

Hematological markers of systemic inflammation potentially associated with migraine in pediatric patients

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ABSTRACT

Objective: The aim of this study was to evaluate potential neuroinflammatory processes in pediatric migraine using hematological inflammatory indices and to examine their associations with age and gender.

Materials and Methods: This retrospective cross-sectional study included 90 children diagnosed with migraine and healthy control group, conducted between August 1, 2019, and August 1, 2025. Complete blood count parameters were analyzed for all participants. The neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and other hematological inflammatory markers were calculated. Comparisons were made between the migraine and control groups. Additionally, the migraine group was subdivided according to age, gender, and treatment status, and subgroup analyses were performed.

Results: Platelet-to-lymphocyte ratio values were significantly higher in the migraine group than in the control group. In gender-based comparisons, a statistically significant difference was observed only in red blood cell (RBC) counts, whereas no gender-related differences were detected in other inflammatory parameters. Within the migraine group, lymphocyte counts decreased in the older age subgroup, while platelet counts and NLR values showed a significant increase. Among patients receiving flunarizine treatment, no significant differences were observed in inflammatory markers, except for mean corpuscular volume (MCV).

Conclusion: Platelet-to-lymphocyte ratio may serve as a marker of increased inflammatory burden in pediatric patients with migraine. The age-related increase in inflammatory indices may reflect neuroinflammatory processes involved in migraine pathophysiology. These findings highlight the importance of considering age in the clinical evaluation of pediatric migraine patients.

Keywords: Child, flunarizine, migraine, neuroinflammation, platelet

Introduction

Migraine is a primary headache disorder characterized by pulsatile or throbbing headache accompanied by photophobia, phonophobia, nausea, and vomiting, and it is commonly observed in childhood (1). The World Health Organization has identified migraine as one of the top ten causes of disability worldwide (2). The prevalence of migraine in children is approximately 10%, and it has a substantial negative impact on school performance and quality of life (3). Although no significant gender differences are observed in migraine prevalence during the prepubertal period, migraine occurs more frequently in girls during adolescence (4).

The diagnosis of migraine in children differs in certain aspects from that in adults. Headache attacks in children are typically shorter in duration. The pain may be unilateral or bilateral. However, similar to adults, childhood migraine is expected to exhibit at least two core features, including a pulsatile quality, moderate to severe intensity, and worsening with routine physical activity. In addition, at least one associated symptom, such as nausea, vomiting, photophobia, or phonophobia, is required for diagnosis. However, children may have difficulty expressing symptoms such as photophobia and phonophobia; instead, they may demonstrate behaviorals, such as seeking a dark and quiet environment (5).

Neurogenic inflammation plays a key role in the pathophysiology of migraine. Migraine-related headache is thought to result from activation of the trigeminovascular system, which consists of peripheral trigeminal nerve fibers that innervate the vascular structures of the dura mater (6). Various cytokines, including tumor necrosis factor (TNF), interleukin-1 (IL-1), and adiponectin, are involved in regulating inflammatory processes, altering pain thresholds, increasing trigeminal nerve sensitization, and the development of migraine attacks (7). Experimental studies have demonstrated significantly increased TNF- α expression and macrophage presence in the trigeminal ganglia during inflammatory processes (8). In addition, increased serum concentrations of IL-1 β , IL-6, IL-8, and TNF- α have been reported during migraine attacks (9). A meta-analysis has shown that serum CRP, IL-1 β , IL-6, and TNF- α levels are higher in patients with migraine than in healthy controls. These findings support the role of inflammation in the pathophysiology of migraine (10).

The NLR and MLR are practical hematological parameters used to assess the presence and severity of systemic inflammation. These indices are calculated by dividing peripheral neutrophil and monocyte counts by lymphocyte counts (11). Previous pediatric studies have reported significant associations between NLR, MLR, and PLR values and various diseases, suggesting that these parameters may serve as useful diagnostic and therapeutic biomarkers (12,13). Recent studies indicate that inflammation may play a role in the pathophysiology of childhood migraine and highlight inflammatory response markers as potential biomarkers. Therefore, this study aimed to investigate whether NLR, MLR, and PLR are potential markers associated with inflammatory processes in childhood migraine.

Materials and Methods

This single-center, retrospective cross-sectional study was conducted at Balıkesir University Health Practice and Research Hospital between August 1, 2019, and August 1, 2025. A total of 90 pediatric patients diagnosed with migraine according to the International Classification of Headache Disorders, 3rd edition (ICHD-3), were included. During the same period, children who presented to the pediatric and Pediatric Neurology-1 outpatient clinics for routine follow-up and had no history of headache (n=100) were included as the control group.

Patients with signs of acute infection, chronic inflammatory diseases, hematological disorders, a history of autoimmune disease, those receiving systemic corticosteroids or immunomodulatory therapy, and those with incomplete medical records were excluded from the study.

Data Collection

Demographic data were retrospectively obtained from medical records. Laboratory data were collected from complete blood count (CBC) results obtained from peripheral venous blood samples drawn at the time of admission. CBC parameters included white blood cell count (WBC), RBC, hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count (PLT), platelet distribution width (PDW), and neutrophil, lymphocyte, monocyte, and eosinophil counts.

Calculation of inflammatory hematological indices

The following inflammatory ratios were calculated from the complete blood count data:

- NLR: calculated by dividing the neutrophil count by the lymphocyte count
- PLR: calculated by dividing the platelet count by the lymphocyte count
- MLR: calculated by dividing the monocyte count by the lymphocyte count

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Data were presented as number (n), minimum–maximum values, and mean and standard deviation. Group comparisons were performed using the independent samples t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. A p value of <0.050 was considered statistically significant.

Results

A total of 190 participants were included in the study. The ages of the participants ranged from 5 to 18 years, with a mean age of 12.0 ± 3.6 years. When stratified by age groups, the majority of participants were in the 5–13-year age range (Table I).

The clinical characteristics of the participants are summarized in Table II. Regarding attack frequency, the most common

Table I: Demographic characteristics of the migraine and control groups

Variables	Migraine group*	Control group*
Age group		
5–12 years	39 (43.3)	74 (74)
12–18 years	51 (56.7)	26 (26)
Gender		
Female	52 (57.8)	45 (45)
Male	38 (42.2)	55 (55)
Treatment		
Yes	10 (11)	-
No	80 (89)	-

*: n(%)

Table II: Clinical characteristics of participants with migraine

Variables	n (%)
Attack Frequency	
Every day	24 (26.6)
2–6 times per week	35 (38.8)
Once per week	10 (11.1)
1–3 times per month	21 (23.3)
Attack Duration	
<1 hour	18 (20)
1–3 hours	46 (51.1)
3–6 hours	16 (17.7)
More than 6 hours	10 (11.1)
Migraine Type	
Without aura	83 (92.2)
With aura	7 (7.8)
Family History	
Present	56 (62.2)
Absent	34 (37.8)

Table III: Comparison of age and hematological parameters between the migraine and control groups

Variables	Migraine group*	Control group*	p
Total number of patients	90	100	
Age (years)	12.18±3.63	9.84±2.99	<0.010 [‡]
WBC (×10 ³ /μL)	7.44±2.21	7.59±2.06	0.636 [‡]
RBC (×10 ⁶ /μL)	4.91±0.39	4.94±0.36	0.460 [‡]
Hb (g/dL)	13.29±1.25	13.07±0.93	0.160 [‡]
Hct (%)	39.46±3.19	38.63±2.62	0.520 [‡]
MCV (fL)	80.59±5.67	78.36±4.85	0.040 [‡]
MCHC (g/dL)	33.52±1.45	33.85±0.71	0.470 [‡]
RDW (%)	13.78±1.10	14.14±1.02	0.190 [‡]
Neutrophils (×10 ³ /μL)	4.20±1.87	3.94±1.70	0.301 [‡]
Lymphocytes (×10 ³ /μL)	2.44±0.73	2.73±0.84	0.011 [‡]
Monocytes (×10 ³ /μL)	0.57±0.18	0.59±0.20	0.622 [‡]
Eosinophils (×10 ³ /μL)	0.18±0.17	0.26±0.23	0.090 [‡]
Platelets (×10 ³ /μL)	312.41±82.00	327.57±86.37	0.166 [‡]
NLR	1.87±1.10	1.59±0.99	0.710 [‡]
MLR	0.25±0.11	0.23±0.09	0.103 [‡]
PLR	134.27±37.80	130.92±66.70	0.046 [‡]

*: mean±SD †: Mann-Whitney U test, ‡: Independent samples t-test

pattern was 2–6 attacks per week (38.8%), followed by daily attacks (26.6%), 1–3 attacks per month (23.3%), and once-weekly attacks (11.1%). In terms of attack duration, most participants reported attacks lasting 1–3 hours (51.1%), whereas 20% had attacks lasting less than 1 hour, 17.7% reported durations of 3–6 hours, and 11.1% experienced attacks lasting more than 6 hours. The majority of patients were diagnosed with migraine without aura (92.2%), whereas migraine with aura was less frequent (7.8%). A positive family history of migraine was present in 62.2% of the participants.

Evaluation of complete blood count parameters revealed that WBC values ranged from 3.4 to 17.7×10³/μL, RBC values from 4.08 to 6.09×10⁶/μL, hemoglobin levels from 10.1 to 17.4 g/dL, and hematocrit values from 30.5% to 49.6%. MCV ranged from 58.1 to 92.4 fL, MCHC from 25.3 to 37.0 g/dL, and RDW from 12.1% to 17.7%.

Regarding platelet parameters, platelet counts ranged from 140 to 637×10³/μL, plateletcrit (PCT) from 0.14% to 0.45%, and PDW from 15.7 to 18.2 fL. Neutrophil counts ranged from 1.0 to 11.4×10³/μL, lymphocyte counts from 0.5 to 6.0×10³/μL, monocyte counts from 0.0 to 1.1×10³/μL, and eosinophil counts from 0.0 to 1.3×10³/μL.

When inflammatory hematological indices were evaluated, the NLR ranged from 0.43 to 8.60, the PLR ranged from 65.46 to 638.00, and the MLR ranged from 0.00 to 1.00.

As shown in Table III, statistically significant differences were observed between the migraine and control groups with respect to age ($p<0.010$), lymphocyte count ($p=0.011$), MCV ($p=0.040$), and PLR ($p=0.046$). Compared with the control group, patients with migraine were older and had lower lymphocyte counts as well as higher MCV and PLR values. No statistically significant differences were detected between the groups for the remaining parameters.

As shown in Table IV, male patients exhibited significantly higher RBC counts than female patients ($p<0.001$), whereas

Table IV: Comparison of hematological parameters by gender in the migraine group

Variables	Female group*	Male group*	p
Total number of patients	52	38	
WBC (×10 ³ /μL)	7.43±1.98	7.47±2.50	0.935 [‡]
RBC (×10 ⁶ /μL)	4.79±0.38	5.09±0.34	<0.001 [†]
Hb (g/dL)	13.10±1.10	13.56±1.39	0.085 [‡]
Hct (%)	39.46±3.19	38.63±2.62	0.183 [‡]
MCV (fL)	81.63±6.03	79.16±4.87	0.041 [‡]
MCHC (g/dL)	33.37±1.43	33.73±1.48	0.240 [‡]
RDW (%)	13.73±1.15	13.83±1.03	0.667 [‡]
Neutrophils (×10 ³ /μL)	4.26±1.65	4.13±2.15	0.737 [‡]
Lymphocytes (×10 ³ /μL)	2.40±0.73	2.50±0.72	0.516 [‡]
Monocytes (×10 ³ /μL)	0.55±0.17	0.60±0.20	0.191 [‡]
Eosinophils (×10 ³ /μL)	0.18±0.20	0.20±0.13	0.544 [‡]
Platelets (×10 ³ /μL)	306.75±74.60	320.16±91.62	0.644 [‡]
NLR	1.91±0.87	1.82±1.38	0.710 [‡]
MLR	0.24±0.08	0.26±0.15	0.364 [‡]
PLR	134.37±36.01	134.13±40.61	0.455 [‡]

*: mean±SD, †: Mann-Whitney U test, ‡: Independent samples t-test

Table V: Comparison of hematological parameters according to age categories in the migraine group

Variables	Migraine age group 1 (5–12 years)*	Migraine age group 2 (12–18 years)*	p
WBC (×10 ³ /μL)	7.53±2.68	7.38±1.78	0.752 [‡]
RBC (×10 ⁶ /μL)	4.93±0.28	4.91±0.46	0.468 [‡]
Hb (g/dL)	13.09±0.76	13.44±1.51	0.193 [‡]
Hct (%)	38.89±2.16	39.89±3.76	0.202 [‡]
MCV (fL)	79.10±2.78	81.72±6.95	0.029 [‡]
MCHC (g/dL)	33.72±1.35	33.37±1.53	0.261 [‡]
RDW (%)	13.64±0.84	13.88±1.26	0.293 [‡]
Neutrophils (×10 ³ /μL)	3.92±2.07	4.42±1.69	0.205 [‡]
Lymphocytes (×10 ³ /μL)	2.74±0.85	2.21±0.51	<0.001 [†]
Monocytes (×10 ³ /μL)	0.59±0.19	0.56±0.17	0.388 [‡]
Eosinophils (×10 ³ /μL)	0.2 ±0.14	0.16±0.19	0.081 [‡]
Platelets (×10 ³ /μL)	343.36±88.80	288.75±68.24	0.020 [†]
NLR	1.48±0.71	2.17±1.26	0.030 [‡]
MLR	0.23±0.09	0.27±0.13	0.140 [‡]
PLR	131.13±34.75	136.67±40.15	0.550 [‡]

*: mean±SD, †: Mann-Whitney U test, ‡: Independent samples t-test

female patients had significantly higher MCV values ($p=0.041$). No significant gender-related differences were detected for the other hematological parameters (all $p>0.050$).

When migraine patients were divided into two age-based categories as Group 1 (5–12 years) and Group 2 (12–18 years), statistically significant differences were observed in MCV ($p=0.029$), lymphocyte count ($p<0.001$), platelet count ($p=0.029$), and NLR ($p=0.030$).

A statistically significant difference was observed only in MCV, which was significantly lower in patients receiving treatment compared to those not receiving treatment ($p<0.010$). No statistically significant differences were found between the treated and untreated groups in terms of age, white blood cell count, RBC count, hemoglobin, hematocrit, platelet count, leukocyte subtypes, or inflammatory ratios including NLR, MLR and PLR.

Table VI: Comparison of hemogram parameters in migraine patients receiving and not receiving treatment

Migraine group	Treated*	Untreated*	p
Age (years)	13.60±3.34	12.00±3.65	0.580 [‡]
WBC (×10 ³ /μL)	7.19±1.31	7.48±2.30	0.700 [‡]
RBC (×10 ³ /μL)	5.14±0.57	4.89±0.36	0.163 [†]
Hb (g/dL)	12.63±1.39	13.37±1.21	0.750 [‡]
Hct (%)	37.86±3.70	39.66±3.09	0.125 [†]
MCV (fL)	74.59±10.36	81.34±4.35	<0.010 [‡]
MCHC (g/dL)	33.32±1.33	33.55±1.48	0.640 [‡]
RDW(%)	14.30±1.38	13.71±1.05	0.109 [‡]
Neutrophils (×10 ³ /μL)	3.97±1.05	4.23±1.95	0.676 [‡]
Lymphocytes (×10 ³ /μL)	2.25±0.43	2.46±0.75	0.385 [‡]
Monocytes (×10 ³ /μL)	0.64±0.11	0.57±0.19	0.219 [‡]
Eosinophils (×10 ³ /μL)	0.29±0.37	0.17±0.13	0.380 [‡]
Platelets (×10 ³ /μL)	324.80±81.82	310.86±82.40	0.599 [†]
NLR	1.81±0.55	1.88±1.16	0.842 [‡]
MLR	0.29±0.08	0.25±0.12	0.206 [‡]
PLR	148.74±42.56	132.46±37.06	0.215 [†]

*: mean±SD, †: Mann–Whitney U test, ‡: Independent samples t-test

Discussion

Migraine is one of the most common primary headache disorders in childhood and primarily affects the central nervous system. However, accumulating evidence suggests that migraine is not only a neurovascular disorder but also a condition with a significant inflammatory component (14). In our study, the migraine group demonstrated lower lymphocyte counts, higher MCV levels, and increased PLR values compared with the control group. These findings suggest that such hematological alterations may represent indirect reflections of the neuroinflammatory processes involved in migraine pathophysiology. Accordingly, readily available complete blood count parameters, particularly lymphocyte count, MCV, and PLR, may serve as practical, inexpensive, and clinically applicable indicators of neuroinflammatory activity in childhood migraine.

Previous studies have likewise emphasized the role of immune-mediated inflammation in pediatric migraine. Elevated levels of proinflammatory cytokines, including interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α), as well as pentraxin-3 (PTX-3), a marker involved in both acute and chronic inflammation, have been reported in children with migraine (10,15). Increased levels of these biomarkers indicate immune activation both within the central nervous system and in the peripheral circulation. Monocytes and lymphocytes are key cellular components of the innate and adaptive immune response. Proinflammatory mediators released during migraine attacks may enhance monocyte activation and promote their differentiation into macrophages. Alterations in lymphocyte counts may likewise be associated with immune regulation and systemic inflammatory processes. Although some studies have not demonstrated a significant association between lymphocyte subgroups and pediatric migraine, a mild reduction in lymphocyte counts during the attack period has been reported (16). Since our findings were obtained during the interictal period, the observed hematological changes may reflect chronic low-grade systemic inflammation accompanying migraine rather than transient inflammatory responses occurring during acute attacks.

In our study, MCV values were significantly higher in pediatric migraine patients compared with controls. Although MCV is primarily used in the differential diagnosis of anemia, increasing evidence suggests that erythrocyte indices may also be influenced by systemic inflammation, oxidative stress, and vascular alterations. However, no previous study has clearly demonstrated elevated MCV levels in patients with migraine. On the contrary, available data indicate either no significant difference or lower MCV values in migraine patients compared with controls. For instance, Şahin et al. (17) reported that MCV levels in pediatric migraine patients were comparable to those of the control group, with no statistically significant difference. In adult patients, Ertekin found that individuals with chronic migraine had significantly lower MCV levels compared with those suffering from tension-type headache (18). In our study, the observed increase in MCV may reflect subtle inflammatory, metabolic, or oxidative changes associated with the pathophysiology of pediatric migraine rather than a simple hematological variation. Given that current evidence remains limited and inconsistent, further prospective multicenter studies are warranted to clarify the clinical significance of this finding.

In our study, no significant differences were found in NLR and MLR between migraine patients and controls, suggesting that changes in neutrophil and monocyte counts may have occurred proportionally to lymphocyte changes. Because migraine-related inflammation is typically chronic rather than acute, neutrophil counts may remain relatively stable. If lymphocyte counts decrease while neutrophil counts remain stable or decrease proportionally, NLR may not show a significant increase. Similarly, parallel changes in monocyte and lymphocyte counts may result in stable MLR values. For example, one clinical study reported decreased monocyte counts and increased MLR in migraine patients (19). In our study, the absence of significant differences in MLR may be explained by similar directional changes in monocyte and lymphocyte counts. Furthermore, ratios such as NLR and MLR are often considered markers of infectious or acute inflammatory processes; therefore, their sensitivity may be limited in sterile inflammatory conditions such as migraine.

PLR, defined as the ratio of peripheral platelet count to lymphocyte count, is a readily accessible marker reflecting systemic inflammation. In our study, PLR was found to be increased in pediatric migraine patients. An elevated PLR may theoretically result from an increase in platelet count, a decrease in lymphocyte count, or a combination of both. In the present study, lower lymphocyte counts may have contributed to the higher PLR values observed in the migraine group. In a pediatric migraine study, platelet counts in the migraine group were found to be significantly lower than those in the tension-type headache group (20). However, other studies have suggested that platelet activation, rather than absolute platelet count alone, may play a more important role in migraine pathophysiology. Activated platelets can release proinflammatory mediators, serotonin, and vasoactive substances that may contribute to neurovascular dysfunction and trigeminovascular activation during migraine attacks (21). Therefore, an increased PLR in our study may reflect the combined effect of relative lymphocyte reduction and heightened platelet-related inflammatory activity, supporting

a possible association between migraine and low-grade inflammatory processes. Therefore, the observed increase in PLR should be interpreted with caution, and further well-designed studies are warranted to clarify the underlying biological mechanisms and its potential relationship with neuroinflammatory processes in pediatric migraine.

The prevalence and clinical characteristics of migraine change with age. In our study, no significant differences were observed according to gender, whereas significant differences were identified between age groups. Migraine attacks in preschool-aged children are often shorter in duration and atypical, whereas school-aged children and adolescents tend to exhibit more classical features, with increasing prevalence (1). For example, it has been reported that the frequency of chronic migraine doubles around the age of 12 and that overall migraine prevalence exceeds 18% during adolescence (22). Early-onset migraine may be associated with genetic predisposition or developmental stages of the immune system. Because the immune system is not fully mature during early childhood, migraine attacks at younger ages may manifest through different inflammatory responses, such as cyclic vomiting syndrome or abdominal pain (23). Hormonal and neuroendocrine changes also influence migraine frequency until adolescence. While migraine prevalence is similar between boys and girls before puberty, it tends to be 2–3 times higher in girls after puberty (24). Consistent with these findings, our study demonstrated significant age-related differences but no significant gender-related differences between groups.

Within the migraine group, a significant difference between genders was observed only in erythrocyte count, whereas no differences were found in lymphocyte, monocyte, platelet counts, or inflammatory parameters such as NLR. This finding may be explained by the fact that RBC count in pediatric populations is more strongly influenced by physiological and biological factors than by inflammation. Erythrocyte count is a gender-sensitive parameter in childhood, particularly near puberty, as androgens stimulate erythropoiesis, resulting in higher RBC levels in boys (25). In contrast, lymphocyte and platelet counts, as well as NLR, are more closely related to immune activation and systemic inflammation and are therefore expected to be independent of gender in pediatric migraine (26).

Significant differences in lymphocyte count, platelet count, and NLR values were observed between age groups in our study. This may reflect age-related changes in immune system maturation and hematological responses. Although migraine prevalence increases toward school age and adolescence, studies have shown that prevalence is approximately 5% in children aged 5–10 years and rises to around 15–18% during adolescence, particularly between 12 and 15 years of age (27). Large pediatric reference studies of hemogram-based inflammatory markers have demonstrated that parameters such as NLR, PLR, and LMR vary with age, showing distinct distributions from infancy to adolescence (28). This phenomenon may be explained by immune system maturation, with lymphocyte predominance in early childhood and increasing neutrophil responses with advancing age. Additionally, platelets are known to play roles not only in hemostasis but also in inflammation and immune

modulation, which may lead to age-related variations in platelet counts and platelet-based indices. Accordingly, age-dependent variability in NLR and other inflammatory indices has been reported in neuroinflammatory conditions such as pediatric migraine, supporting the age-related differences observed in our study (29).

No significant differences in hematological parameters were observed between migraine patients receiving flunarizine treatment and those not receiving treatment. However, this finding should be interpreted with caution, as the retrospective design, lack of standardized treatment duration, and relatively small sample size limit the ability to draw definitive conclusions regarding treatment effects.

Flunarizine primarily acts on central calcium channels, with unclear effects on systemic inflammation (30). Previous studies have suggested that combination therapies may influence inflammatory markers; however, such findings cannot be directly extrapolated to flunarizine monotherapy (31). Therefore, our results do not provide sufficient evidence to determine whether flunarizine has a measurable effect on peripheral inflammatory parameters, and further prospective studies are needed to clarify this relationship.

Conclusion

In this study, PLR values were significantly higher in pediatric migraine patients than controls. This finding suggests that migraine in childhood may be associated with inflammatory processes. The inflammatory response in pediatric migraine appears to be independent of gender. Age-based analysis demonstrated significantly higher inflammatory markers in the 12–18 age group compared with the 5–12 age group, age-related increases in inflammatory markers may reflect immune system maturation. These findings indicate that pediatric migraine may be associated with age-sensitive inflammatory mechanisms and suggest that PLR may serve as a readily accessible inflammatory marker in clinical practice. Flunarizine treatment showed no effect on inflammatory parameters.

Limitations

This study has several limitations. Only interictal migraine patients were evaluated, and inflammatory marker changes during migraine attacks were not assessed. The cross-sectional and single-center design limits causal inference and generalizability. Furthermore, the inability to perform subgroup analyses based on flunarizine dose, treatment duration, and pediatric age groups partially restricts interpretation of treatment-related inflammatory changes. Therefore, detailed subgroup analyses of hematological parameters according to specific pediatric age groups could not be performed. Although it is well established that hematological parameters show the most pronounced physiological variations during the neonatal and infancy periods, and tend to be relatively stable in later childhood, certain parameters such as hemoglobin (Hb), MCV, and MCHC may still vary according to age and gender during adolescence. In addition, existing literature demonstrates heterogeneity in age-related reference ranges of

hematological parameters across different populations, which may be influenced by ethnic background, nutritional status, and environmental factors. Accordingly, the inability to perform age-stratified analyses represents an important limitation of this study. Future studies with larger sample sizes and stratification according to age and pubertal stage are needed to provide a more detailed evaluation of hematological parameters in pediatric populations.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Balikesir University (06.01.2026, reference number: 2025/365).

Contribution of the authors

Study conception and design: ÖKA,HA; data collection: OKA,HA; analysis and interpretation of results: OKA,HA,OK; draft manuscript preparation: OKA,HA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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