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Diagnostic value of red blood cell indices and peripheral inflammatory markers in migraine patients during the interictal period

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Abstract

Objectives: Current data show that migraine patients exhibit a widespread pro-inflammatory systemic state, present even during the interictal period, becoming even more pronounced during attacks. This study aimed to investigate the potential of red blood cell indices and peripheral inflammatory biomarkers (PIB) measured in the interictal period to distinguish migraine from tension-type headache (TTH). *Methods*: This retrospective cross-sectional study included 410 individuals aged 18 to 69 years, comprising 213 (52.0%) with migraine and 197 (48.0%) with tension-type headache (TTH). Peripheral markers of inflammation, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), white blood cell (WBC) count, C-reactive protein (CRP), pan-immune inflammation value (PIV), systemic immune inflammation index (SII) and other blood indices such as hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), platelet distribution width (PDW), ferritin, vitamin B12 and folic acid values were calculated. *Results*: Interictal hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), ferritin, mean platelet volume (MPV), platelet distribution width (PDW), and LMR were significantly *lower*, whereas red cell distribution width (RDW), platelet count (PLT), PLR, NLR, C-reactive protein (CRP), PIV, and SII were significantly *higher* in migraine patients compared with TTH patients. The ROC curve analysis revealed that a PIV cutoff of 206.09 demonstrated 94.8% sensitivity and 89.3% specificity, while an SII cutoff of 535.28 resulted in 91.5% sensitivity and 89.3% specificity in distinguishing migraine from TTH.
Conclusions: The SII and PIV indices may be potential biomarkers for distinguishing migraine from TTH. These indices may also help monitor treatment efficacy based on individual inflammatory response profiles during clinical follow-up.

Keywords: Migraine, peripheral Inflammatory biomarkers, red blood cell indices.

INTRODUCTION

Migraine is a primary headache disorder that causes significant disability and affects millions worldwide.[1] While the pathophysiology of migraine is not fully understood, recent evidence suggests neurogenic inflammation in the meninges[2], occuring within the trigeminal system as a result of neural activity (both central and peripheral), plays a key role.[3] Neural activity causes the release of chemokines and proinflammatory cytokines, which increase vascular permeability in meningeal vessels, resulting in leukocyte migration and glial cell activation.[4]

Significant increases in peripheral levels of proinflammatory cytokines have been observed in migraine patients during both attacks and the interictal period. In particular, during the interictal period, the anti-inflammatory cytokine IL-10 decreases[5], while levels of the proinflammatory chemokine IL-8 markedly increase in the peripheral circulation.[6] TNF-α is an important proinflammatory cytokine involved in migraine pathology.[7] Although some reports have shown no significant differences in TNF-α and IL-1β levels during attacks and the interictal period[8-11], another study found significantly higher TNF-α levels in the peripheral circulation

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in both chronic and episodic migraine patients compared with healthy controls. However, no significant relationship was found between CRP levels and migraine in this study.[12] Previous studies have reported that CRP, which increases in response to inflammation, may play a role in the pathogenesis of migraine.[13-15] This indicates that the role of CRP in migraine pathogenesis remains controversial. Consequently, there is a proinflammatory systemic condition in migraine patients during both attacks and the interictal period.[16]

Beyond CRP and total white blood cell count, peripheral inflammatory markers derived from differential white blood cell counts have been shown to predict clinical outcomes in various medical conditions.[17,18] Numerous studies have demonstrated that factors such as NLR, MLR, PLR, MPV, and RDW are associated with inflammatory processes.[19,20] Additionally, recent studies have proven that new inflammatory markers derived from complete blood count parameters, such as SII and PIV, based on aggregate parameters of platelets, monocytes, neutrophils, and lymphocytes, are more sensitive in clinical monitoring.[21]

Although the potential association between migraine and peripheral inflammatory and red blood cell indices has been investigated, it is unclear whether these indices play a role in the pathogenesis of migraine or whether they can be distinguished from non-migraine headaches. NLR and NMR, especially those that are elevated during headache attacks in migraine patients, suggest that inflammation plays a role in migraine and that peripheral inflammatory indices may be useful to support the diagnosis of migraine. Current data suggest that migraine sufferers exhibit a common pro-inflammatory systemic condition, which is present even between attacks and becoming even more pronounced during attacks. In light of recent data on the pathophysiology of migraine[22], we aimed to assess the diagnostic significance of SII and PIV values, along with NLR, PLR, and LMR, in investigating the possible proinflammatory systemic process in migraine patients during the interictal period. We also examined how white cell subgroups and variations in erythrocyte values relate to this process. Such evidence may be useful in demonstrating the efficacy of migraine treatment during clinical follow-up. In addition, although a few studies have compared these markers between migraine patients and healthy controls, there has been no comparison of proinflammatory markers between migraine and TTH.

METHODS

Study population

This retrospective observational study analyzed data from Siirt Training and Research Hospital, a Ministry of Health–affiliated state hospital, between January 2022 and December 2024 using the SISOFT clinical database. Diagnoses were based on the International Classification of Headache Disorders (ICHD-IIIβ) criteria[23], and groups were classified according to International Classification of Diseases (ICD-10) codes. Patients with the G43 diagnostic code were assigned to the migraine group, and those with the G44.2 code to the TTH group.

A total of 410 patients aged 18-69 years were included in the study, comprising 213 (52.0%) migraine patients and 197 (48.0%) TTH patients. All patients had been diagnosed at least 6 months earlier and were under regular follow-up in the headache outpatient clinic. A detailed headache history, including time of headache onset, mean duration of attack and pain intensity, presence of aura, triggering factors, and accompanying symptoms, was obtained by a neurologist. A headache diary was used for follow-up, allowing patients to document the frequency of migraine attacks, pain intensity (using a visual analog scale), attack duration, and medication use. In addition, prophylactic treatment protocols (β-blockers, antidepressants (SSRIs, SNRIs, TCAs) and antiepileptic drugs (AEDs) were documented.

Patients with chronic diseases such as inflammatory, immune, infectious or allergic conditions, cardiovascular diseases, diabetes mellitus, hypertension, rheumatic diseases (e.g., rheumatoid arthritis), major psychiatric disorders (schizophrenia, psychosis, major depression), epilepsy, head trauma, dementia, Parkinson's disease, neurodegenerative or demyelinating diseases, cerebrovascular stroke, brain tumor, migraine attack within the last week, and those taking any NSAIDs, ,paracetamol or triptans, during this period were excluded.

Peripheral inflammatory markers

Peripheral blood samples collected at the first outpatient clinic visit were analyzed for peripheral inflammatory markers and red blood cell indices, including $N \times 10^9/l$,

L×10^9/l, M×10^9/l, PLT, NLR, LMR, PLR, PDW, MPV, PIV, SII, CRP, WBC, MCV, MCH, MCHC, HBG, RDW, ferritin, vitamin B12, and folic acid. NLO was calculated as neutrophil count / lymphocyte count, LMR as lymphocyte / monocyte count, and PLR as platelet/lymphocyte count, Systemic Immune-Inflammation Index (SII) was calculated using the formula: neutrophil count × platelet count / lymphocyte count.[24] Pan-Immune Inflammation Value (PIV) was calculated as: neutrophil count × platelet count × monocyte count / lymphocyte count.[25] All haemogram parameters were calculated using an automated blood analyser (Hematologic Analyzer; Beckman Coulter Inc., Brea, CA, USA).

Statistical analysis

All statistical analyses were primarily conducted using IBM SPSS Statistics v29.0 (IBM Corp., Armonk, NY, USA). In response to the reviewer's request for internal validation, additional bootstrap resampling (2,000 iterations) and 10-fold cross-validation procedures were performed with Python v3.11, employing open-source libraries including scikit-learn (v1.3) and numpy (v1.26).

The normality of continuous variables was assessed with the Kolmogorov–Smirnov test. Continuous variables are presented as mean ± standard deviation or median (min–max), while categorical variables are expressed as frequencies (n, %). Group comparisons were performed using the Mann–Whitney U test for non-normally distributed variables, and categorical variables were analyzed using the chi-square test. Homogeneity of variances was tested with Levene's test.

To identify significant risk factors for migraine, logistic regression with backward elimination was applied, with age and sex entered as covariates to control for potential confounding. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic value of PIV and SII and to determine optimal cut-off points.

To mitigate potential overfitting, internal validation was performed. For each index (PIV, SII), AUCs were computed with stratified bootstrap resampling (2,000 iterations) to obtain bias-corrected 95% confidence intervals. In addition, 10-fold stratified cross-validation using logistic regression (predictors: PIV and SII) was conducted to estimate out-of-sample discrimination and classification accuracy.

A two-sided p-value <0.05 was considered statistically significant for all analyses, unless otherwise specified.

RESULTS

A total of 410 patients were included, comprising 213 (52.0%) with migraine and 197 (48.0%) with TTH. Descriptive statistics and group comparisons are given in Table 1. Migraine was significantly associated with female sex (p=0.000). The difference between the groups in terms of age was also statistically significant (p=0.003).

Compared with TTH patients, migraineurs showed higher WBC (p<0.001), platelet counts (p<0.001), RDW-CV (p<0.001), neutrophil counts (p<0.001), monocyte counts (p<0.001), CRP (p<0.001), NLR (p<0.001), PLR (p<0.001), PIV (p<0.001), and SII (p<0.001). Conversely, they had lower Hb (p=0.001), MCV (p=0.037), MCH (p=0.004), MCHC (p=0.010), PDW (p=0.003), MPV (p=0.002), lymphocyte counts (p=0.006), ferritin (p=0.005), and LMR (p<0.001). No significant differences were found for other variables presented in Table 1 (p>0.05).

To obtain a logistic model capable of accurately predicting systemic proinflammation condition in migraineurs, variables listed in Table 2 were first examined using univariate analysis. Multivariate logistic regression analysis was conducted with migraine diagnosis (migraine vs. TTH) as the dependent variable to identify factors that significantly discriminate between two groups.

The backward elimination method yielded the final model (Table 2), which correctly classified 94. 4% of cases. Model fit was confirmed by the Hosmer-Lemeshow test (X^2=6.893, p>0.05).

Results of the multivariate logistic regression (Table 2) showed that each one-unit increase in PIV increased the risk of systemic proinflammation in migraineurs by 1.026 times (OR: 1.026; 95% CI: 1.017-1.035, p=0.000), while each one-unit increase in SII increased the risk by 1.019 times (OR: 1.019; 95% CI: 1.013-1.025, p=0.000). Changes in vitamin B12 levels were not significantly associated with systemic proinflammation risk (OR: 1.004; 95% CI: 0.999-1.008, p=0.092). Similarly, folic acid levels showed no significant effect (OR: 1.230; 95% CI: 0.961-1.573, p=0.100).

Following the logistic regression analysis, *ROC analysis* was conducted to determine whether the significant variables included in the model could establish diagnostic cut-off values

Table 1: Descriptive statistics and comparisons of migraine and TTH patients.

Variables	Total n=410	Migraine n=213(52.0%)	TTH n=197(48.0%)	p[&]
Sex, F, n (%)	322 (78.5%)	184 (86.4%)	138 (70.1%)	0.000[#]
Age	37.84 ± 12.85 37.0 (18.0-70.0)	35.84 ± 11.83 36.0 (18.0-70.0)	40.02 ± 13.58 39.0 (18.0-70.0)	0.003[&]
WBC	7.30 ± 1.86 7.06 (2.94-19.44)	7.94 ± 2.08 7.78 (2.94-19.44)	6.62 ± 1.29 6.49 (4.0-12.10)	0.000[&]
HGB	13.20 ± 1.63 13.10 (8.70-18.30)	12.88 ± 1.56 13.0 (8.70-16.70)	13.54 ± 1.65 13.40 (9.40-18.30)	0.001[&]
Platelets	288.01 ± 68.70 281.0 (129.0-648.0)	314.56 ± 68.33 306.0 (136.0-648.0)	259.31 ± 56.62 251.0 (129.0-441.0)	0.000[&]
MCV	85.50 ± 8.12 87.20 (29.90-98.90)	84.67 ± 8.29 86.6 (56.50-98.90)	86.40 ± 7.84 88.0 (29.90-98.60)	0.037[&]
MCH	287.47 ± 2.97 28.2 (17.70-33.1)	27.02 ± 3.24 27.9(17.70-33.0)	27.95 ± 2.56 28.5(18.6-33.1)	0.004[&]
MCHC	31.88 ± 1.98 32.0 (13.7-36.8)	31.66 ± 2.29 31.8 (13.7-36.8)	32.12 ± 1.53 32.2 (22.7-35.9)	0.01[0]&
RDW-CV	13.58 ± 1.58 13.3 (10.4-25.4)	13.86 ± 1.80 13.4 (10.4-25.4)	13.28 ± 1.24 13.2 (10.4-17.4)	0.000[&]
PDW	15.49 ± 1.60 16.0 (9.4-17.0)	15.49 ± 1.52 16.0 (9.4-17.0)	15.49 ± 1.69 16.1 (9.8-17.0)	0.003[&]
MPV	10.17 ± 1.28 10.1 (5.9-16.5)	9.98 ± 1.23 9.9 (5.9-16.1)	10.38 ± 1.31 10.3 (7.0-16.5)	0.002[&]
Neutrophils	4.48 ± 1.65 4.13 (1.97-16.47)	5.34 ± 1.73 5.1 (2.45-16.47)	3.54 ± 0.84 3.5 (1.97-6.38)	0.000[&]
Lymphocytes	2.24 ± 0.64 2.2 (0.29-5.37)	2.07 ± 0.62 2.0 (0.29-4.24)	2.43 ± 0.59 2.42 (1.40-5.37)	0.000[&]
Monocytes	0.47 ± 0.46 0.41 (0.10-5.20)	0.55 ± 0.61 0.45 (0.10-5.20)	0.38 ± 0.13 0.38 (0.10-0.94)	0.000[&]
B12	348.65 ± 130.53 322.5(132.0-1293.0)	351.0 ± 133.69 323.0 (176.0-1293.0)	346.11 ± 127.31 321.0(132.0-991.0)	0.583
CRP	2.68 ± 2.47 2.1(0.18-26.70)	3.01 ± 3.0 2.3(0.18-26.70)	2.32 ± 1.66 1.8(0.30-13.90)	0.000[&]
Folate	8.46 ± 1.99 8.5(3.24-15.17)	8.40 ± 2.09 8.4(3.24-15.17)	8.54 ± 1.89 8.56(4.26-13.87)	0.466
Ferritin	30.30 ± 40.31 18.35(2.0-505.3)	25.18 ± 29.23 14.6(2.0-221.0)	35.84 ± 49.06 21.1(2.3-505.3)	0.005[&]
N/L	2.24 ± 1.61 1.88(0.59-19.62)	2.92 ± 1.97 2.48(1.11-19.62)	1.51 ± 0.44 1.44(0.59-3.71)	0.000[&]

Table 1 (continued)

Variables	Total n=410	Migraine n=213(52.0%)	TTH n=197(48.0%)	p[&]
PLT/L	140.14 ± 62.45 130.82(31.51-758.62)	166.00 ± 71.31 152.43(71.39-758.62)	111.44 ± 32.33 106.45(31.51-236.09)	0.000[&]
L/M	5.76 ± 2.98 5.34 (0. 30-27.00)	4.63 ± 2.18 4.46 (0. 30-25.00)	6.99 ± 3.23 6.14 (2.24-27.0)	0.000[&]
PIV= N×P×M/L	305.41 ± 330.13 226.52(20.89-3329.62)	450.54 ± 403.25 348.75(73.17-3229.62)	148.50 ± 62.44 143.55(20.89-375.64)	0.000[&]
SII= N×P/L	640.47 ± 420.38 563.65(89.18-4316.55)	873.54 ± 461.86 729.09(432.35-4316.55)	388.47 ± 123.20 370.55(89.18-787.42)	0.000[&]

TTH: tension-type headache. PIV: Pan-Immune Inflammation Value, SII: Systemic Immune-Inflammation Index. N: Neutrophil, M: Monocyte, PLT and/orP: platelet, L: Lymphocyte
[#]: Chi-Sqaure test, [&]: Mann-Whitney U test.

for distinguishing migraine patients during the interictal period from those with TTH. The evaluation from the ROC analysis indicated that the PIV and SII variables had significant cut-off values (Table 3).

The ROC analysis confirmed the diagnostic value of both PIV and SII. For PIV, the AUC was 0.958 (95% CI: 0.938–0.976; p<0.01), with a cut-off of 206.09 yielding 94.8% sensitivity and 89.3% specificity. For SII, the AUC was 0.962 (95% CI: 0.947–0.978; p<0.01), with a cut-off of 535.28 providing 91.5% sensitivity and 89.3% specificity in discriminating migraine from TTH during the interictal period (Figure 1).

Discrimination was high for both indices. The AUC for PIV was 0.9567; the bootstrapped mean AUC was 0.9566 (95% CI 0.9365–0.9744) with an optimal cut-off of 209.69 (sensitivity 0.944; specificity 0.888). The AUC for SII was 0.9624; the bootstrapped mean AUC was 0.9625 (95% CI 0.9457–0.9768) with an optimal cut-off of 536.39 (sensitivity 0.915; specificity 0.893). Ten-fold cross-validation of a logistic model combining PIV and SII yielded a mean accuracy of 0.922 (SD 0.042) and a mean AUC of 0.985 (SD 0.012). Together, these findings indicate that PIV and SII are strong and stable discriminatory markers for differentiating migraine from TTH, even after rigorous internal validation.

DISCUSSION

Evidence from animal models has shown that in migraine pathophysiology, mast cells around the meningeal vessels, as well as glia and astrocytes in the trigeminal ganglion and trigeminal caudal nucleus, contribute to neurogenic inflammation. This results in the production of pro-inflammatory mediators and cytokines that maintain trigeminal fiber sensitivity. Clinical data support this mechanism, showing increased pro-inflammatory cytokines, a predominance of Th1 lymphocytes, and reduced regulatory lymphocyte subgroups in migraine patients, both during attacks and in the interictal period.[22] It is possible that the systemic proinflammatory state promotes trigemino-vascular activation in the dural and pial vessels,

Table 2: Multivariate logistic regression analysis results

Variable	B	SE	Wald	P	OR	95% CI for Exp (B)	
						Lower	Upper
PIV	0.026	0.004	35.287	***0.000***	1.026	1.017	1.035
SII	0.019	0.003	43.558	***0.000***	1.019	1.013	1.025
B12	0.004	0.002	2.846	0.092	1.004	0.999	1.008
Folate	0.207	0.126	2.706	0.100	1.230	0.961	1.573

B: regression coefficient, SE: standard error, OR: odds ratio, CI: confidence interval, PIV: *Pan-Immune Inflammation Value, SII: Systemic Immune-Inflammation Index.*

Table 3: ROC analysis results

Variables	AUC	SE	p	95% CI Lower-Upper	Cut-off	Sensitivity	Specificity
PIV	0.958	0.010	***0.000***	0.938-0.976	206.09	***94.8%***	***89.3%***
SII	0.962	0.008	***0.000***	0.947-0.978	535.28	***91.5%***	***89.3%***

AUC: area under the curve, SE: standard error, CI: confidence interval, PIV: Pan-Immune Inflammation Value, SII: Systemic Immune-Inflammation Index.

triggering the onset of a migraine attack.[16]

Systemic inflammatory indices are ratio indices calculated from platelets, inflammatory activators (neutrophils/monocytes), and inflammatory regulators (lymphocytes). They are considered effective indicators of systemic inflammation and immune balance and play an important role in the diagnosis, prognosis, and therapeutic evaluation of various diseases. While traditional markers such as white blood cell count and CRP are commonly used to assess inflammation, next-generation indices like PIV and SII provide a more sensitive and comprehensive evaluation. Our results showed that, compared to TTH patients, migraine patients had higher NLR and PLR values and lower LMR values. During the interictal period, migraine patients exhibited increased neutrophil and monocyte counts (inflammatory activators) and decreased lymphocyte counts (inflammatory regulators), corresponding to elevated NLR, reduced LMR, and higher platelet counts contributing to increased PLR. Furthermore, the study highlights the strong diagnostic value of PIV and SII indices as biomarkers for distinguishing migraine from TTH, with high sensitivity and specificity.

Red blood cell (RBC) indices, including MCV, MCH, MCHC, and RDW, are important markers in anemia. Considering that 60-70% of iron in the body is stored in hemoglobin and erythrocytes, the importance of iron in our system cannot be denied.[26] Studies have demonstrated that in anemia or latent iron deficiency, MCH decreases[27,28], while iron deficiency is characterized by low MCV and high RDW.[29] In addition, an increase in RDW has been associated with impaired iron mobilization[30] and inflammatory markers such as IL-6 and CRP, indicating membrane instability.[31-33] The interaction between iron levels and neuroinflammation in migraine, a neurogliovascular disease where neuroinflammation plays a significant role, can affect the disease's progression. While iron deficiency can impair neurotransmitter transport or

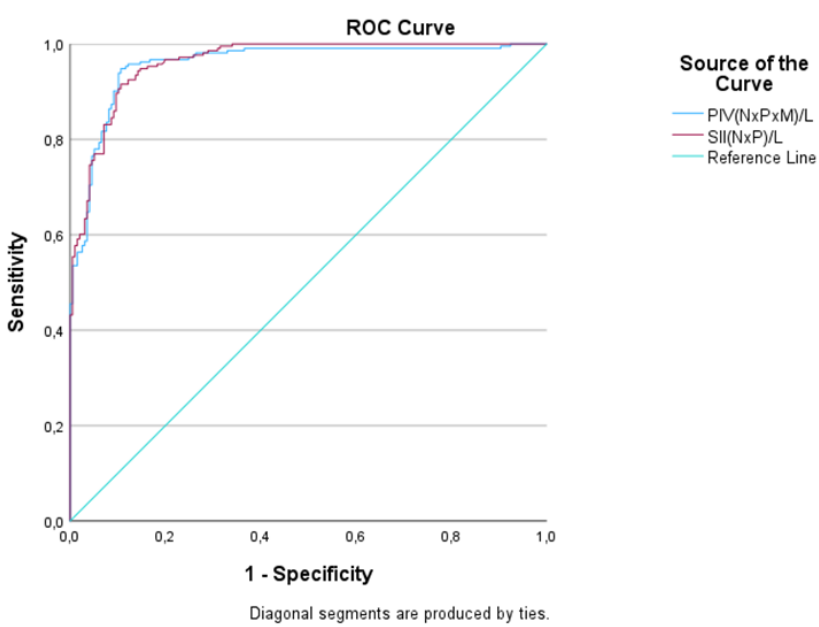

Figure 1. ROC curve.

exacerbate inflammation, iron overload increases oxidative stress and neuroinflammation.[26] In chronic migraine patients, there is significantly greater iron accumulation in multiple subcortical nuclei, especially the nucleus accumbens, compared to episodic migraine.[34] In our study, hematological parameters such as Hb, MCV, MCH, MCHC, and ferritin levels were low, while RDW was elevated, whereas B12 and folic acid levels were not significantly different in migraine patients. Although the relationship between migraine and iron levels is not yet fully understood, the decrease in ferritin and red cell indices in this study, particularly in migraine patients, suggests that iron plays an important role in the pathogenesis of migraine during the interictal period.

MPV and PDW are common indicators of platelet volume. Inflammation can alter MPV by affecting the thrombopoiesis process. High MPV values can be observed in mild inflammatory states, indicating platelet activation and participation in inflammatory processes. However, in severe inflammatory states, MPV values may decrease.[35] The volume of platelets decreases due to an increase in platelet consumption in the inflammatory process. Inflammatory agents stimulate immature platelet precursors in the bone marrow, causing smaller platelets to be released into circulation, while larger and more active platelets are simultaneously consumed at inflammatory sites.[36,37] MPV reflects both pro-inflammatory and pro-thrombotic conditions and regulates thrombopoiesis.[35] PDW varies with platelet activity. Under physiological conditions, the variability between MPV and PDW is always in the same direction. However, the prognostic value of PDW has not been well-studied, and its reliability as an indicator of platelet activation is still questioned.[38-40] In this study, the PDW and MPV values were lower in migraineurs than in TTH patients, supporting the presence of a systemic proinflammatory state in migraineurs.

In contrast, TTH involves uncontrolled endogenous pain modulation and peripheral myofascial nociception.[41] Data on cytokines in TTH are limited.

Despite the robustness of our findings, some limitations must be acknowledged. Firstly, CBC-derived indices are indirect markers of systemic inflammation and may not accurately reflect neuroinflammatory processes within the central nervous system or meninges. The cross-sectional design of this study prevented longitudinal assessment of how these indices fluctuate in relation to migraine activity or treatment response. Secondly, exceptionally high AUC values (~0.96) may raise overfitting concerns. To mitigate this, we performed internal validation using bootstrap resampling and 10x cross-validation, both of which verified the stability of our results. However, independent external validation in larger, multicenter cohorts is required for these indices to be applied in routine clinical practice. Thirdly, the migraine and TTH groups were not matched in terms of age and gender, which could reveal potential confounding factors. However, this imbalance reflects the natural epidemiology of migraines, which are more common in younger individuals and women. To solve this problem, age and gender were included as covariates in multivariate logistic regression analysis. Another limitation was the lack of information about menopausal status, which may have affected ferritin and red blood cell indexes in female participants.

In conclusion, this study revealed that red cell indices and white cell-derived peripheral inflammatory markers showed significant differences in migraine patients compared to TTH patients. The data obtained from peripheral blood samples of migraine patients indicate a proinflammatory systemic condition even in the interictal period. We propose that not only white cell subgroups but also red blood cell indices contribute to this diagnostic process. In addition, the SII and PIV indices may serve as potential biomarkers for distinguishing migraine from TTH. Finally, while our results suggest that PIV and SII may serve as supporting markers to distinguish migraine from TTH, they should not yet be considered definitive biomarkers. However, future studies with matched control groups are warranted to validate our findings and further reduce potential bias.

DISCLOSURE

Ethics: Ethical approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Siirt University (2025/01/01/5-128122). Informed consent has been obtained from all participants.

Data availability: The data supporting this study's findings are available on request from the corresponding author.

Conflict of interests: None

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