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Evaluation of Monocyte/Lymphocyte, Neutrophil/Lymphocyte, and Platelet/Lymphocyte Ratios in Patients with Temporal Lobe Epilepsy

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Abstract

Objective: This study aimed to determine the levels of monocyte/lymphocyte, neutrophil/lymphocyte, and platelet/lymphocyte (PLR) ratios in patients with mesial temporal lobe epilepsy, which is considered to be a chronic inflammatory brain disease, by comparing with healthy individuals of similar age and gender and to reveal the role of these values in the disease process.

Methods: In our retrospective single-center study, 76 patients who were diagnosed with mesial temporal lobe epilepsy and 47 healthy volunteers of similar age and gender were included.

Results: While neutrophil/lymphocyte and monocyte/lymphocyte ratio values were statistically significantly higher in the patient group, there was no difference between the 2 groups in terms of platelet/lymphocyte ratio. It was found that the presence of mesial temporal sclerosis, febrile convulsion, or trauma, and seizure type and frequency did not cause any changes on neutrophil/lymphocyte, monocyte/lymphocyte, and platelet/lymphocyte ratio values. There was a positive and statistically significant correlation between disease duration and neutrophil/lymphocyte, monocyte/lymphocyte, and platelet/lymphocyte ratio values. It was determined that values above 0.2 for monocyte/lymphocyte ratio and 1.99 for neutrophil/lymphocyte ratio can be used in the diagnosis of mesial temporal lobe epilepsy with high sensitivity and specificity.

Conclusions: Considering that patients with mesial temporal lobe epilepsy have higher monocyte/lymphocyte and neutrophil/lymphocyte ratio values and neutrophil/lymphocyte and monocyte/lymphocyte ratio values increase as the duration of the disease increases; it can be suggested that patients with mesial temporal lobe epilepsy have increased inflammatory activity compared to healthy controls, this activity continues to increase as the duration of the disease increases and contributes to the progressive process of mesial temporal lobe epilepsy.

Keywords: Monocyte/lymphocyte ratio, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, mesial temporal lobe epilepsy, inflammation

INTRODUCTION

Epilepsy is a chronic brain disorder characterized by unprovoked seizures.[1] Epileptic seizure is a clinical condition that occurs when the normal activity of the brain is disrupted as a result of temporary abnormal electrical activity in nerve cells. Epileptic seizures can be classified under 3 headings as generalized, focal, or unknown onset. Generalized seizures are those that diffusely begin in the brain and maybe convulsive or non-convulsive.

Epilepsy is observed in all age groups, but its incidence varies markedly with age, and 30% of new cases with epilepsy begin in childhood.[2] This serious neurological disorder is the most common neurological disorder in children and is a major cause of mortality and disability.[2] In adults, the incidence of new cases with epilepsy over the age of 65 years is high. The prevalence of epilepsy in the community is approximately 1%-3%.[3]

Approximately 60% of all epilepsies are focal epilepsy, and approximately one-third of these patients have temporal lobe epilepsy (TLE). Temporal lobe epilepsy is the most common form of localization-related epilepsy and is also the form that is most effectively treated with current surgical procedures.[4] Most patients with TLE have a family history or history of infection, trauma, or febrile convulsions in early childhood. While seizures can be controlled for a limited time with medical treatment, the progression of the disease cannot be stopped. According to the classification of epileptic syndromes, TLE is divided into 2 main groups: the first and most common of focal epilepsies is mesial TLE (MTLE), in which the main seizures occur in temporal medial structures such as the hippocampus, entorhinal cortex, amygdala, and parahippocampal gyrus. Approximately 30% of MTLE patients have seizures that do not respond to current antiepileptic drug therapy.[4,5] The most prominent feature of MTLE is hippocampal sclerosis, which is characterized by loss of hippocampal neurons accompanied by gliosis and abnormal axonal sprouting.[6,7] The second type is lateral TLE, where the seizure affects the temporal neocortex, which includes the superior, middle, and inferior temporal regions, the temporal-occipital and temporal-parietal junctions, and the sensory connectivity areas of hearing, vision, and speech functions.[8] Various clinical features are used for the initial differentiation

of mesial and lateral temporal lobe seizures. While fear, "déja vu" and "jamais vu," emotions, olfactory hallucinations, epigastric sensation, and autonomic changes are observed in mesial temporal lobe seizures, simple sensory hallucinations (auditory, vestibular, or gustatory), receptive aphasia, and focal sensorimotor phenomena are frequently observed in lateral temporal lobe seizures.[9] The underlying pathophysiology of TLE is not clearly understood. Recent studies have revealed that TLE is a progressive process and uncontrolled progressive inflammation may play a role in this condition.[10,11] Increasing evidence has shown that the immune system plays an important role especially in the emergence of MTLE.[12-14] In an autopsy study conducted by Kan et al.[15] the neocortical and hippocampal tissues of patients diagnosed with MTLE were pathologically examined, and proteins showing the link between increased inflammatory cells and cytokines and chemokines were detected compared to controls.[15] In addition, it has been found that inflammation contributes to the emergence or progression of epilepsy in animal models of epilepsy.[16] In recent studies, it has been suggested that the administration of anti-inflammatory drugs in addition to traditional antiepileptic drugs for providing seizure control in epileptic patients may be more effective in controlling seizures and stopping the progression of the disease than antiepileptic drugs alone.[17]

Today, numerous studies have revealed that monocyte/lymphocyte (MLR), neutrophil/lymphocyte (NLR), and platelet/lymphocyte (PLR) ratios are associated with the progression and prognosis of the disease in many diseases, including inflammatory brain disorders.[18,19] Actually, high NLR and PLR values are associated with poor prognosis and short survival in many cancers, including brain gliomas and metastases.[20,21] These ratios, which are easily obtained from complete blood count, can be superior to other inflammatory parameters because they do not require additional cost and are easily accessible.

Therefore, this study aimed to determine the levels of MLR, NLR, and PLR, which are potential new biomarkers of inflammation, in patients with MTLE, which is considered a chronic inflammatory brain disease, by comparing them with healthy controls of similar age and gender and to reveal the possible role of these values in the disease course.

METHODS

Establishment of the Patient and Control Groups

This retrospectively designed study included 76 patients aged 18 years and over, who applied to Sivas Cumhuriyet University Faculty of Medicine Neurology Department between January 01, 2010, and December 01, 2020, and were diagnosed with MTLE based on seizure type, anamnesis, and cranial magnetic resonance (c.MRI) imaging. There was no gender restriction among the patients.

Patients with chronic heart, lung, or kidney failure, connective tissue disease, hematological or psychiatric disease, malignancy, acute/chronic inflammatory or autoimmune disease or thyroid disorder, having a history of infection in the last 2 weeks, using immunosuppressants or anti-inflammatory drugs, having a neurodegenerative disease or mental retardation, having neuroleptic drug, alcohol or illegal substance abuse, having a history of the acute coronary syndrome, acute cerebrovascular disease or surgery in the last 3 months, and being pregnant were not included in our study.

Our control group, on the other hand, consisted of 47 healthy volunteers similar to our patient group in age and gender, and without comorbidity and regular drug use, who were examined in our outpatient clinic and gave blood samples for other reasons.

The informed consent form was obtained from each patient and control, and only the patients who gave consent were included in the study.

Ethics committee approval of our study was obtained from the Non-Interventional Ethics Committee of Sivas Cumhuriyet University (Date: March 10, 2021, Decision no: 2021-03/02).

Questioning Individuals in the Study Group and Evaluating Parameters

For all patients included in the study, age, gender, age of onset of epilepsy, duration of disease, seizure type, seizure frequency (including focal seizures with or without affected consciousness), family history, febrile convulsion (simple or complex) or trauma, the presence of mesial temporal sclerosis (MTS), serum neutrophil, lymphocyte and monocyte counts, and MLR, NLR, and PLR values obtained by dividing these values by each other were evaluated. Similarly, age, gender, blood neutrophil, lymphocyte and monocyte count, and MLR, NLR, and PLR levels were measured for controls.

Evaluation of Blood Parameters

Relevant measurements were made from blood samples taken from the right antecubital vein into dry and Ethylenediaminetetraacetic acid (EDTA) tubes while the patients were in the resting position. While dry tubes were used for biochemical analysis, tubes with EDTA were used in hematological tests. Complete blood counts were performed on the Diagon branded Mindray BC-6800 device, and neutrophil, platelet, and monocyte counts were obtained from these measurements. MLR, NLR, and PLR values were found by dividing these values by each other.

Biochemical analyses (glucose and creatinine levels) were performed with a fully automated nephelometric method using the same brand kits on the Beckman Coulter AU5800 device (Beckman Coulter Inc, Hialeah, Florida).

Evaluation with Cranial Magnetic Resonance Imaging

Cranial imagings performed by the Department of Radiology of Sivas Cumhuriyet University on a magnetic resonance imaging device of Siemens branded Magnetom Aera 1.5 Tesla 2013 model were evaluated with the automation system over the Sectra Uniview system. A radiologist and a neurologist specialist, independent of each other, evaluated the images for any abnormality, the presence of MTS was determined accordingly, and the patients were included in the study accordingly.

Statistical Analysis

The data obtained from our study were evaluated by using the Statistical Package for the Social Sciences Version 22.0. (IBM SPSS Corp.; Armonk, NY, USA). When the parametric test assumptions were fulfilled (Kolmogorov–Smirnov), the significance test of the difference between the 2 means was used while comparing the measurements obtained from 2 independent groups. On the other hand, when parametric test assumptions could not be fulfilled, the Mann–Whitney *U* test was used. The Kruskal–Wallis test was used when comparing measurements obtained from more than 2 independent groups.

The chi-square test was employed to evaluate the data obtained by counting. The Pearson correlation analysis was utilized while examining the relationship between the values; receiver operating characteristic analysis was used to find the cut-off value for the values. The error level was taken as $P < .05$.

RESULTS

In our study, 76 patients diagnosed with MTLE and 47 healthy volunteers were evaluated. The mean age was 34.9 3± 12.72 years for the patient group and 32.34 ± 5.16 years for the control group (P =.19). When the patient and control groups were evaluated in terms of age and gender, there was no statistically significant difference between the 2 groups. When these groups were compared according to their laboratory findings, there was no difference between the 2 groups in terms of glucose, creatinine values, hemoglobin, white blood cell, monocytes, and lymphocyte counts; however, lymphocyte and platelet counts were statistically significantly higher in the control group (P=.08 and P=.001, respectively). Similarly, when the patient and control groups were evaluated in terms of ratios, NLR and MLR values were statistically significantly higher in the patient group (P=.01 and P=.02, respectively), but no difference was observed between the 2 groups in terms of PLR (Table 1). When the seizure types in the patient group were evaluated, it was found that 47.3% of the patients had focal-onset seizures with impaired awareness (n=36) and 52.6% (n=40) had seizures that changed from focal to bilateral tonic-clonic seizures. Among the patients, 15.8% (n=12) had family history, 38.2% of the patients had febrile convulsion (n=29), 11.8% had a history of trauma (n=9), and 47.4% had MTS (n=36). While 33 (43.4%) of the patients had seizures once a year or less frequently, 33 (43.4%) had seizures 2-12 times a year. The frequency of seizures in 10 patients was more than 12 in a year (Table 1).

Then, NLR, MLR, and PLR values in the patient group were reassessed according to the presence of the history of MTS, febrile convulsions, or trauma, the seizure type (focal-onset seizure with impaired awareness/seizure that changed from focal to bilateral tonic-clonic seizure), and seizure frequency (1 or less frequently in a year, 2-12 times in a year, more than 12 in a year). It was revealed that the presence of MTS, febrile convulsion (simple/complex), or trauma did not cause any change in NLR, MLR, and PLR values. Similarly, there was no change in NLR, MLR, and PLR values according to seizure type and seizure frequency (Table 2).

In addition, when the correlation between disease duration and NLR, MLR, and PLR values was evaluated, there was a statistically significant correlation between disease duration and NLR, MLR, and PLR values (r=0.36, r=0.25, and r=0.28; P = .002, P=.03, P=.02, respectively). Accordingly, NLR, MLR, and PLR values increased as the duration of the disease increased, but these correlations were statistically weak. In addition, when the presence of a correlation between the age of onset of the disease and NLR, MLR, and PLR values was evaluated, no statistically significant correlation was found (P > .05) (Table 3).

When the receiver operating characteristic analysis was applied for these 3 values, the cut-off value for NLO was 1.99 [AUC (area under

Table 1. Comparison of Baseline Demographic/Clinical Characteristics and Laboratory Findings of the Patient and Control Groups

	Patient Group (n=76)	Control Group (n=47)	X^2	P
Female, n (%)	40 (60.5)	28 (60)	6.85	.94
Age(mean ± SD)	34.93 ± 12.72	32.34 ± 5.16		.19
Clinical features				
Disease duration	16 (2-51)	-		
Age of onset of disease	14.5 (1-40)	-		
Seizure type		-		
Focal-onset seizure with impaired awareness	36 (47.3%)			
Seizure changing from focal to bilateral tonic-clonic seizure	40 (52.6%)			
Presence of family history	12 (15.8%)	-		
Seizure frequency (including focal seizures with/without consciousness)		-		
Once a year or less	33 (43.4%)			
Between 2 and 12 per year	33 (43.4%)			
More than 12 per year	10 (13.1%)			
History of febrile convulsion (simple/complex)	29 (38.2%)	-		
Presence of trauma	9 (11. 8%)	-		
Presence of MTS	36 (47.4%)	-		
Biochemical analyses				
Glucose (mg/dL) (mean ± SD)	145.9 ± 72.8	141.7 ± 73.3		.28
Creatinine (mg/dL) (median)(IR)	0.9 (0. 5-1.4)	0.8 (0.5-1.3)		.36
Whole blood count values				
Hb (g/dL) (median) (IR)	14.6 (11.6-15.2)	14.1 (11.1-16.1)		.21
WBC (10^9/mL) (median) (IR)	7.55 (4.23–12.4)	7.02 (4.61–10. 14)		.19
Monocytes (10^9/mL) (median) (IR)	0.46 (0.20-0.87)	0.42 (0.24-0.78)		.35
Neutrophil (10^9/mL) (median) (IR)	4.25 (2.21-10.47)	3.97 (2.18-7.12)		.09
Lymphocyte (10^9/mL) (median) (IR)	2.04 (0.53-3.20)	2.19 (1.36-3.62)		*.008*
Platelet (10^9/mL) (median) (IR)	230 (155-437)	269 (165-416)		*.001*
Ratios				
NLR (median) (IR)	2.4 (0.89-17.32)	1.8 (0.97-3.80)		*.01*
MLR (median) (IR)	0.22 (0.08-0.81)	0.19 (0.11-0.33)		*.02*
PLR (median) (IR)	125.01 (52.36-426.92)	122.79 (72.05-208.61)		.66

SD, standard deviation; IR, interquartile range; MTS, mesial temporal sclerosis; Hb, hemoglobin; WBC, white blood cell; NLR, neutrophil/lymphocyte ratio; MLR, monocyte/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

Table 2. Comparison of NLR, MLR, and PLR Values According to MTS, Febrile Convulsion, Presence of Trauma, Seizure Type, and Seizure Frequency

	Presence of MTS			Seizure Type			Seizure Frequency				Febrile Convulsion			Presence of Trauma		
	MTS+	MTS–	*P*	X	Y	*P*	A	B	C	*P*	FC+	FC–	*P*	Trauma+	Trauma–	*P*
NLR	2.4 (0.91-12.77)	2.38 (0.89-17.32)	.89	2.09 (0.97-10.61)	2.66 (0.89-17.32)	.13	2.40 (0.91-10.66)	2.66 (0.89-17.32)	2.64(1.05-12.77)	.20	2.98 ± 2.11	3.26 ± 3.10	.72	2.30 ± 0.91	3.27 ± 2.89	.42
MLR	0.22 (0.08-0.81)	0.20 (0.08-0.66)	.93	0.22 (0.12-0.69)	0.21 (0.08-0.61)	.39	0.20 (0.08-0.66)	0.23 (0.08-0.81)	0.24(0.16-0.51)	.53	0.27 ± 0.16	0.28 ± 0.16	.84	0.24 ± 0.10	0.28 ± 0.17	.81
PLR	135.85 (76.25-426.92)	119.03 (52.36-358.49)	.66	125.01 (76.25-244.72)	123.68 (52.36-426.92)	.99	121.69 (52.36-272.97)	135.46 (75.90-426.92)	139.77 (76.74-413.41)	.64	143.71 ± 67.17	140.78 ± 72.99	.49	129.03 ± 61.49	143.63 ± 71.35	.47

X, focal-onset seizure with impaired awareness; A, seizure changing from focal to bilateral tonic-clonic seizure; A, 1 or less seizure per year; B, 2-12 seizures per year; C, more than 12 seizures per year; MTS, mesial temporal sclerosis; FC, febrile convulsion (simple/complex); NLR, neutrophil/lymphocyte ratio; MLR, monocytes/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

Table 3. Evaluation of the Relationship Between NLR, MLR, and PLR Values, Disease Duration, and Age of Onset of Disease

		Disease Duration	Age of Onset of Disease
NLR	Pearson correlation	0.36	−0.07
	Sig. (2-tailed)	0.002	0.57
MLR	Pearson correlation	0.25	0.06
	Sig. (2-tailed)	0.03	0.59
PLR	Pearson correlation	0.28	−0.16
	Sig. (2-tailed)	0.02	0.18

NLR, neutrophil/lymphocyte ratio; MLR, monocyte/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

the curve): 0.67, 95% CI: 0.57-0.76, sensitivity=68.4%, specificity=61.7%)], and the cut-off value for MLR was 0.2 (AUC: 0.63, 95% CI: 0.53-0.73, sensitivity=60.5%, specificity=57.4%). The size of the AUC was insignificant as it contained a 95% CI of 0.50 found in the receiver operating characteristic analysis for the PLR, and therefore, no cut-off value was given for a PLR. If given, the cut-off value would be 116.34 (sensitivity=63.2%, specificity=42.6%) (Figure 1).

DISCUSSION

Based on the results of this study, it can be said that patients with MTLE had higher MLR and NLR values compared to healthy volunteers of the same age and gender, MLR and NLR values increased as the disease duration increased, and values above 0.2 for MLR and above 1.99 for NLR can be used in the diagnosis of MTLE with higher sensitivity and higher specificity.

It has been demonstrated that systemic inflammation may trigger epileptic seizures by disrupting the function of the blood–brain barrier.[21] In a recent study, it was found that the white blood cell count increased after seizures in patients with generalized- and focal-onset seizures, supporting that epileptic seizures are a neuroinflammatory process.[22] It has been demonstrated that serum interleukin-1 beta (IL-1b) levels increase in patients with epileptic seizures. This causes the impaired blood–brain barrier and increased systemic inflammation, which contributes to the onset of neuronal hyperexcitability and epileptic seizures, so that more neutrophils are transferred to the brain.[23] After the activation of neutrophils, which are the cells that first invade the inflammation site, they cause the release of cytotoxic oxygen derivatives and elastase, which have important roles in the continuation of the inflammatory process.[24] Peripheral monocytes, which are in the same family with microglial cells, one of the best-known cells of the central nervous system, contribute to the immune response through a wide variety of cell death ligands and cytokines released from the surfaces of monocytes, leading to an increase in the inflammatory state.[25] On the other hand, lymphocytes, especially T lymphocytes, play a role in limiting inflammation, especially with IL-10 expression.[26] This condition was initially associated with poor prognosis in ischemic cerebro or cardiovascular diseases accompanied by lymphopenia. Platelets, on the other hand, contribute to both inflammation and the development of thrombosis by producing molecules with both proinflammatory and prothrombotic activities. Therefore, NLR and MLR values obtained by dividing the neutrophil and monocyte counts by the lymphocyte count are considered as inflammatory biomarkers, while the PLR value obtained by dividing the platelet count by the lymphocyte count is both an inflammatory and a thrombotic indicator.[26-28]

It is known that increased NLR, MLR, and PLR values are useful biomarkers in showing disease activity and prognosis in many brain

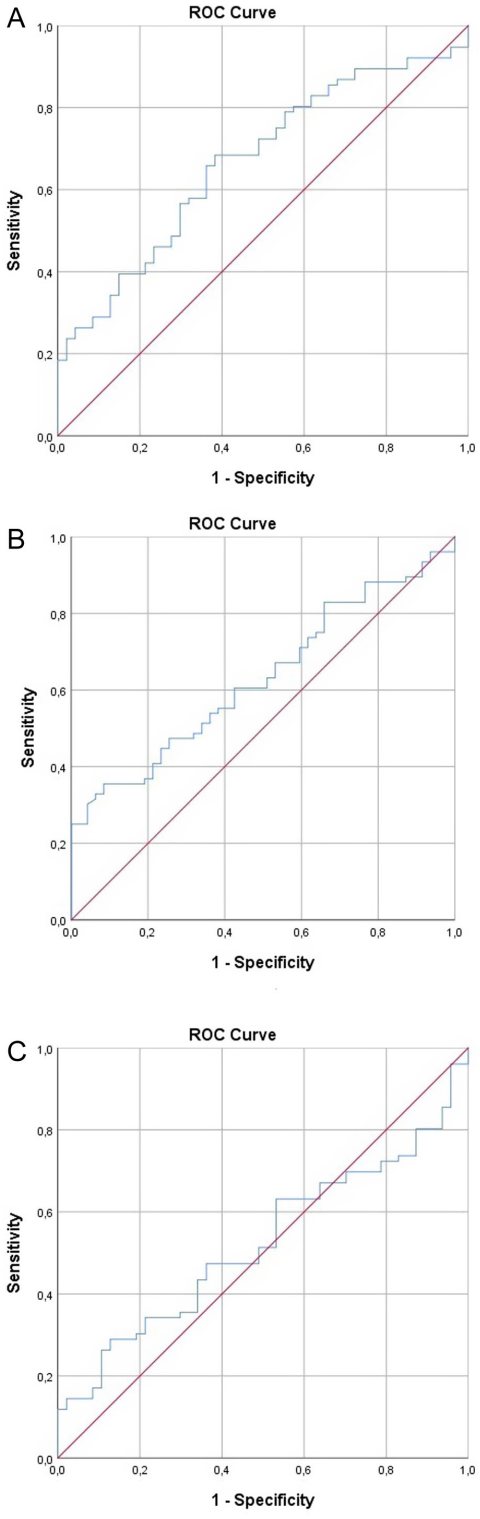

Figure 1. (A) Cut-off value for NLR = 1.99 (AUC: 0.67, 95% CI: 0.57-0.76, sensitivity = 68.4%, specificity = 61.7%), (B) cut-off value for MLR = 0.2 (AUC: 0.63, 95% CI: 0.53-0.73, sensitivity = 60.5%, specificity = 57.4%), (C) the AUC size is insignificant as the 95% CI found in the receiver processing characteristic analysis for the PLR is 0.50, and therefore, no cut-off value is given for a PLR. If given, the cut-off value would be 116.34 (sensitivity = 63.2%, specificity = 42.6%). AUC, area under the curve; NLR, neutrophil/lymphocyte ratio; MLR, monocyte/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

tumors such as brain metastases and gliomas, and in inflammatory brain diseases.[18-20] In a study conducted by Güneş et al.[29] a close relationship was found between NLR, PLR, and neutrophil-related inflammation and generalized epileptic seizure. It was determined that the risk of epileptic seizures increased 1.95 times with a 1-unit increase in NLR.[29] In addition, recent studies have shown that these ratios increase in children with simple and complex febrile convulsions.[30,31] In these studies, it was determined that the increase in NLR level was more pronounced in children with complex febrile convulsions. This may be explained by the fact that the complex febrile convulsion is associated with a stronger inflammatory response, which causes more IL-1b induction, resulting in an increase in neutrophil count and tissue migration.[32] In another study conducted by Ozdemir et al.[33] higher NLR values were found in children with convulsive status epilepticus, and it was hypothesized that neutrophil-related inflammation had an important role in the pathophysiology of status epilepticus.[33] In our study, similar to these studies, higher NLR and MLR values were found in the patient group compared to the controls. However, in these studies, unlike our study, samples were taken in the ictal period and the relationship between inflammation and epileptic seizures was revealed. The high NLR and MLR values detected in the blood samples taken during the interictal period in our study were thought to be associated with inflammation, which plays a role in the pathophysiology of MTLE.[12-15] In another study similar to our study, conducted on patients with TLE, NLR and PLR values were evaluated and it was found that these ratios were higher in the patient group than in the control group, although not statistically significant.[34] In our study, similar to this study, the NLR value was higher in the patient group, and unlike this study, this higher value was statistically significant. In addition, in our study, the MLR value was also statistically significantly higher in the patient group, similar to NLR. Similar to this study, there was no significant difference between the 2 groups in terms of PLR values. Moreover, no correlation was found between disease activity and NLR, MLR, and PLR values in this study. Similarly, again in our study, there was no change in NLR, MLR, and PLR values according to the presence of MTS, febrile convulsion (simple/complex) or trauma history, and seizure type and seizure frequency. In addition, it was stated that there was a positive correlation between NLR and PLR values, seizure duration, and history of febrile convulsions (simple/complex) in this study, although not statistically significant. However, since this correlation was not statistically significant, it was concluded that NLR and PLR values were not specific and sensitive for diagnosing TLE. In our study, similar to this study, no correlation was found between NLR, PLR, and MLR values and MTS, febrile convulsion (simple/complex), and presence of trauma or age of onset of disease, seizure type, and seizure frequency. Different from the study conducted by Baran et al.[34] there was a same-directional and statistically significant relationship between NLR, MLR, and PLR values and disease duration, although it was weak in our study. The reason for this difference may be that the number of patients in our study was higher than in the other study. The same-directional and statistically significant relationship between NLR, MLR, and PLR values and disease duration in our study can be interpreted as inflammation, which is thought to play a role in the pathophysiology of MTLE, continues to increase throughout the process, contributing to the progression of the disease.

Study Limitations

Our study has several limitations. First of all, our study is a single-center retrospective study and the number of patients is too small to make further comments. Due to the insufficient number of patients, the number of patients who received each antiepileptic drug alone or in combinations of 2 or 3 was statistically insignificant. Therefore, the

antiepileptic drug information taken by the patient during the design phase of the study was eliminated and could not be evaluated. In addition, unfortunately, the past history of febrile convulsions in the anamnesis of each patient could not be obtained reliably and in detail, and therefore, simple or complex febrile seizures could not be differentiated in patients. Moreover, other inflammatory markers were not evaluated in our study, and it was not examined whether these 3 ratios had a relationship with other inflammatory markers. In addition, c. MRI examinations of the patients included in our study were performed on a 1.5 Tesla device in our hospital, and our study was insufficient to show some pathologies in this respect.

As a result, considering that patients with MTLE have higher MLR and NLR values and NLR and MLR values increase in parallel with disease duration, it can be suggested that patients with MTLE have increased inflammatory activity compared to healthy individuals, this activity continues to increase as the disease duration increases, and this activity contributes to the progressive process of MTLE. There is a need for more detailed and extensive prospective studies on this subject in the future.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sivas Cumhuriyet University (Date: March 10, 2021, Decision no: 2021-03/02).

Informed Consent: Written informed consent was obtained from patients.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The authors have no conflicts of interest to declare.

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