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Systemic Immune-inflammation Index in Patients with Migraine: Clinical, Scale and Radiological Characteristics

Migrenli Hastalarda Sistemik İmmün-enflamasyon İndeksi: Klinik, Skala ve Radyolojik Özellikler

Duygu ARSLAN MEHDIYEV, Zeynep ÖZÖZEN AYAS, Gülgün UNCU

Eskişehir City Hospital, Clinic of Neurology, Eskişehir, Turkey

ABSTRACT

Aim: Migraine is a common neurological disorder in which inflammation plays a role in its pathophysiology. Systemic immune inflammation index (SII) (platelet x neutrophil/lymphocyte) is a vital parameter that indicates inflammatory response and is used in follow-up and evaluation of prognosis for various diseases. The aim of this study is to compare the hematological parameters of patients with migraine and healthy controls and to determine the correlation between SII with the clinical features of migraine and migraine-related hyperintense lesions on brain magnetic resonance imaging (MRI).

Materials and Methods: Migraine patients over 18 years old, who were admitted to the neurology outpatient clinic in a 48-month period, were included in the study. Healthy individuals were included in the study as the control group. Age, gender, duration of migraine diagnosis, migraine attack frequency, presence of aura, smoking, family history, presence of systemic disease, visual analog scale and migraine disability scale scores, presence of migraine-related hyperintense lesions on brain MRI were recorded for all patients in the study. Hemoglobin (Hb), red cell distribution width (RDW), neutrophil, lymphocyte, thrombocyte counts and SII values of the control group and migraine patients were compared.

Results: Hb, lymphocyte, thrombocyte, and RDW levels were significantly higher in migraine patients (n=150) than in the control group (n=178) (p=0.03, p=0.05, p=0.002, p=0.000, respectively). SII was found to be significantly higher in female patients with a diagnosis of migraine compared to males (p=0.01). RDW value was significantly higher in patients with hyperintense lesions on MRI than in those without lesions (p=0.001).

Conclusion: In our study, it is thought that RDW in patients with migraine may be a marker for the presence of migraine-related hyperintense lesions on MRI. However, although SII had a difference between genders in migraine, it has been observed that it is not a parameter that will contribute to the prediction for the disease for now.

Keywords: Migraine, inflammation, red cell distribution width, magnetic resonance image

ÖZ

Amaç: Migren fizyopatolojisinde enflamasyonun rol oynadığı sık görülen nörolojik bir hastalıktır. Sistemik immün-enflamatuvar indeks (SII) (trombosit x nötrofil/lenfosit) enflamatuvar yanıtı gösteren ve pek çok hastalık için takipte ve prognozu değerlendirmede önemli bir parametredir. Çalışmamızın amacı, migren hastalarının hematolojik parametrelerinin sağlıklı kontrollerle kıyaslanması ve SII'nin migren kliniği ile ve beyin manyetik rezonans görüntülemedeki (MRG) migren-ilişkili hiperintens lezyonlarla arasındaki bağlantıyı saptamaktır.

Gereç ve Yöntem: Çalışmaya, 48 aylık süreçte nöroloji polikliniğine başvuran ve migren tanısıyla izlenen 18 yaş üzeri hastalar alındı. Çalışmaya kontrol grubu olarak sağlıklı bireyler dahil edildi. Çalışmadaki tüm hastaların yaş, cinsiyet, migren tanısının süresi, migren atak sıklığı, aura varlığı, sigara içiciliği, aile hikayesi, sistemik hastalık varlığı, görsel analog skala ve migrene bağlı dizabilite ölçeği skorları, beyin MRG'de migren-ilişkili hiperintens lezyonların varlığı kaydedildi. Kontrol grubu ve migren hastalarının hemoglobin (Hb), eritrosit dağılım hacmi (RDW), nötrofil, lenfosit, trombosit ve SII değerlerine bakılarak birbirleriyle karşılaştırıldı.

Bulgular: Hb, lenfosit, trombosit ve RDW düzeyleri migrenli hastalarda (n=150), kontrol grubuna göre (n=178) anlamlı oranda yüksekti (sırasıyla p=0,03, p=0,05, p=0,002, p=0,000). Migren tanılı kadın hastalarda erkeklere kıyasla SII anlamlı olarak daha yüksek saptandı (p=0,01). MRG'de hiperintens lezyonu olan hastalarda, olmayanlara göre RDW değeri anlamlı düzeyde daha yüksek tespit edildi (p=0,001).

Address for Correspondence: Zeynep ÖZÖZEN AYAS MD, Eskişehir City Hospital, Clinic of Neurology, Eskişehir, Turkey
Phone: +90 505 903 96 05 **E-mail:** zozozen@hotmail.com **ORCID ID:** orcid.org/0000-0002-9302-5543
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Sonuç: Çalışmamızda migrenli hastalarda RDW'nin MRG'deki migren-ilişkili hiperintens lezyon varlığı açısından bir belirteç olabileceği düşünülmektedir. Ancak SII'nin migrende cinsiyetler arası farklılığı olsa da, hastalık için şimdilik öngörüye katkıda bulunacak bir parametre olmadığı gözlenmiştir.

Anahtar Kelimeler: Migren, enflamasyon, eritrosit dağılım genişliği, manyetik rezonans görüntüleme

INTRODUCTION

Headache is a common complaint in society, which almost everyone experiences at least once and is the most common reason for admission to a neurology outpatient clinic. Among the primary headaches, migraine is the third most common disease in the world and the third most common disease that causes disability in both men and women under the age of 50 years[1]. The overall prevalence of migraine is 12%, 18% in women and 6% in men[2]. In Turkey, the prevalence of migraine in the age group of 15-55 years is 16.4%; 21.8% in women and 10.9% in men[3].

Although the pathophysiology of migraine remains unclear, it is currently accepted that it starts with cortical spreading depolarization and results in peripheral and central sensitization. With this depolarization wave stimulating the trigeminovascular system, various neuropeptides are secreted, causing vascular dilatation and sterile neurogenic inflammation resulted from the extravasation of plasma proteins. Sterile neurogenic inflammation is the mechanism responsible for the pain phase[4].

There are studies regarding the use of inflammation and related biomarkers in many diseases. As the neutrophil count increases in response to inflammation, the lymphocyte count decreases, so the neutrophil/lymphocyte ratio can be used as an inflammation marker[5]. Systemic immune-inflammation index (SII) is a parameter that shows inflammation and immune status calculated using neutrophil/lymphocyte ratio and thrombocyte value[6]. It was shown that SII could be used as a marker in different cancer types such as hepatocellular carcinoma, small cell lung cancer, pancreatic cancer, and cervical cancer and in the prognosis of many diseases such as coronary artery disease and Severe acute respiratory syndrome-Coronavirus-2[6-9].

Since there is a neurogenic inflammation in migraine, studies have been performed to evaluate the neutrophil/lymphocyte ratio[10-12]. It was also shown that platelet activation may play a role in the pathophysiology of migraine[13]. Studies in which neutrophil, lymphocyte, monocyte and thrombocyte values and their ratios to each other in migraine patients have been studied[14,15]. However, as of May 2022, there is no publication in the literature evaluating the relationship of SII with migraine. Our study, which presents these data for the first time, makes a significant contribution to the literature. We designed this study to understand the relationship between SII and migraine, as it is a marker of inflammation and sterile neurogenic inflammation plays a role in the pathogenesis of migraine.

The purpose of our study is to examine hemoglobin (Hb), red cell distribution width (RDW), neutrophil, lymphocyte and platelet values in patients diagnosed with migraine, as well as SII level, which is a crucial parameter in inflammation. Also, the clinical characteristics of migraine patients and the presence of migraine-related hyperintense lesions on magnetic resonance imaging (MRI) and their correlation with clinical and blood parameters were investigated.

MATERIALS AND METHODS

Patients over the age of 18 years, who were followed up with the diagnosis of migraine according to the International Classification of Headache Disorders (ICHD) and who were admitted to Eskişehir City Hospital Neurology Outpatient Clinic between November 1, 2018, and November 1, 2020, were included in the study. Individuals over the age of 18 years, who were referred for work-school applications and were not diagnosed with systemic diseases including migraine, were included in the study as the control group. The presence of aura, nausea, vomiting, and photo-phonophobia was recorded in patients diagnosed with migraine. The duration of the diagnosis of migraine, the frequency of pain, smoking, family history in terms of migraine, and presence of a systemic disease was questioned. The diseases classified as systemic diseases in our study included diabetes, hypertension, asthma, chronic obstructive pulmonary disease, and thyroid diseases. The severity of migraine pain was calculated using the visual analog scale (VAS) and functional loss using the Migraine Disability Scale (MIDAS)[16,17].

In the VAS evaluation, the headache was grouped as mild (1-3 points), moderate (4-6 points), severe (7-8 points), and very severe (9-10 points).

MIDAS is a practical questionnaire used to evaluate the degree of migraine, consisting of 7 parts. While the first five questions evaluate functionality, the frequency and severity of pain are scored in the last two questions. The total score is graded as grade I between 0 and 5 points, grade II between 6 and 10, grade III between 11 and 20, and grade IV between 21 and above[18].

Demographic characteristics, Hb, RDW, lymphocyte, thrombocyte, neutrophil, and SII values of the patient and control groups were recorded. These values were compared between subgroups in migraine patients and between migraine patients and healthy controls.

Patients with a diagnosis of migraine were divided into cases with periventricular white matter localization in brain MRI, hyperintense lesions smaller than 5 mm and the number of the lesions limited with 4-12 and patients without lesions in brain MRI. It was checked whether there was any difference in clinical features and hemogram parameters in patients with and without migraine-related hyperintense lesions in MRI.

According to the ICHD[1], patients with headaches other than migraine and ischemic and/or vasculitic lesions in brain MRI were not included in the study. Those with the signs of active infection were also excluded from the study.

Approval for this study was obtained from the Non-invasive Clinical Studies Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (number: E-25403353-050.99-122340, date: 15.12.2020).

Statistical Analysis

Mean, standard deviation, median, interquartile difference, ratio, and frequency values were used in the descriptive statistics of the data. The distribution of variables was determined with the Kolmogorov-Smirnov test. In quantitative data analysis, the independent sample t-test was used in groups with normal distribution and the Mann-Whitney U test in groups that did not show normal distribution. The chi-square and Fisher exact tests analyzed the qualitative data, and the Spearman correlation analysis was used for non-parametric data in correlation analysis. Statistical Package for the Social Sciences 21.0 program was used in the analyses. A p value of <0.05 was considered statistically significant in all analyses.

RESULTS

A total of 150 migraine patients, 121 (80.7%) female and 29 (19.3%) male, were included in the study. Of the healthy individuals in the control group, 129 (72.5%) were female, and 49 (27.5%) were male. The mean age of migraine patients was 33.25±8.93 years, while the mean age of the healthy control group was 30.77±9.77 years.

The mean duration of diagnosis of migraine was 7.58 years (0.8-35), the frequency of pain was 8.71 (0.08-30) month on average, and the mean VAS score was 8.37 (3-10) (Table 1). The mean monthly pain frequency was found to be 8.71 (0.08-30) and the mean VAS score was 8.37 (3-10) (Table 1). It was determined that 22.7% (34) of the migraine patients were MIDAS grade I, 24% (36) were grade II, 20.7% (31) were grade III, and 32.7% (49) were grade IV (Table 1). Eighty-four (56%) patients had a family history, 58 (38.7%) patients were found to be smoking, and 28 (18.7%) patients (9 patients with hypertension, 6 with diabetes mellitus, 6 with thyroid disorder, 4 with chronic obstructive pulmonary disease and 3 with asthma) had a comorbid systemic disease (Table 1). Considering the clinical features, photo/phonophobia was detected in 136 (90.7%) patients, aura in 69 (46%) patients, nausea in 106 (70.7%) patients, and vomiting in 50 (33.3%) patients (Table 1). All patients included in the study underwent brain MRI, and a hyperintense lesion on MRI was detected in 57 (38%) patients (Table 1).

The blood parameters of the migraine and control groups were compared. Hb level, RDW, thrombocyte, and lymphocyte counts were significantly higher in the migraine group than in the control group (p=0.03, p=0.000, p=0.002, p=0.05, respectively) (Table 2).

When the migraine group was compared by gender, it was found that platelet, RDW, and SII values were significantly

Table 1. Clinical features of migraine patients

Variables	Migraine (n=150) Mean±standard deviation (minimum-maximum) / n (%)	
MIDAS	2.63±1.16 1-4	
The duration of the diagnosis	7.58±7.47 0-35	
The frequency of pain	8.71±8.47 0-30	
VAS	8.37±1.44 3-10	
Family history	n	%
Yes	84	56
No	66	44
Smoking	n	%
Yes	58	38.7
No	92	61.3
Systemic disease	n	%
Evet	28	18.7
Hayır	122	81.3
Hyperintense lesion on MRI	n	%
Yes	57	38
No	93	62
Photophonophobia	n	%
Yes	136	90.7
No	14	9.3
Nausea	n	%
Yes	106	70.7
No	44	29.3
Vomiting	n	%
Yes	50	33.3
No	100	66.7
Aura	n	%
Yes	69	46
No	81	54

MIDAS: Migraine Disability Scale, VAS: Visual analog scale, MRI: Magnetic resonance imaging

higher in women than in men, but the Hb values were significantly lower (Table 3).

Control group data were compared according to gender. Age and Hb values were markedly lower in women than in men, and RDW values were markedly higher (p=0.001, p<0.001, p=0.01, respectively). SII value did not differ significantly between men and women in the control group (Table 4).

Considering the correlation of clinical and laboratory data with each other, it was seen that Hb level was positively correlated with smoking.

Table 2. Comparison of blood parameters of migraine-control group

	Migraine (n=150) Mean±standard deviation (minimum-maximum)	Control (n=178) Mean±standard deviation (minimum-maximum)	p value
Hb	14.02±1.47 9-18	13.7±1.38 10-17	**p=0.03***
RDW	13.75±2.97 10-39	11.87±1.39 2-19	**p<0.001****
Neutrophil	4450±1477 1750-11160	4365±1217 1760-7380	p=0.97
Thrombocyte	266.288±66.390 85000-481000	245.083±49.901 153000-441000	**p=0.002***
Lymphocyte	2340±712 1050-5300	2182±586 930-4860	**p=0.05***
SII	541.530±2.73 158673-1900100	521.021±2.29 156922-1525465	p=0.7

*p<0.05, **p<0.001.

Hb: Hemoglobin, RDW: Red cell distribution width, SII: Systemic inflammatory index

Table 3. Comparison of the clinical and laboratory values of the migraine group by gender

	Female (n=121) Mean±standard deviation (minimum-maximum)	Male (n=29) Mean±standard deviation (minimum-maximum)	p value
Age	34±9 18-62	31±8 20-47	p=0.13
The duration of the diagnosis	8±7 0-35	7±7 0-30	p=0.17
The frequency of pain	8±8 0-30	10±7 1-30	p=0.17
VAS	8±1 3-10	8±7 6-10	p=0.99
MIDAS	3±1 1-4	3±7 1-4	p=0.08
Hb	13±1 9-16	16±1 13-18	**p<0.001****
RDW	14±3 10-39	13±2 11-19	**p=0.01***
Neutrophil	4410±1477 1750-11160	4614±1491 2960-9470	p=0.69
Thrombocyte	273.464±67488 154000-481000	236.034±52580 85000-327000	**p=0.01***
Lymphocyte	2273±626 1050-3860	2618±958 1490-5300	p=0.14
SII	564.134±282010 158673-1900100	447.217±215927 165952-1118044	**p=0.01***

*p<0.05, **p<0.001.

Hb: Hemoglobin, RDW: Red cell distribution width, SII: Systemic inflammatory index, MIDAS: Migraine Disability Scale, VAS: Visual analog scale

The presence of hyperintense lesions on MRI was found to be positively associated with the RDW count. Platelet count was negatively correlated with family history and smoking (Table 5).

RDW value was positively correlated with hyperintense lesions on MRI. When the migraine group was compared by the presence of hyperintense lesions in MRI, the attack frequency and RDW values were found to be significantly higher in those with hyperintense lesions on MRI. There was no significant relationship between neutrophil, lymphocyte, thrombocyte, and SII and MRI lesions (Table 6).

When migraine patients were compared in terms of the presence of aura, the mean age and duration of illness of those with aura were significantly higher than those without aura (p=0.008, p=0.01, respectively). No significant differences were observed between patients with and without aura in Hb, RDW, and SII values.

Family history of migraine was positive in 55.3% of women and 56.6% of men.

When patients diagnosed with migraine were compared for smoking, it was found that Hb levels were significantly higher in smokers compared to non-smokers (p=0.007), and platelet count was significantly lower (p=0.01).

When the migraine group was compared for the presence of systemic disease, it was found that the mean age of those with the systemic disease was significantly higher (p=0.004) compared to those without systemic disease.

When the relationship of Hb level with the presence of smoking and systemic disease was evaluated, it was revealed that there was a predictive relationship between smoking and Hb (sig: 0.009) (Table 7).

The relationship of smoking and systemic diseases with the presence of hyperintense lesions on MRI was not found to be significantly predictive (Table 8).

Table 4. Comparison of the control group by gender

	Female (n=129) Mean±standard deviation (minimum-maximum)	Male (n=49) Mean±standard deviation (minimum-maximum)	p value
Age	33.25±8.93 18-62	36±9.22 18-66	**p=0.001****
Hb	13±1 10-16	15±0.9 13-17	**p<0.001****
RDW	12±1.57 2-19	11.5±0.66 10-14	**p=0.01***
Neutrophil	4413±1233 1930-7380	4237±1177 1760-7180	p=0.38
Thrombocyte	248.455±54.065 153000-441000	236.204±35.727 171000-339000	p=0.29
Lymphocyte	2187±611 930-4860	2187±611 930-4860	p=0.99
SII	533.520±236.374 199169-1525465	488115±211025 156992-1061219	p=0.16

*p<0.05, **p<0.001.

Hb: Hemoglobin, RDW: Red cell distribution width, SII: Systemic inflammatory index

Table 5. Correlation of clinical and laboratory data of the migraine group

Variable		Hb	RDW	SII	Lymphocyte	Neutrophil	Thrombocyte
Hyperintense lesion on MRI	R	-0.033	0.264**	0.075	-0.103	-0.006	-0.077
	P	0.691	0.001	0.362	0.211	0.945	0.348
Family history	R	0.158	-0.128	-0.061	-0.025	0.091	**-0.173***
	P	0.054	0.118	0.455	0.766	0.269	**0.035**
Smoking	R	**0.236****	0.037	-0.077	0.074	0.142	**-0.194***
	P	**0.004**	0.652	0.350	0.366	0.082	**0.017**

Hb: Hemoglobin, RDW: Red cell distribution width, SII: Systemic inflammatory index, MRI: Magnetic resonance imaging

Table 6. Comparison of the migraine group according to the presence of lesions in MRI

	Presence of lesions in MRI (n=57) Mean±standard deviation (minimum-maximum)	Absence of lesions in MRI (n=93) Mean±standard deviation (minimum-maximum)	p value
Gender **Female** **Male**	**n** **%** 47 82.5 10 17.5	**n** **%** 74 79.6 19 20.4	p=0.66
Age	34.84±8.44 20-55	32.27±9.12 18-62	p=0.08
The duration of the diagnosis	7.31±7.2 0-35	7.7±7.6 0-30	p=0.86
The frequency of pain	6.9±7.34 0-30	9.78±8.9 1-30	**p=0.03***
VAS	8.46±1.46 3-10	8.32±1.4 4-10	p=0.51
MIDAS	2.44±1.13 1-4	2.75±1.16 1-4	p=0.1
Hb	13.28±1.82 9-18	13.38±1.16 9-18	p=0.71
RDW	14.29±2.3 10-25	13.41±3.28 11-39	**p=0.001***
Neutrophil	4413±1233 1930-7380	4237±1177 1760-7180	p=0.94
Thrombocyte	263263±66444 146000-481000	268.045±66.651 85000-461000	p=0.34
Lymphocyte	2271±744 1170-5140	2382±693 1050-5300	p=0.21
SII	552479±2.68 158673-1582094	534819±2.78 165952-1900100	p=0.36

*p<0.05.

Hb: Hemoglobin, RDW: Red cell distribution width, SII: Systemic inflammatory index, MRI: Magnetic resonance imaging, MIDAS: Migraine Disability Scale, VAS: Visual analog scale

Table 7. Linear regression analysis of hemoglobin level with the presence of smoking and systemic disease

Model		Unstandardized coefficients		Standardized coefficients	T	Sig.
		B	Standard error	Beta		
1	**(Constant)**	13.143	0.186		70.780	0.000
	Smoking	0.732	0.276	0.212	2.649	0.009
	Systemic disease	-0.461	0.345	-0.107	-1.336	0.184

a. Dependent variable: hemoglobin

Table 8. Binary logistic regression analysis of the relationship between smoking and systemic consumption with the presence of hyperintense lesion on MRI

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI for EXP(B)	
								Lower	Upper
	Smoking (1)	-0.040	0.349	0.013	1	0.908	0.960	0.485	1.903
	Systemic disease (1)	-0.737	0.475	2.413	1	0.120	0.478	0.189	1.213
	Constant	-0.737	0.242	9.287	1	0.002	0.478		

a. Dependent variable: hyperintense lesion on MRI. Variable(s) entered on step 1: smoking, systemic disease.

CI: Confidence interval, MRI: Magnetic resonance imaging

DISCUSSION

Migraine is a chronic disease that affects a large part of society and causes loss of labour and economic and social impact, especially in young adults. In this study, the characteristics of headache and hematological parameters that may guide the diagnosis, prognosis, and radiological findings of migraine disease diagnosed with associated symptoms were investigated.

The annual prevalence of migraine in the general population was reported to be 12% and it was found that the prevalence was mainly between the ages of 30 and 39 years in studies[19,20]. Similarly, the mean age of migraine patients in our study was found to be 33.25±8.93 years.

While the annual and lifetime prevalence of migraine is 18% and 33%, respectively, in women, this rate is 6% and 13%, respectively, in men. Migraine, which is three times more common in women, was found to have a female/male ratio of approximately 4 in our study[21.]

Migraine is a disease in which a genetic background and environmental and lifestyle factors are combined. About 70% of migraine patients have first-degree relatives with a history of migraine, and it has been reported that the risk of migraine increases fourfold in the relatives of patients with aura[22].

Our study found that 56% of the patients had a history of migraine in their first-degree family members. Although the prevalence of migraine is higher in women, it has been reported that the genetic predisposition in men is similar or higher than in women[23]. Again, in a recent study, monthly migraine frequency was associated with genetic predisposition only in men[24]. Although the number of male patients was less in our study, family history was found in similar rates (55.3% and 56.6%) in males and females.

In patients with migraines, the presence of aura generally associated with brainstem dysfunction is seen in approximately one-third of patients[22]. In our study, 46% of patients with migraines were found to have an aura. Our study observed that the mean age and duration of disease diagnosis of migraine patients with aura were higher than those without aura. It is thought that this difference may be related to the fact that people with long-term illness better recognize the nature and auras of the disease over time. No significant difference was found between Hb, RDW, and SII values between migraine patients with and without aura in our study.

It is known that there are hyperintense lesions in the subcortical and white matter that do not cause any clinical symptoms in brain MRI examinations of migraine patients. In our study, hyperintense involvement in migraine-associated white matter was observed in 38% of brain MRI. It was reported as 43.1% in a recent study and 32% in the study of Zhang et al.[25,26]. Methodological differences in studies are thought to alter the results. Age, presence of aura, the severity of headache, and duration of migraine have been reported to be risk factors for the development of white matter hyperintensities[25]. Although there was no significant difference in these risk factors in our study, it was found that the frequency of attacks was significantly higher in those with MRI hyperintense lesions than those without. In addition, the relationship between the presence of hyperintense lesions in MRI and the elevation of RDW suggests that RDW may be a marker for the presence of lesions.

Migraine and anemia are two common diseases that can be seen in young people, and a clear relationship between them has not been defined. In a study, the Hb level measured in migraine attacks was found within normal limits, and no significant difference was found with the control group[27]. On the other hand, it was shown that Hb values measured during the non-attack period were lower in migraine patients compared to healthy control, and in a study consisting of 100 patients in which patients were evaluated during an attack, it was shown that Hb values significantly decreased during an acute migraine attack[11,14]. In our study, Hb and RDW values were found to be significantly higher in migraine patients compared to the control group ($p=0.03$ and $p<0.001$, respectively). RDW, which indicates erythrocyte distribution width and shows anisocytosis, is expected to increase in cases of decreased Hb and iron deficiency. However, we think that the expected relationship between Hb and RDW may not have been observed since iron parameters were not evaluated in our study, and multifactorial reasons may affect the results.

A population-based, large cross-sectional study showed that migraine prevalence was lower in 2385 women, especially in patients with Hb values below 11.5 g/dL[28]. In society, low Hb levels are already more common in females[29]. In our study, when women and men in the migraine and healthy control groups were compared within themselves, as expected in both groups, the Hb level was found to be low, and the RDW level was higher in women than in men. Also, in correlation analyses, no relationship was found between Hb and RDW values of migraine patients and clinical characteristics (pain frequency, migraine diagnosis time, pain severity, nausea, vomiting, photo-phonophobia).

It is thought that platelet activation may be increased in patients with migraines, and this may be a part of sterile neurogenic inflammation in migraine etiology[30]. One study revealed that the platelet level was increased in migraine patients compared to controls[11]. On the other hand, some studies do not show a statistically significant difference in platelet levels in adult and pediatric migraine patients than in controls[12,31]. In our study, when the migraine and control groups were compared, platelet

values were significantly higher in patients diagnosed with migraines than in the control group (p=0.002). In addition, in our study, when migraine patients were compared in terms of gender, platelet value was found to be significantly higher in women compared to men, but no significant difference was observed between men and women in the control group. These data suggest that platelets may play a role in the inflammatory vascular process in the pathogenesis of migraine, which may be more pronounced, especially in women.

SII is a parameter for clinical worsening and invasive ventilation support in Coronavirus disease-2019 disease[32]. In evaluating the risk of major cardiovascular events in coronary artery disease, it was found to be prognostically significant in many types of cancer[6,8]. No study evaluating the systemic inflammatory index related to headache or migraine was found.

In our study, the SII value was significantly higher in women with migraine than in men. No similar difference was found between men and women in the control group. It was found that female gender was associated with high SII value only in the presence of migraine. It suggests that high SII values may lead to a diagnosis of migraine in women although not in all migraine patients, especially in women with a more common disease. The absence of similar changes in male patients may be related to the low number of male patients in our study. Studies involving larger patient populations are needed.

Lymphocyte values were significantly higher in patients diagnosed with migraine than controls. It is expected that there is a neurogenic inflammation in migraine and neutrophils increase while lymphocytes decrease in inflammation. However, contrary to expectations, lymphocyte counts were found to be high in migraine patients in our study. This result may be related to taking blood samples during the inter-attack period, not during an attack.

Inflammatory markers were also expected to be higher in patients with MRI lesions, with the prediction that white matter lesions that can be seen in brain MRI in migraine patients are caused by inflammation. A study has shown that white matter lesions on MRI are seen more frequently in patients with a higher neutrophil/lymphocyte ratio[10]. However, no significant relationship was found between laboratory parameters such as neutrophil, lymphocyte, thrombocyte, and SII values and MRI lesions in our study.

When the neutrophil/lymphocyte ratio, which is considered an inflammation marker, is considered during the attack period of migraine patients, it was significantly higher[14,27] but the same relationship could not be demonstrated in the period between attacks[12]. Our study concluded that inflammation markers were not high because the patients were evaluated in the outpatient clinic during or outside the attack.

In the relationship between migraine and RDW, inflammation and oxidative stress play a role by changing iron metabolism. The erythrocyte half-life is shortened, and the response of the bone marrow to erythropoietin decreases. It was reported that there is a positive correlation between RDW inflammation and cytokines[33,34]. In our study, it should be considered that it can be used in diagnosis and prognosis because the RDW level was significantly higher in both migraine patients compared to controls and MRI positive patients compared to MRI negative ones.

As shown and expected in previous studies, it is found that smokers have higher Hb levels and lower platelet levels[31]. In our study, the mean age of patients with systemic diseases was higher, and the frequency of systemic diseases such as diabetes and hypertension increased with age, which supports this finding.

Study Limitations

The study's limitations are its retrospective nature, failure to obtain laboratory values during a migraine attack, and failure to look for concurrent inflammatory cytokines.

CONCLUSION

In our study, we could not find a significant relationship between the clinic and MRI lesions and SII, but we found that SII significantly increased in the control group, especially in female patients compared to men. This result has revealed that studies in which SII can provide more guidance in the diagnosis of female patients and/or with more male patients are needed. We have found that RDW and thrombocyte elevation in blood parameters may be much more significant than Hb and lymphocytes in migraine patients. The presence of RDW correlation with MRI lesions suggested that RDW could guide in diagnosis, follow-up, and prognosis.

Since our study was conducted in the inter-attack period, there is a need for comprehensive studies to be conducted by including more cases that look for similar blood parameters during the attack period and compare with each other.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Non-invasive Clinical Studies Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (number: E-25403353-050.99-122340, date: 15.12.2020).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.A.M., Z.Ö.A., Concept: D.A.M., G.U., Design: D.A.M., Z.Ö.A., G.U., Data Collection or Processing: D.A.M., Z.Ö.A., G.U., Analysis or Interpretation: D.A.M., Z.Ö.A., Literature Search: D.A.M., Z.Ö.A., G.U., Writing: D.A.M.

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