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Hematological Parameters and Inflammation in Primary Headache Types: A Retrospective Study of Migraine and Chronic Tension-Type Headache

Emiş Cansu Yaka

Clinic of Neurology, University of Health Sciences Türkiye, İzmir City Hospital, İzmir, Türkiye

Abstract

BACKGROUND/AIMS: Headache disorders, particularly migraine and chronic tension-type headache (CTTH), are highly prevalent neurological conditions contributing substantially to global disability. Hematologic and inflammatory markers have been proposed as potential indicators of migraine, yet findings remain inconsistent. This study aimed to examine sex-, age-, and subtype-specific differences in hematologic and inflammatory indices among patients with migraine and CTTH, and healthy controls.

MATERIALS AND METHODS: We conducted a retrospective cross-sectional case-control study in the neurology outpatient clinic between December 2024 and March 2025. Medical records and same-day laboratory results for patients diagnosed with migraine (chronic or episodic) or with CTTH were reviewed. Participants were classified according to the International Classification of Headache Disorders, 3rd edition criteria. Complete blood counts were used to calculate the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and composite indices, including red cell distribution width to mean corpuscular volume ratio (RDW/MCV), platelet distribution width to platelet count ratio, and hemoglobin (Hb) to RDW ratio.

RESULTS: A total of 1,074 participants were included in the study. Compared with CTTH and controls, migraine patients had lower Hb and hematocrit levels, and higher RDW, NLR, and PLR values (all $p<0.01$). In the migraine subgroup analysis, patients with aura had lower lymphocyte counts and higher NLR compared with those without aura ($p<0.001$). Patients with chronic migraine had higher platelet counts and higher Migraine Disability Assessment scores (38.5 vs. 16; $p<0.001$).

CONCLUSION: Migraine is associated with modest but consistent alterations in hematologic and inflammatory markers, particularly elevated RDW and NLR, supporting systemic immune-vascular involvement and the potential of these markers as adjunctive biomarkers.

Keywords: Chronic tension-type headache, hematologic indices, inflammation, migraine, neutrophil-to-lymphocyte ratio

INTRODUCTION

Headache disorders are among the most common neurological conditions worldwide, and they impose substantial burdens on individuals and societies. Migraine is a disabling, recurrent headache disorder frequently involving nausea, photophobia, phonophobia, and aura.[1] Over the past decades, the global impact of migraine has increased, with current estimates indicating over a billion affected people and a rise in disability-adjusted life years.[2,3] Tension-type headache (TTH), though generally milder, is more pervasive: many people experience it episodically or recurrently during their lifetimes.

A crucial step in tailored treatment and prevention is understanding the biological causes and epidemiology of these headache disorders. One of the most consistent epidemiological features of migraine is its

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ORCID IDs of the authors: E.C.Y. 0000-0001-6413-8015.

Corresponding author: Emiş Cansu Yaka
E-mail: emiscansu@gmail.com
ORCID ID: orcid.org/0000-0001-6413-8015

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pronounced female preponderance. The prevalence of migraines in women is roughly two to four times higher than in men after puberty.[4] Women typically report longer attack durations, more frequent recurrences, and greater disability.[5] Hormonal fluctuations, especially in estrogen, frequently influence migraine risk and severity, impacting the trigeminovascular, vascular, and neural pathways.[4,6,7] By contrast, TTH demonstrates a more uniform sex distribution in some cohorts; despite mixed data, certain studies report a slight male predominance or equal distribution.[8,9]

Biological and hematologic factors may underlie the sex- and age-related differences observed in headache disorders. It is well known that males tend to have higher hemoglobin (Hb) and hematocrit levels than females, reflecting physiological sex differences in erythropoiesis and blood volume.[10] On the other hand, females often exhibit elevated red cell distribution width (RDW) and platelet count, which may be related to differences in hematologic regulation, iron metabolism, and microvascular dynamics.[11] Baseline sex-based differences in hematologic metrics should be considered when exploring links between these metrics and headache disorders.

Researchers have been investigating associations between hematologic or inflammatory biomarkers and headache phenotypes. Peripheral blood ratios-such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and derived composite indices-are useful because they are inexpensive, readily available, and may reflect systemic inflammatory balance. Several studies have examined their links to migraine, albeit with inconsistent findings.[12-15] For example, Sarıcam[13] found that PLR and neutrophil-monocyte ratio were higher in the migraine group than in the control group, whereas differences in NLR were not significant among the subgroups. Likewise, Gül et al.[15] found that RDW was notably elevated in participants with migraine and that it remained an independent predictor after multivariate adjustment. Moreover, in emergency settings, some studies have evaluated whether NLR or PLR can help distinguish migraine from nonspecific headaches.[16,17]

However, findings in the literature remain inconsistent. Some population-based studies did not find robust associations between inflammatory cell counts and migraine during interictal periods, suggesting that attack timing, prophylactic therapy, or selection biases might have influenced the results.[18] Moreover, numerous studies are limited by small sample sizes, lack of subgroup stratification (e.g., by aura or chronicity), or insufficient control for confounders.

In light of this complex background, this study aimed to examine a broad panel of hematologic and inflammation-related indicators across diagnostic groups [migraine, chronic tension-type headache (CTTH), and healthy controls].

By combining demographic, hematologic, and inflammatory data, we aimed to contribute to the evolving understanding of migraine phenotypes, risk stratification, and the pathophysiologic role of systemic immune-vascular interaction.

MATERIALS AND METHODS

This retrospective, cross-sectional, case-control study included 1,074 adults (203 males and 871 females) who attended the neurology outpatient clinic between December 2024 and March 2025. Medical records and same-day laboratory results of patients diagnosed with migraine (chronic or episodic) or CTTH who had visited the clinic at least three times within the previous 12 months were reviewed. The study participants were adults aged 18-65 who met the International Classification of Headache Disorders-3 (ICHD-3) (1) criteria for either migraine or CTTH. Migraine patients were further subdivided into episodic and chronic migraine groups based on attack frequency, and into subgroups with or without aura based on clinical features. The control group comprised individuals with no history of primary headache disorders or chronic pain disorders. All participants were clinically stable, were in an interictal period lasting at least 72 hours before blood sampling, and had not used corticosteroids, non-steroidal anti-inflammatory drugs, triptans, and other anti-inflammatory/antiplatelet drugs for at least two weeks. The control group consisted of individuals who presented to the same outpatient clinics for non-headache-related complaints during the study period. Controls had no history of primary headache disorders or chronic pain conditions. To ensure comparability, the same exclusion criteria that were applied to the migraine and CTTH groups-including systemic inflammatory diseases, acute or chronic infections, hematological disorders, malignancy, and recent use of medications affecting inflammatory parameters-were also applied to the control group.

Participants were excluded if they had systemic inflammatory or autoimmune diseases, hematological or oncological disorders, chronic systemic illnesses (such as diabetes, renal, hepatic, thyroid, or cardiovascular disease), or any acute infection within the preceding four weeks. Pregnant or breastfeeding women, active smokers, individuals who use alcohol or other substances, and those on anticoagulants or hormonal therapy were not included. Individuals who, in the past three months, underwent surgery, experienced trauma, or received blood transfusions, as well as those with incomplete clinical or laboratory data, were not included in the analysis.

Ethics Approval and Consent to Participate

The University of Health Sciences Türkiye, İzmir City Hospital Non-Interventional Ethics Committee (approval number: 2024/232, date: 04.12.2024) approved the study, which was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Data Collection and Clinical Assessment

Demographic characteristics, including age and sex, were recorded for all participants. Structured interviews and medical records provided clinical details, such as migraine type, presence of aura, and headache severity. Aura status was determined according to ICHD-3 criteria and recorded from neurologist documentation in the outpatient clinic notes and from structured patient interviews. Headache severity and migraine-related disability were assessed using the visual analog scale and the Migraine Disability Assessment (MIDAS) questionnaire,[19] respectively.

Hematological Measurements

All participants provided venous blood samples after at least eight hours of fasting, during the interictal period for those with migraine or CTTH. The blood samples were assessed via an automated hematology analyzer (Sysmex XN-1000, Kobe, Japan) within 60 minutes of collection. The following parameters were measured: Hb, hematocrit, mean corpuscular volume (MCV), RDW, platelet count, and platelet

distribution width (PDW). White blood cell counts, including neutrophil and lymphocyte counts, were also recorded.

From these primary parameters, several inflammatory and composite indices were calculated:

- NLR = Neutrophil count/lymphocyte count
- PLR = Platelet count/lymphocyte count
- The RDW/MCV, PDW/PLT, RDW/PLT, and Hb/RDW were computed to assess variability in erythrocyte and platelet distributions.

Statistical Analysis

Statistical analyses were conducted using R software version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Normality of continuous variables was assessed via the Shapiro-Wilk test. Depending on the data distribution, Student's t-test or the Wilcoxon rank-sum test was used to compare two independent groups, and one-way ANOVA or the Kruskal-Wallis test was used to compare more than two groups. Categorical variables were analyzed using the chi-square test or Fisher's exact test when cell counts were fewer than five. In addition to univariable analyses, a multivariable logistic regression analysis was performed to identify independent factors associated with migraine. Variables showing a p-value <0.10 in univariable analyses and clinically relevant covariates were entered into the multivariable model. Age, sex, RDW, NLR, and PLR were included in the final model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Model fit was assessed using the omnibus chi-square test, Nagelkerke R^2, and the Hosmer-Lemeshow goodness-of-fit test. Statistical significance was determined by a p-value less than 0.05.

RESULTS

The study included 1,074 subjects; 203 were male (18.9%) and 871 were female (81.1%), with a mean age of 41.5±10.9 years. The distribution of diagnostic groups differed significantly by sex (p<0.001). As shown in Table 1, migraine was more prevalent among females (55.9%), whereas CTTH was more frequent among males (40.8%). Males exhibited significantly higher Hb and hematocrit, while females had higher RDW and platelets (all p<0.001). MCV also differed between sexes (p=0.011). Sex-related differences were observed in several hematological indices, including PLR, RDW/MCV, PDW/PLT, and Hb/RDW ratios (all p<0.001).

When participants were categorized by headache type (Table 2), age and sex distributions differed significantly among groups (p<0.001 for both). CTTH patients were older (47.8±9.5 years) than the migraine group (38.1±9.7 years) and the control group (39.3±11.6 years). The migraine group was predominantly female (89.0%). whereas CTTH had a higher proportion of males (23.9%). Compared with other groups, migraine patients had lower Hb and hematocrit (p<0.001) and higher RDW (p=0.005). Neutrophil and lymphocyte counts differed significantly across groups (p<0.001). Accordingly, NLR values were significantly higher in the migraine group (p<0.001). PDW values were lowest among CTTH patients (p<0.001), while the migraine group had the highest PLR (p=0.002). RDW/MCV and Hb/RDW ratios showed statistically significant differences between groups (p=0.046 and p<0.001, respectively).

In the comparison between episodic and chronic migraine subgroups (Table 3), demographic and hematological parameters were largely similar The MIDAS score was significantly higher in the chronic migraine group (38.5 vs. 16, p<0.001). The chronic migraine group also had a higher platelet count (p=0.047). In addition, the PDW/PLT ratio differed between subtypes (p=0.036).

As shown in Table 4, a comparison of migraine patients with and without aura revealed that those with aura were slightly younger (36.8 vs. 38.3 years; p=0.251) and had significantly lower lymphocyte counts and percentages (both p<0.001). NLR values were significantly higher in patients with aura (p<0.001). These findings suggest a distinct inflammatory balance in aura-associated migraine.

When the study population was stratified by age (Table 5), participants aged >40 years had a higher prevalence of CTTH (44.1% vs. 18.2%; p<0.001) than those aged ≤40 years, while migraine was more frequent in the younger group (62.3% vs. 41.5%; p<0.001). Hb levels were slightly higher in participants aged ≤40 years (p=0.059), whereas RDW was significantly greater among those aged >40 years (p<0.001). PDW/PLT ratios were higher in participants aged ≤40 years (p=0.028), whereas Hb/RDW ratios were lower in participants aged >40 years (p=0.001).

As shown in Table 6, univariable logistic regression analysis demonstrated that female sex (OR =4.03, 95% CI: 2.68-6.09, p<0.001), higher NLR (OR =1.40, 95% CI: 1.15-1.74, p=0.001), and higher PLR (OR =1.00, 95% CI: 1.00-1.01, p=0.018) were associated with migraine. In the multivariable model, female sex remained a strong independent predictor of migraine (OR =4.04, 95% CI: 2.63-6.22, p<0.001). Additionally, higher NLR was independently associated with migraine after adjustment (OR=1.32, 95% CI: 1.08-1.67, p=0.012). RDW and PLR did not retain statistical significance in the adjusted analysis. The overall model demonstrated an acceptable goodness-of-fit (Hosmer-Lemeshow χ^2 =10.304, p=0.244) with a Nagelkerke R^2 of 0.114.

DISCUSSION

The study included 1,074 participants, and we observed consistent differences in demographics, hematologic, and inflammatory indices when considering sex, headache diagnosis (migraine, CTTH, controls), migraine subtypes, and age groups. The results add to the existing literature on primary headache heterogeneity and highlight peripheral hematologic markers as potential correlates of underlying biological processes. Overall, migraine was associated with subtle but consistent alterations-particularly elevated RDW and NLR-which may reflect low-grade inflammatory or oxidative processes. Variations in these disturbances by sex, aura status, and age may indicate biologically heterogeneous presentations of migraine. In this study, multivariable logistic regression analysis identified female sex and elevated NLR as independent factors associated with migraine, whereas RDW and PLR were no longer statistically significant after adjustment. The strong association with female sex is consistent with extensive epidemiological evidence demonstrating a marked female predominance in migraine, likely mediated by hormonal and neurovascular mechanisms.[4,20]

A prominent observation was that migraine showed female predominance (55.9%), whereas CTTH was more frequent in males (40.8%). This is consistent with epidemiological research showing that migraines predominantly affect women, particularly after puberty, with a female-to-male ratio of 2:1-3:1.[4,20,21] Hormonal fluctuations, especially estrogen-related mechanisms, may modulate vascular and inflammatory pathways involved in migraine.[6] In the American

Migraine Prevalence and Prevention cohort, Buse et al.[20] confirmed that sex is a crucial factor in migraine biology, as they demonstrated sex-based differences in prevalence and disability. Our data show that composite indices (PLR, RDW/MCV, PDW/PLT, Hb/RDW) differ by sex; thus, biomarker interpretation must be sex-specific. Stratified analyses by hormonal status, aura, and comorbidities are crucial for defining biologically meaningful migraine phenotypes.

Migraine patients showed lower Hb and hematocrit levels but higher RDW, NLR, and PLR compared with CTTH and controls; PDW was lowest in CTTH. These findings may point to subtle systemic alterations related to subclinical inflammatory or oxidative mechanisms.[22] Similarly, according to Özdemir et al.,[12] patients with TTH also present with increased NLR and PLR values compared with controls, suggesting that systemic inflammatory processes may be a factor in migraine and CTTH. The value of peripheral immune markers, including NLR, PLR, and C-reactive protein (CRP), is supported by their findings in differentiating primary headache disorders and in assessing inflammatory load.[12]

The mechanisms behind increased RDW include cytokine-driven suppression of erythropoiesis or the release of immature red blood cells (anisocytosis); oxidative stress or iron dysregulation may exacerbate red cell heterogeneity.[21,23] Higher NLR values may reflect a relative predominance of neutrophil counts, which has been interpreted as a marker of systemic inflammatory balance in previous studies.

RDW, which quantifies red cell size variability, has been studied as a marker of inflammation and oxidative stress.[23,24] Previous studies demonstrated that those with migraines had higher RDW, with RDW remaining an independent predictor after adjustment.[5,25] Our findings are consistent with previous reports and further demonstrate differences in RDW not only between migraine patients and controls, but also between migraine patients and CTTH patients. To clarify temporal dynamics, longitudinal studies could assess RDW and related indices across ictal-interictal periods and during migraine progression (from episodic to chronic). Combining complete blood count (CBC)-derived measurements with cytokines [interleukin (IL)-1 beta, IL-6, tumor

Table 1. Baseline characteristics by sex

	Overall, n (%) n=1074	Male, n (%) n=203	Female, n (%) n=871	p
Age (years)*	41.5±10.89	41.8±12.4	41.4±10.5	0.777
Age				0.854
≤40 years old	488 (45.5)	94 (46.3)	394 (45.3)	
>40 years old	585 (54.5)	109 (53.7)	476 (54.7)	
Study group				**<0.001**
Control	180 (16.8)	60 (29.6)	120 (13.8)	
Migraine	547 (50.9)	60 (29.6)	487 (55.9)	
Chronic tension-type headache	347 (32.3)	83 (40.8)	264 (30.3)	
Migraine type				0.203
Episodic	355 (64.9)	34 (56.7)	321 (65.9)	
Chronic	192 (35.1)	26 (43.3)	166 (34.1)	
Presence of aura	60 (11.0)	10 (16.7)	50 (10.3)	0.201
MIDAS score*	18 (8-65)	19 (9-58)	18 (8-65)	0.161
VAS score*	8 (7-9.5)	8 (7-9)	8 (7-9.5)	0.610
Hb (g/dL)*	13.0±1.5	14.5±1.5	12.7±1.3	**<0.001**
Hematocrit (%)*	38.6±4.0	42.5±4.0	37.8±3.4	**<0.001**
MCV (fL)*	84.3±11.9	85.0±6.6	84.1±12.8	**0.011**
RDW (%)*	14.3±1.8	13.7±1.8	14.4±1.7	**<0.001**
Neutrophil (x10³/µL)*	4.2 (1.5-17.7)	4.1 (1.5-9.7)	4.2 (1.6-17.7)	0.060
Lymphocyte (x10³/µL)*	2.1 (0.4-4.92)	2.19 (0.8-4.92)	2.1 (0.4-4.9)	0.840
Lymphocyte (%)*	30.1 (3.6-75.5)	31.2 (8.5-75.5)	29.9 (3.6-65.8)	0.074
Platelets (x10³/µL)*	265 (26-1489)	245 (26-1489)	268 (64-688)	**<0.001**
PDW (%)*	16.5±1.4	16.3±1.7	16.53±1.3	0.618
NLR*	2.00 (0.8-23.0)	1.9 (0.8-10.4)	2.0 (0.8-23.0)	0.053
PLR*	124.4 (16.3-827.2)	114.1 (16.3-827.2)	125.6 (25.6-437.5)	**<0.001**
RDW/MCV ratio*	0.16 (0.03-0.47)	0.16 (0.12-0.41)	0.16 (0.03-0.47)	**<0.001**
PDW/PLT ratio*	0.06 (0.0-0.62)	0.07 (0-0.62)	0.06 (0.02-0.28)	**<0.001**
RDW/PLT ratio*	0.05 (0.01-0.45)	0.06 (0.01-0.45)	0.05 (0.02-0.26)	**0.011**
Hb/RDW ratio*	0.95 (0.34-1.43)	1.1 (0.47-1.43)	0.93 (0.34-1.33)	**<0.001**

*Numeric variables were presented as median (minimum-maximum) or as mean ± SD.
Hb: Hemoglobin, MCV: Mean corpuscular volume, MIDAS: Migraine Disability Assessment, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution width, PDW: Platelet distribution width, PLR: Platelet-to-lymphocyte ratio, VAS: Visual analog scale, PLT: Platelet count ratio, SD: Standard deviation.

necrosis factor-alpha, high-sensitivity CRP] or endothelial function tests may provide greater insight into inflammatory-vascular interactions.

The observation of higher NLR values in migraine is consistent with hypotheses suggesting a role for innate immune mechanisms. The neutrophil-to-lymphocyte axis reflects systemic inflammation and is a prognostic factor in multiple neurological diseases.[16,24] However, its value outside of acute episodes is uncertain, since NLR may vary depending on the timing of attacks or comorbidities.[16] Future trials might assess whether anti-inflammatory or antioxidant treatments alter these hematologic signatures and reduce the attack burden.

Platelet indices offer complementary insight. The release of serotonin, thromboxanes, and other vasoactive and proinflammatory mediators from platelets affects neurovascular reactivity. Increased PLR might indicate platelet activation alongside lymphocyte suppression. PDW and derived ratios (PDW/PLT) reflect platelet size variability and reactivity. The current study's finding of higher PLR in patients with migraine is consistent with studies linking platelet activity to migraine development.[14] Conversely, the lower PDW observed in CTTH may indicate a less reactive platelet phenotype. Based on these findings, migraine, compared with CTTH, may be associated with peripheral hematologic patterns compatible with a pro-inflammatory-oxidative profile. Future studies should focus on multivariable biomarker models that incorporate RDW, NLR, and platelet indices and could be enhanced by machine learning to distinguish migraine subtypes and predict therapeutic response.

Within the migraine cohort, episodic and chronic subtypes showed minimal hematologic differences, except that chronic migraine showed higher platelet counts and altered PDW/PLT ratios. Chronic cases had higher MIDAS scores, which indicate a greater disease burden, as expected. The absence of major differences in RDW or NLR may indicate that migraine chronicity is not solely related to an intensification of systemic inflammation but may involve central sensitization and neuroplasticity.[26] Combining neuroimaging measures (such as white matter hyperintensities and perfusion) or immunogenomic data with peripheral biomarkers may reveal links between systemic and central mechanisms.

Patients with migraine with aura were younger, had fewer lymphocytes, and had higher NLRs than those without aura. This pattern may be compatible with differences in immune balance in aura-associated migraine, potentially due to lymphocyte redistribution or immune modulation. Previous studies of serial systemic immune inflammation indices showed fluctuating immune profiles in individuals with and without aura, implying immune changes associated with aura rather than static trait differences.[26]

Age-related patterns further supported biological variability. CTTH was more common in older participants and was associated with a lower Hb/RDW ratio and higher RDW, which may be related to oxidative stress or age-related changes in erythropoiesis. Younger individuals exhibited higher PDW/PLT ratios, which may indicate increased platelet activity. However, NLR and PLR did not change significantly with age, suggesting

Table 2. Comparison of demographic and hematological parameters among control, migraine, and tension-type headache groups

	Control, n (%) n=180	Migraine, n (%) n=547	Chronic tension-type headache, n (%) n=347	p
Age (years)*	39.3±11.6	38.1±9.7	47.8±9.5	<0.001
Age				
≤40 years old	95 (53.1)	304 (55.6)	89 (25.7)	<0.001
>40 years old	84 (46.9)	243 (44.4)	258 (74.3)	
Sex				
Male	60 (33.3)	60 (11.0)	83 (23.9)	<0.001
Female	120 (66.7)	487 (89.0)	264 (76.1)	
Hb (g/dL)*	13.4±1.6	12.8±1.5	13.1±1.5	**<0.001**
Hematocrit (%)*	39.5±4.2	38.0±3.9	39.2±3.8	**<0.001**
MCV (fL)*	83.8±7.9	83.9±7.0	85.1±18.0	0.640
RDW (%)*	14.2±1.9	14.4±1.7	14.1±1.8	**0.005**
Neutrophil (x10³/µL)*	4.0 (1.5-9.7)	4.2 (2.0-17.7)	4.3 (1.9-10.2)	**<0.001**
Lymphocyte (x10³/µL)*	2.2 (0.7-4.9)	2.0 (0.4-4.3)	2.3 (0.8-4.92)	**<0.001**
Lymphocyte (%)*	32.1 (8.5-65.8)	29.5 (3.6-51.9)	30.3 (8.6-75.5)	**<0.001**
Platelets (x10³/µL)*	249.5 (101-688)	267 (26-1489)	266 (125-513)	0.082
PDW (%)*	16.8±0.6	16.8±0.6	15.8±2.2	**<0.001**
NLR*	1.8 (0.8-9.7)	2.1 (0.8-23.0)	2.0 (0.8-10.4)	**<0.001**
PLR*	121.2 (54.0-305.0)	127.7 (16.3-827.2)	118.6 (39.5-377.0)	**0.002**
RDW/MCV ratio*	0.16 (0.13-0.45)	0.16 (0.13-0.47)	0.16 (0.03-0.41)	**0.046**
PDW/PLT ratio*	0.16 (0.13-0.45)	0.16 (0.13-0.47)	0.16 (0.03-0.41)	**<0.001**
RDW/PLT ratio*	0.06 (0.03-0.26)	0.05 (0.01-0.45)	0.05 (0.03-0.14)	0.066
Hb/RDW ratio*	0.96 (0.45-1.36)	0.93 (0.34-1.43)	0.96 (0.44-1.39)	**<0.001**

*Numeric variables were presented as median (minimum-maximum) or mean ± SD.
Hb: Hemoglobin, MCV: Mean corpuscular volume, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution width, PDW: Platelet distribution width, PLR: Platelet-to-lymphocyte ratio, PLT: Platelet count ratio, SD: Standard deviation.

that the systemic inflammatory balance remains relatively constant in adults. These results emphasize that age affects blood and headache characteristics.

Even though the results were statistically significant, the biomarker differences were small and overlapped between groups. This pattern suggests limited discriminative performance at the individual patient level, despite statistical significance. Accordingly, RDW-, NLR-, and PLR-based indices should be interpreted as adjunctive markers of low-grade inflammatory balance rather than stand-alone diagnostic tools for primary headache classification. Consequently, these indices may not be sufficient as stand-alone diagnostic tools, though they could help indicate inflammation or differentiate migraine subtypes. Their clinical utility likely lies in combination with other parameters within multimodal predictive frameworks. In addition, multiple hematologic indices were examined across several subgroup comparisons without formal adjustment for multiple testing. This increases the possibility of type I error, and therefore the observed associations should be interpreted with caution.

Taken together, these findings further support NLR as a more robust inflammatory marker in migraine than other CBC-derived indices. NLR reflects the balance between innate and adaptive immune responses and has been proposed as a marker of inflammatory burden in migraine, although prior studies have reported heterogeneous results depending on study design and attack timing.[13,16,17] In contrast, RDW and PLR were not independently associated with migraine after adjustment, suggesting that their univariable associations may reflect sex-related hematologic differences or shared inflammatory pathways rather than migraine-specific effects.[15,25] Although the explanatory power of the model was modest, these findings highlight NLR as a more robust inflammatory marker in migraine compared with other CBC-derived indices.

Study Limitations

Several limitations must be acknowledged. First, the retrospective design limits causal inference and introduces potential selection and information biases. In addition, a cross-sectional design precludes causal inference; therefore, it remains unclear whether hematologic alterations precede or result from migraine. Longitudinal monitoring across ictal and interictal periods is warranted. Furthermore, CBC indices are non-specific and are influenced by systemic conditions. Integrating cytokine, vascular biomarker, or endothelial function test measurements could help clarify the links. Future studies incorporating high-sensitivity CRP, cytokine profiles, and endothelial and vascular biomarkers are needed

Table 3. Comparison of demographic and hematological parameters between episodic and chronic migraine groups

	Episodic, n (%) n=355	Chronic, n (%) n=92	p
Age (years)*	38.0±9.8	38.3±10.2	0.530
Age			
≤40 years old	204 (57.5)	100 (52.1)	0.263
>40 years old	151 (42.5)	92 (47.9)	
Sex			
Male	34 (9.6)	26 (13.5)	0.203
Female	321 (90.4)	166 (86.5)	
Presence of aura	40 (11.3)	20 (10.4)	0.872
MIDAS score*	16 (8-22)	38.5 (21-65)	**<0.001**
VAS score*	8 (7-9)	8 (7-9.5)	0.851
Hb (g/dL)*	12.8±1.4	12.8±1.5	0.590
Hematocrit (%)*	38.0±3.7	38.1±4.2	0.829
MCV (fL)*	84.1±6.5	83.5±7.8	0.533
RDW (%)*	14.3±1.6	14.5±1.8	0.257
Neutrophil (x10³/µL)*	4.2 (2.0-17.7)	4.2 (2-10.3)	0.213
Lymphocyte (x10³/µL)*	2.0 (0.4-4.3)	2.1 (1.1-4.3)	0.328
Lymphocyte (%)*	29.1 (3.6-48.1)	30.3 (6.3-51.9)	0.090
Platelets (x10³/µL)*	260 (26-1489)	271 (118-510)	0.047
PDW (%)*	16.9±0.6	16.8±0.5	0.079
NLR*	2.1 (0.8-23.0)	2.0 (0.8-6.1)	0.120
PLR*	127.4 (16.3-827.2)	128.5 (49.6-339.2)	0.556
RDW/MCV ratio*	0.16 (0.13-0.34)	0.16 (0.13-0.47)	0.270
PDW/PLT ratio*	0.06 (0.01-0.62)	0.06 (0.03-0.15)	**0.036**
RDW/PLT ratio*	0.05 (0.01-0.45)	0.05 (0.02-0.12)	0.066
Hb/RDW ratio*	0.93 (0.34-1.43)	0.93 (0.46-1.28)	0.498

*Numeric variables were presented as median (minimum-maximum) or mean ± SD.
Hb: Hemoglobin, MCV: Mean corpuscular volume, MIDAS: Migraine disability assessment, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution width, PDW: Platelet distribution width, PLR: Platelet-to-lymphocyte ratio, VAS: Visual analog scale, PLT: Platelet count ratio, SD: Standard deviation.

to better characterize the underlying mechanisms and validate whether CBC-derived indices accurately reflect migraine-related inflammatory and vascular pathways.

Additionally, the clinic-based sample may overrepresent individuals who are more symptomatic, thereby limiting generalizability. Inflammatory markers may be affected by the timing of blood sampling. Even with a large sample, the impact was small. Moreover, the substantial overlap between groups limits clinical interpretability and precludes using these indices as diagnostic classifiers in routine practice. Diagnostic precision and prognostic accuracy might be enhanced in future studies through composite biomarker models and advanced statistical methods. Although multivariable regression analysis was performed, residual confounding cannot be entirely excluded, and the model included a limited number of hematologic variables.

CONCLUSION

Migraine patients exhibit small but consistent variations in blood and inflammatory measures, especially increased RDW and NLR, compared with CTTH patients and control subjects. Biological differences in these relationships are influenced by sex, age, aura, and chronicity. Although not diagnostic in isolation, these indices may provide valuable adjunctive insights into migraine pathophysiology. However, given the modest effect sizes and overlapping distributions, these markers should be considered supportive rather than diagnostic. These findings should be considered exploratory and require confirmation in longitudinal studies incorporating multivariable analytical approaches. Future longitudinal and multimodal studies are warranted to validate these hematologic and inflammatory markers as potential clinical tools.

Table 4. Comparison of demographic and hematological parameters between migraine patients with and without aura

	No, n (%) n=487	Yes, n (%) n=60	p
Age (years)*	38.3±9.8	36.8±8.9	0.251
Age			0.553
≤40 years old	268 (55.0)	36 (60.0)	
>40 years old	219 (45.0)	24 (40.0)	
Sex			0.201
Male	50 (10.3)	10 (16.7)	
Female	437 (89.7)	50 (83.3)	
Migraine type			0.872
Episodic	315 (64.7)	40 (66.7)	
Chronic	172 (35.3)	20 (33.3)	
MIDAS score*	18 (8-65)	18 (11-54)	0.418
VAS score*	8 (7-9.5)	8 (7-9)	0.779
Hb (g/dL)*	12.8±1.4	13.0±1.7	0.427
Hematocrit (%)*	38.0±3.8	38.4±4.5	0.338
MCV (fL)*	83.8±7.1	84.3±6.2	0.967
RDW (%)*	14.4±1.7	14.2±1.3	0.498
Neutrophil (x10^3/µL)*	4.2 (2-17.7)	4.5 (2.4-16.2)	0.352
Lymphocyte (x10^3/µL)*	2.1 (0.4-4.3)	1.8 (0.9-3.2)	**<0.001**
Lymphocyte (%)*	29.8 (3.6-48.1)	26.4 (8.1-51.9)	**<0.001**
Platelets (x10^3/µL)*	267 (64-1489)	259.5 (26-407)	0.168
PDW (%)*	16.8±0.5	16.8±0.7	0.907
NLR*	2.1 (0.8-23.0)	2.3 (0.8-10.1)	**<0.001**
PLR*	127.3 (25.6-827.2)	139.8 (16.3-340.0)	0.095
RDW/MCV ratio*	0.16 (0.13-0.47)	0.16 (0.13-0.26)	0.789
PDW/PLT ratio*	0.06 (0.01-0.28)	0.06 (0.04-0.62)	0.193
RDW/PLT ratio*	0.05 (0.01-0.21)	0.05 (0.04-0.45)	0.259
Hb/RDW ratio*	0.93 (0.34-1.31)	0.93 (0.53-1.43)	0.564

*Numeric variables were presented as median (minimum-maximum) or mean ± SD.
Hb: Hemoglobin, MCV: Mean corpuscular volume, MIDAS: Migraine Disability Assessment, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution width, PDW: Platelet distribution width, PLR: Platelet-to-lymphocyte ratio, VAS: Visual analog scale.

Table 5. Comparison of demographic and hematological parameters between participants aged ≤40 and >40 years

	≤40 years old, n (%) n=488	>40 years old, n (%) n=585	p
Age (years)*	31.8±6.6	49.5±6.3	**<0.001**
Sex			
Male	94 (19.3)	109 (18.6)	0.854
Female	394 (80.7)	476 (81.4)	
Study group			
Control	95 (19.5)	84 (14.4)	**<0.001**
Migraine	304 (62.3)	243 (41.5)	
Chronic tension-type headache	89 (18.2)	258 (44.1)	
Migraine type			
Episodic	204 (67.1)	151 (62.1)	0.263
Chronic	100 (32.9)	92 (37.9)	
Presence of aura	36 (11.8)	24 (9.9)	0.553
MIDAS score*	18 (8-62)	18 (9-65)	0.283
VAS score*	8 (7-9)	8 (7-9.5)	0.423
Hb (g/dL)*	13.1±1.5	12.9±1.5	0.059
Hematocrit (%)*	38.8±4.0	38.5±3.9	0.215
MCV (fL)*	83.9±7.3	84.7±14.6	0.650
RDW (%)*	14.1±1.6	14.4±1.9	**<0.001**
Neutrophil (x10³/µL)*	4.3 (1.6-17.7)	4.1 (1.5-14.8)	0.331
Lymphocyte (x10³/µL)*	2.1 (0.8-4.92)	2.2 (0.4-4.9)	0.053
Lymphocyte (%)*	29.6 (8.1-65.8)	30.6 (3.6-75.5)	0.062
Platelets (x10³/µL)*	260.5 (26-1489)	265 (64-688)	0.138
PDW (%)*	16.7±1.0	16.4±1.6	0.245
NLR*	2.1 (0.8-10.4)	1.9 (0.8-23.0)	0.053
PLR*	124.9 (16.3-827.2)	122.7 (25.6-437.5)	0.583
RDW/MCV ratio*	0.16 (0.13-0.47)	0.16 (0.03-0.41)	0.067
PDW/PLT ratio*	0.06 (0.01-0.62)	0.06 (0-0.28)	**0.028**
RDW/PLT ratio*	0.05 (0.01-0.45)	0.05 (0.02-0.21)	0.879
Hb/RDW ratio*	0.96 (0.44-1.43)	0.94 (0.34-1.39)	**0.001**

*Numeric variables were presented as median (minimum-maximum) or mean ± SD.
Hb: Hemoglobin, MCV: Mean corpuscular volume, MIDAS: Migraine Disability Assessment, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution width, PDW: Platelet distribution width, PLR: Platelet-to-lymphocyte ratio, VAS: Visual analog scale.

Table 6. Univariable and multivariable logistic regression analysis of factors associated with the migraine

	Univariable				Multivariable		
Characteristic	**N**	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Age	719	0.99	0.97, 1.01	0.189	0.99	0.97, 1.00	0.122
Sex	719						
Male		-	-		-	-	
Female		4.03	2.68, 6.09	**<0.001**	4.04	2.63, 6.22	**<0.001**
RDW	719	1.06	0.96, 1.19	0.260	1.00	0.90, 1.12	0.984
NLR	719	1.40	1.15, 1.74	**0.001**	1.32	1.08, 1.67	**0.012**
PLR	719	1.00	1.00, 1.01	**0.018**	1.00	1.00, 1.01	0.515

Omnibus (model χ^2) =1.74, p=0.187 Nagelkerke R^2 =0.114 Hosmer-Lemeshow testi: χ^2 =10.304, p=0.244.
CI: Confidence interval, OR: Odds ratio, NLR: Neutrophil-to-lymphocyte ratio, RDW: Red cell distribution Width, PLR: Platelet-to-lymphocyte ratio.

MAIN POINTS

- This study demonstrates sex-, age-, and subtype-specific variations in hematologic and inflammatory indices among individuals with migraine and chronic tension-type headache.
- Migraine was associated with increased red cell distribution width, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio, supporting the hypothesis that low-grade systemic inflammation contributes to migraine pathophysiology.
- The results highlight the potential utility of complete blood count-derived indices as accessible adjunctive biomarkers for differentiating primary headache disorders.
- Hematologic differences showed substantial overlap between groups, underscoring their adjunctive rather than diagnostic role.

ETHICS

Ethics Committee Approval: The University of Health Sciences Türkiye, İzmir City Hospital Non-Interventional Ethics Committee (approval number: 2024/232, date: 04.12.2024) approved the study, which was conducted in accordance with the Declaration of Helsinki.

Informed Consent: All participants provided written informed consent.

DISCLOSURES

Financial Disclosure: The author declared that this study received no financial support.

Declaration Regarding the Use of Artificial Intelligence and Artificial Intelligence-Assisted Technologies

During the preparation of this manuscript, the author utilized Grammarly as an artificial intelligence (AI)-assisted tool to support language editing, improve clarity and coherence of the text, and assist in rephrasing sentences for academic style. The scientific content, data interpretation, statistical analyses, and final conclusions were independently reviewed, verified, and approved by the author. The author takes full responsibility for the accuracy, integrity, and originality of the manuscript. The use of this AI tool did not affect the study design, data collection, data analysis, or interpretation of the results.

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018; 38(1): 1-211.
2. Ge R, Chang J, Cao Y. Headache disorders and relevant sex and socioeconomic patterns in adolescents and young adults across 204 countries and territories: an updated global analysis. J Headache Pain. 2023; 24(1): 110.
3. Chen ZF, Kong XM, Yang CH, Li XY, Guo H, Wang ZW. Global, regional, and national burden and trends of migraine among youths and young adults aged 15-39 years from 1990 to 2021: findings from the global burden of disease study 2021. J Headache Pain. 2024; 25(1): 131.
4. Vetvik KG, MacGregor EA. Sex differences in the epidemiology, clinical features, and pathophysiology of migraine. Lancet Neurol. 2017; 16(1): 76-87.
5. Lipton RB, Nicholson RA, Reed ML, Araujo AB, Jaffe DH, Faries DE, et al. Diagnosis, consultation, treatment, and impact of migraine in the US: results of the OVERCOME (US) study. Headache. 2022; 62(2): 122-40.
6. Krause DN, Warfvinge K, Haanes KA, Edvinsson L. Hormonal influences in migraine - interactions of oestrogen, oxytocin and CGRP. Nat Rev Neurol. 2021; 17(10): 621-33.
7. Faria V, Höfer B, Klimova A, von der Hagen M, Berner R, Sabatowski R, et al. Sex and age-related patterns in pediatric primary headaches: observations from an outpatient headache clinic. Front Neurol. 2024; 15: 1441129.
8. Yadav P, Bradley AL, Smith JH. Recognition of chronic migraine by medicine trainees: a cross-sectional survey. Headache. 2017; 57(8): 1267-72.
9. Dabilgou AA, Dravé A, Kyelem JMA, Sawadogo Y, Napon C, Millogo A, et al. Frequency of headache disorders in neurology outpatients at Yalgado Ouedraogo University Teaching Hospital: a 3-month prospective cross-sectional study. SN Compr Clin Med. 2020; 2(1): 301-07.
10. Shamliyan TA, Choi JY, Ramakrishnan R, Miller JB, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults. J Gen Intern Med. 2013; 28(9): 1225-37.
11. Onwuekwe I, Onyeka T, Aguwa E, Ezeala-Adikaibe B, Ekenze O, Onuora E. Headache prevalence and its characterization amongst hospital workers in Enugu, South East Nigeria. Head Face Med. 2014; 10: 48.
12. Özdemir HH, Dönder A. Evaluation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and c-reactive protein in tension-type headache patients. J Neurosci Rural Pract. 2021; 12(3): 566-70.
13. Sarıcam G. Relationship between migraine headache and hematological parameters. Acta Neurol Belg. 2021; 121(4): 899-905.
14. Turan ÖF, Gedikaslan Ş. Utilizing biomarkers for rapid assessment of headache in the emergency department. Disaster and Emergency Medicine Journal. 2025; 10(1): 1-8.
15. Gül ZB, Çelik RGG, Selçuk B, Aksoy S, Gül M, Soysal A. New indicator of inflammation in migraine: red blood cell distribution. Haydarpasa Numune Med J. 2021;61(2):166-171.
16. Onder H, Deliktas MM. May neutrophil to lymphocyte ratio serve a role in the prediction of clinical features of migraine? J Neurol Res. 2020; 10(2): 38-43.
17. Ha WS, Chu MK. Altered immunity in migraine: a comprehensive scoping review. J Headache Pain. 2024; 25(1): 95.
18. Acarsoy C, Ruiter R, Bos D, Ikram MK. No association between blood-based markers of immune system and migraine status: a population-based cohort study. BMC Neurol. 2023; 23(1): 445.
19. Stewart WF, Lipton RB, Kolodner K, Liberman J, Sawyer J. Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. Cephalalgia. 1999; 19(2): 107-14; discussion 74.
20. Buse DC, Loder EW, Gorman JA, Stewart WF, Reed ML, Fanning KM, et al. Sex differences in the prevalence, symptoms, and associated features of migraine, probable migraine and other severe headache: results of the American Migraine Prevalence and Prevention (AMPP) study. Headache. 2013; 53(8): 1278-99.
21. Wu J, Fu L, Deng Z, Li H, Zhong L, Gao R, et al. A study of changes in hematologic parameters in patients with migraine. Clin Exp Immunol. 2025; 219(1): uxae113.
22. Lee SH, Kim JH, Kwon YS, Sohn JH. Role of peripheral inflammatory markers in patients with acute headache attack to differentiate between migraine and non-migraine headache. J Clin Med. 2022; 11(21): 6538.
23. Lippi G, Cervellin G, Mattiuzzi C. Migraine and erythrocyte biology: a review. Int J Lab Hematol. 2014; 36(6): 591-7.

24. Morgan CT, Nkadimeng SM. The role of inflammation in migraine headaches: a review. FASEB Bioadv. 2025; 7(7): e70033.

25. Celikbilek A, Zararsiz G, Atalay T, Tanik N. Red cell distribution width in migraine. Int J Lab Hematol. 2013; 35(6) :620-8.

26. Wijeratne T, Murphy MJ, Wijeratne C, Martelletti P, Karimi L, Apostolopoulos V, et al. Serial systemic immune inflammation indices: markers of acute migraine events or indicators of persistent inflammatory status? J Headache Pain. 2025; 26(1): 7.