro-Ophthalmology*. 2025;45(2):e114-e116.

15. Salgado C, Vilson F, Miller NR, Bernstein SL. Cellular Inflammation in Nonarteritic Anterior Ischemic Optic Neuropathy and Its Primate Model. *Archives of Ophthalmology*. 2011;129(12):1583-1591.
16. Kashani E, Nourigheimasi S, Valisno J, et al. Diagnostic significance of neutrophil-to-lymphocyte ratio in non-arteritic anterior ischemic optic neuropathy: a meta-analysis. *Eur J Med Res*. 2024;29(1):562.
17. Bernstein SL, Johnson MA, Miller NR. Nonarteritic anterior ischemic optic neuropathy (NAION) and its experimental models. *Prog Retin Eye Res*. 2011;30(3):167-187.
18. Wang Q, Zhong W, Xiao Y, et al. Pan-immune-inflammation value predicts immunotherapy response and reflects local antitumor immune response in rectal cancer. *Cancer Sci*. 2025;116(2):350-366.
19. Yolbas S, Yildirim A, Gozel N, Uz B, Koca SS. Hematological Indices May Be Useful in the Diagnosis of Systemic Lupus Erythematosus and in Determining Disease Activity in Behçet's Disease. *Medical Principles and Practice*. 2016;25(6):510.
20. Ozgonul C, Sertoglu E, Mumcuoglu T, Kucukevcilioglu M. Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Novel Biomarkers of Primary Open-Angle Glaucoma. *J Glaucoma*. 2016;25(10):e815-e820.
21. Karaca EE, Özmen MC, Ekici F, Yüksel E, Türkoğlu Z. Neutrophil-to-lymphocyte ratio may predict progression in patients with keratoconus. *Cornea*. 2014;33(11):1168-1173.
22. Elbeyli A, Kurtul BE, Ozcan DO, Ozcan SC, Dogan E. Assessment of Red Cell Distribution Width, Platelet/lymphocyte Ratio, Systemic Immune-inflammation Index, and Neutrophil/lymphocyte Ratio Values in Patients with Central Retinal Artery Occlusion. *Ocul Immunol Inflamm*. 2022;30(7-8):1940-1944.
23. Liu Z, Perry LA, Penny-Dimri JC, et al. The association of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio with retinal vein occlusion: a systematic review and meta-analysis. *Acta Ophthalmol*. 2022;100(3):e635-e647. doi:10.1111/AOS.14955
24. Timur İEE, Tarım B, Şeker ED, Uğurlu N. The relation between serum inflammatory marker levels and serous retinal detachment in macular edema secondary to retinal vein occlusion. *Photodiagnosis Photodyn Ther*. 2023;42:103591. doi:10.1016/j.pdpdt.2023.103591
25. Bisgaard AK, Pihl-Jensen G, Frederiksen JL. The neutrophil-to-lymphocyte ratio as disease activity marker in multiple sclerosis and optic neuritis. *Mult Scler Relat Disord*. 2017;18:213-217. doi:10.1016/j.msard.2017.10.009