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Evaluation of hematologic inflammation parameters and cranial magnetic resonance imaging findings in patients with trigeminal neuralgia

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ABSTRACT

Aims: This study aimed to evaluate the relationship between trigeminal neuralgia (TN) and hematological parameters, including leukocyte-based inflammatory indices, and to explore their association with cranial magnetic resonance imaging (MRI) findings.

Methods: A retrospective analysis was conducted on 114 patients with newly diagnosed TN and 114 healthy control groups with comparable demographic characteristics. Clinical, laboratory, and cranial MRI data were collected from hospital records. White matter abnormalities were identified via cranial MRI, and inflammatory indices were calculated as follows: neutrophil-to-lymphocyte ratio (NLR)=Neutrophil count/lymphocyte count, platelet-to-lymphocyte ratio (PLR)=Platelet count/lymphocyte count, Systemic Immune-Inflammation Index (SII)=Platelet count×neutrophil count/lymphocyte count, and Systemic Inflammatory Response Index (SIRI)=Neutrophil count×monocyte count/lymphocyte count.

Results: TN patients showed significantly higher leukocyte counts (7.4±1.8 vs. 6.0±1.9 $\times 10^3$/µl, $p<0.001$), neutrophil counts (4.2±1.1 vs. 2.8±0.8$\times 10^3$/µl, $p<0.001$), CRP levels (median: 2.6 vs. 0.8 mg/dl, $p<0.001$), and inflammatory indices (NLR, PLR, SII, and SIRI; $p<0.001$ for all) compared to control group. White matter abnormalities were detected in 16.7% of TN patients, predominantly in the frontal (11.4%) and parieto-occipital (7.0%) regions. Patients with white matter abnormalities exhibited significantly higher inflammatory indices than those without. Compared to other inflammatory parameters, SIRI demonstrated the highest diagnostic performance for TN (threshold: 0.7; sensitivity: 84.2%, specificity: 82.5%) and white matter abnormalities (threshold: 1.3; sensitivity: 78.9%, specificity: 82.1%).

Conclusion: Inflammatory markers, particularly SIRI, are significantly elevated in TN patients and are associated with white matter abnormalities. These markers may serve as useful non-invasive tools for predicting TN and related MRI findings.

Keywords: Trigeminal neuralgia, inflammation markers, white matter lesions, cranial MRI, Inflammation Index

INTRODUCTION

Trigeminal neuralgia (TN) is described as sudden, intense, brief, stabbing pain attacks, typically affecting one side of the face and localized to the distribution of one or more branches of the trigeminal nerve.[1] It typically occurs in middle and older age and is more common in women than in men.[2,3] However, the etiology and underlying mechanisms of TN remain insufficiently understood.[4]

Compression of the trigeminal nerve is linked to significant myelin erosion and disintegration due to inflammation, especially at the site of nerve indentation.[5,6] Structural changes related to this compression may impact the functionality of voltage-gated sodium (Nav) channels, which play a significant role in the onset of TN symptoms.[7] It has also been shown that changes in Nav expression play a role in the development of neuropathic and inflammatory pain.[8,9] Moreover, the cerebrospinal fluid of TN patients demonstrates significant increases in inflammatory mediators such as chemokines, pro-inflammatory cytokines, growth factors, and tumor necrosis factor superfamily, suggesting a pathophysiologic role for neuroinflammation.[10,11] Furthermore, neuroimaging studies conducted on TN patients indicate that neuroinflammation could be associated with brain structure and function such as white and gray matter volume changes.[12,13]

Previous rare studies have reported conflicting results regarding the association between systemic inflammatory indices, such as the platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR), measured using a low-cost, more practical, and simpler method, and TN.[14-16] However, the relationship between systemic inflammatory markers and cranial magnetic resonance imaging (MRI) findings in these patients has not yet been investigated. This study aimed to assess the relationship between TN and hematological

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parameters, including leukocyte-based inflammation indices, and to examine their connection to cranial MRI findings.

METHODS

Ethics

Following the principles set forth in the Declaration of Helsinki, this single center retrospective study was conducted at the Atlas University Medicine Hospital Neurology Clinical from January 2021 to November 2023. The study received approval from the Üsküdar University Non-interventional Researches Ethics Committee (Date: 27.11.2023, Decision No: 2023-61). The local ethics committee did not require informed consent because the study was retrospective.

Study Population

A total of 144 patients diagnosed with TN were retrospectively examined. The diagnosis of TN was determined according to the criteria of International Classification of Headache Disorders (ICHD3).[1] Patients with chronic conditions (cerebrovascular disease, central nervous system vasculitis, rheumatologic disease, hypertension, diabetes mellitus, chronic any diseases, hematologic disorders, acute inflammatory diseases), those with a history of TN, those with cranial MRI findings of pathologies such as masses or trauma sequelae, those who had undergone surgery in the past month prior to diagnosis, those using steroids, antibiotics, antivirals, antiplatelet, anticoagulant, or immunosuppressant drugs, those who were pregnant, and those with missing data were excluded from the study. After this exclusion process, 114 patients with newly diagnosed with TN were enrolled in this study. The control group, consisting of 114 healthy individuals who underwent check-up programs, had no comorbidities, had normal brain imaging results, and were matched with TN patients by age and sex, was also included in the study.

Study Protocol

Demographic, clinical, and imaging data were obtained from the hospital's electronic information system and patient records. Blood samples and cranial MRI data for all patients were collected at the time of their initial hospital admission. Prior to starting any treatment, complete blood count and biochemical parameters were measured using venous blood samples taken after a 12-hour fasting period during outpatient evaluations. All samples were analyzed in a single laboratory following the same methodology outlined below. Pain severity was assessed by the patients using the Visual Analogue Scale (VAS), with scores ranging from 1 to 10.

Biochemical Analysis

Venous blood samples were analyzed using a Cell-Dyn 3700 SL device (Abbott Diagnostics, Chicago, USA). Hemoglobin levels were measured photometrically, platelet count via the impedance method, and CRP levels using the immunoturbidimetric method. The inflammatory indices were respectively calculated as follows: NLR=Neutrophil count/lymphocyte count, PLR=Platelet count/lymphocyte count, Systemic Immune-Inflammation Index (SII)=Platelet count×neutrophil count/lymphocyte count, and Systemic Inflammatory Response Index (SIRI)=Neutrophil count× monocyte count/lymphocyte count.

Cranial MRI Evaluation

The patients' cranial MRI images were retrospectively evaluated. All imaging were performed with a 1.5 Tesla MRI machine (Achieva, Philips Medical Systems, Best, The Netherlands). The MRI protocol consisted of various sequences: T1-weighted imaging (T1WI) in axial and sagittal planes, T2-weighted imaging (T2WI) in axial, coronal, and sagittal planes, along with axial and coronal fluid-attenuated inversion recovery (FLAIR). White matter and basal ganglia lesions were assessed using the age-related white matter changes (ARWMC) scale, which evaluates white matter lesions based on their size and location.[17] The brain was divided into five regions for assessment in both hemispheres: (1) frontal region: the anterior portion of the brain, located in front of the central sulcus; (2) parieto-occipital region: the parietal and occipital lobes combined; (3) temporal region: the lateral section of the brain, extending from the posterior part of the Sylvian fissure to the lateral ventricles; (4) infratentorial region: including the brainstem and cerebellum; and (5) basal ganglia and insula: covering the striatum, globus pallidus, thalamus, internal and external capsules, and insula. Lesions were graded as follows: grade 0: no lesions; grade 1: focal lesions; grade 2: lesions with a tendency to merge; grade 3: diffuse involvement of the entire region, with or without U-fiber involvement.

Hyperintense lesions measuring less than 5 mm and numbering between 4 and 12 in the periventricular white matter on cranial MRI were included in the study. Patients were categorized into those with and those without white matter lesions.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). Numerical variables with a normal distribution, as verified by Kolmogorov-Smirnov tests, are presented as mean±standard deviation (SD), while non-normally distributed variables are expressed as median values with interquartile ranges (25^{th}-75^{th} percentile). For group comparisons, the student's T test was used for normally distributed data, and the Mann-Whitney U test was applied for data not meeting normality assumptions. Categorical variables are shown as frequencies and percentages, with comparisons between groups performed using the chi-square or Fisher's exact tests. To identify independent predictors of TN, a multivariable logistic regression analysis was carried out using the backward Wald method. The receiver operating characteristic (ROC) curve analysis was employed to evaluate diagnostic performance, reporting the area under the curve (AUC), standard error (SE), sensitivity, and specificity. The Youden index method was used to determine the optimal cutoff values of hematological parameters or indices for predicting TN and the presence of white matter abnormalities. Comparisons of AUCs were made using a nonparametric approach based on the generalized U-statistics framework, with the covariance matrix estimation method described by DeLong et al.[18] Statistical significance was set at $p<0.05$ (*) for all tests.

RESULTS

The study included 114 control participants (mean age: 49.7±11.9 years) and 114 patients with TN (mean age: 49.5±13.7 years). The two groups had comparable age and gender distributions. The majority of patients with TN had right side dominance (66.7%). In the TN group compared to the control group, the mean leukocyte counts (7.4±1.8 vs. 6.0±1.9×10^3 µl, p<0.001), mean red blood cells (RBC) (4.6±0.5 vs. 4.4±0.5×10^6 µl, p=0.011), mean neutrophil counts (4.2±1.1 vs. 2.8±0.8×10^3 µl, p<0.001), mean monocytes count (0.4±0.1 vs. 0.5±0.1×10^3 µl, p<0.001), and median CRP level (2.6 vs. 0.8 mg/dl, p<0.001) were higher, while the median lymphocyte counts was found to be lower (2.1±0.6 vs. 2.3±0.6×10^3 µl, p<0.001). Also, in the TN group, inflammation indices (NLR, PLR, SII, and SIRI) were found to be higher (Table 1).

The effects of hematological parameters and inflammation indices on TN were analyzed using multivariable regression models. Model I multivariable regression analysis included only hematological parameters. Model II multivariable regression analysis included leukocytes, RBC, CRP, NLR, and PLR, while lymphocyte subtypes were excluded due to high collinearity with NLR and PLR. Model III multivariable regression analysis included leukocytes, RBC, CRP, SII, and SIRI, while lymphocyte subtypes, NLR, and PLR were excluded due to high collinearity with SII and SIRI. Among these, Model III demonstrated superior performance in explaining the variance associated with TN compared to other models. Accordingly, increased CRP (OR=2.85, p<0.001) and SIRI (OR=13.48, p<0.001) levels were identified as independent predictors of TN (Table 2).

Cranial MRI revealed that 16.7% of TN patients exhibited white matter abnormalities. These lesions were predominantly located in the frontal region (11.4%), with fewer cases involving the parieto-occipital (7.0%) and temporal regions (0.9%). In patients with white matter abnormalities compared to those without, the median NLR (2.8 vs. 1.8, p<0.001), median PLR (138.8 vs. 125.3, p=0.016), median SII (751.6 vs. 454.4, p<0.001), and median SIRI (2.1 vs. 1.0, p<0.001) levels were higher. There was no significant difference in VAS scores between the groups (Table 3).

Table 1. Demographic and laboratory findings

Variables	Control group n=114	Trigeminal neuralgia group n=114	p
Age, years	49.7±11.9	49.5±13.7	0.873
Gender, n (%)			
Female	85 (74.6)	85 (74.6)	0.999
Male	29 (25.4)	29 (25.4)	
Side, n (%)			
Left	-	38 (33.3)	-
Right	-	76 (66.7)	
Laboratory findings			
Leukocytes, ×10^3 µl	6.0±1.9	7.4±1.8	<0.001*
RBC, ×10^6 µl	4.4±0.5	4.6±0.5	0.011*
Hemoglobin, g/dl	13.4±1.2	13.2±1.5	0.568
Hematocrit, %	39.9±2.8	39.6±4.0	0.505
Platelets, ×10^3 µl	252.5±50.6	256.6±55.7	0.563
Lymphocytes, ×10^3 µl	2.3±0.6	2.1±0.6	<0.001*
Neutrophils, ×10^3 µl	2.8±0.8	4.2±1.1	<0.001*
Monocytes, ×10^3 µl	0.4±0.1	0.5±0.1	<0.001*
CRP, mg/dl	0.8 (0.1-2.3)	2.6 (2.1-3.3)	<0.001*
NLR	1.0 (0.9-1.6)	1.8 (1.6-2.6)	<0.001*
PLR	107.7 (90.2-120.9)	125.4 (106.6-148.7)	<0.001*
SII	260.8 (228.3-392.6)	480.8 (370.0-668.5)	<0.001*
SIRI	0.5 (0.4-0.7)	1.0 (0.7-1.4)	<0.001*
VAS	-	9.0 (7.0-9.0)	-
Cranial MRI findings, n (%)			
White matter hyperintensity			
No	-	95 (83.3)	-
Yes	-	19 (16.7)	-
Side			
Frontal region	-	13 (11.4)	-
Parieto-occipital region	-	8 (7.0)	-
Temporal region	-	1 (0.9)	-

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: RBC: Red blood cells, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, VAS: Visual Analogue Scale, MRI: Magnetic resonance imaging

Table 2. Independent predictor of trigeminal neuralgia

Variables	Univariable regression		Model I regression		Model II regression		Model III regression	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Leukocytes	1.55 (1.31-1.84)	<0.001*	-	-	-	-	-	-
RBC	2.01 (2.15-2.50)	0.015*	-	-	-	-	-	-
Lymphocytes	0.43 (0.26-0.69)	<0.001*	0.34 (0.15-0.78)	0.011*	Not including		Not including	
Neutrophils	4.72 (4.14-4.10)	<0.001*	2.73 (1.69-4.40)	<0.001*	Not including		Not including	
Monocytes	1.05 (1.03-1.08)	<0.001*	1.05 (1.01-1.09)	0.006*	Not including		Not including	
CRP	3.25 (3.29-3.61)	<0.001*	2.68 (1.79-4.00)	<0.001*	3.08 (2.08-4.56)	<0.001*	2.85 (1.96-4.13)	<0.001*
NLR	6.59 (6.63-6.97)	<0.001*	Not including		7.03 (3.01-16.42)	<0.001*	Not including	
PLR	1.02 (1.01-1.04)	0.001*	Not including		-	-	Not including	
SII	1.03 (1.01-1.05)	<0.001*	Not including		Not including		-	-
SIRI	20.66 (20.18-20.16)	<0.001*	Not including		Not including		13.48 (4.43-40.95)	<0.001*
			Nagelkerke R^2=0.325		Nagelkerke R^2=0.354		Nagelkerke R^2=0.489	

The effects of age and gender were adjusted in the regression analysis. *p<0.05 indicates statistical significance. Abbreviations: OR: Odds ratio, CI: Confidence interval, RBC: Red blood cells, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index

Table 3. Findings associated with white matter in trigeminal neuralgia

	White matter hyperintensity		
Variables	**No (n=95)**	**Yes (n=19)**	**p**
Age, years	48.7±13.8	53.2±12.7	0.200
Gender, n (%)			
Female	71 (74.7)	14 (73.7)	0.923
Male	24 (25.3)	5 (26.3)	
Laboratory findings			
Leukocytes, ×10³ µl	7.1±1.5	8.9±2.2	<0.001*
RBC, ×10⁶ µl	4.6±0.5	4.6±0.4	0.920
Platelets, ×10³ µl	256.4±56.7	257.7±52.0	0.923
Lymphocytes, ×10³ µl	2.1 (1.8-2.5)	1.9 (0.8-2.2)	0.012*
Neutrophils, ×10³ µl	4.0±1.0	4.8±1.1	0.004*
Monocytes, ×10³ µl	0.5±0.1	0.5±0.2	0.406
CRP, mg/dl	2.1 (1.9-2.8)	2.6 (2.4-3.4)	0.036*
NLR	1.8 (1.6-2.3)	2.8 (2.4-5.5)	<0.001*
PLR	125.3 (102.1-144.2)	138.8 (112.1-335.1)	0.016*
SII	454.4 (356.0-640.5)	751.6 (522.8-1476.6)	<0.001*
SIRI	1.0 (0.7-1.2)	2.1 (1.4-2.4)	<0.001*
VAS	8.4±1.4	8.2±1.3	0.489
Moderate	17 (17.9)	4 (21.1)	0.746
Severe	78 (82.1)	15 (78.9)	

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, RBC: Red blood cells, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, VAS: Visual Analogue Scale

Table 4. Findings associated with VAS score in trigeminal neuralgia

	VAS score		
Variables	**Moderate (n=21)**	**Severe (n=93)**	**p**
Age, years	49.0 (36.0-62.0)	51.0 (41.0-60.0)	0.994
Gender, n (%)			
Female	14 (66.7)	71 (76.3)	0.358
Male	7 (33.3)	22 (23.7)	
Laboratory findings			
Leukocytes, ×10³ µl	7.1±1.5	7.5±1.8	0.313
RBC, ×10⁶ µl	4.6±0.3	4.6±0.5	0.935
Platelets, ×10³ µl	274.7±48.6	252.5±56.7	0.100
Lymphocytes, ×10³ µl	2.1±0.4	2.0±0.6	0.817
Neutrophils, ×10³ µl	4.0±1.2	4.2±1.0	0.559
Monocytes, ×10³ µl	0.5±0.1	0.5±0.1	0.572
CRP, mg/dl	2.6 (2.2-3.0)	2.5 (2.0-3.4)	0.405
NLR	1.8 (1.6-2.4)	1.8 (1.6-2.7)	0.324
PLR	135.3 (110.1-177.2)	124.0 (104.4-148.7)	0.236
SII	529.8 (369.8-629.6)	460.0 (370.7-669.5)	0.759
SIRI	0.9 (0.6-1.3)	1.0 (0.7-1.4)	0.236
White matter hyperintensity			
No	17 (81.0)	78 (83.9)	0.746
Yes	4 (19.0)	15 (16.1)	

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: CRP: C-reactive protein, MRI: Magnetic resonance imaging, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, RBC: Red blood cells, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, VAS: Visual Analogue Scale

Demographic and clinical parameters showed no significant differences in patients with moderate and severe pain (Table 4).

Table 5 presents the diagnostic performance of inflammatory markers in predicting TN and white matter abnormalities.

Table 5. Diagnostic performance of inflammation parameters in predicting trigeminal neuralgia and white matter

Variable	AUC±SE	95% CI	Sens. (%)	Spec. (%)	Threshold values
Trigeminal neuralgia (vs. control)					
Leukocytes	0.723±0.03	0.658-0.789	57.0	81.6	≥7×10³ µl
RBC	0.617±0.04	0.545-0.690	43.9	84.2	≥4.7×10⁶ µl
Platelets	0.512±0.04	0.437-0.587	28.9	90.4	≥278×10³ µl
Neutrophils	0.759±0.03	0.710-0.808	70.7	72.5	≥3.2×10³ µl
Lymphocytes	0.625±0.04	0.553-0.698	70.2	21.1	≤1.85×10³ µl
Monocytes	0.566±0.04	0.492-0.641	77.2	42.1	≥0.4×10³ µl
NLR	0.741±0.03	0.689-0.793	69.3	79.5	≥1.7
PLR	0.638±0.04	0.566-0.709	56.1	80.7	≥122.8
SII	0.811±0.03	0.767-0.875	80.6	61.4	≥268.5
SIRI	0.832±0.03	0.776-0.886	84.2	82.5	≥0.7
CRP	0.782±0.03	0.721-0.831	74.3	78.3	>2.4 mg/dl
White matter hyperintensity (vs. normal MRI)					
Leukocytes	0.744±0.07	0.609-0.879	63.2	82.1	8.7×10³ µl
Neutrophils	0.683±0.06	0.589-0.767	71.2	47.8	>3.50×10³ µl
Lymphocytes	0.675±0.07	0.581-0.759	42,1	85.8	≤1.23×10³ µl
NLR	0.799±0.06	0.674-0.924	78.9	80.0	≥2.3
PLR	0.675±0.07	0.533-0.817	42.1	95.8	≥187.8
SII	0.789±0.06	0.661-0.916	89.5	55.8	≥476.7
SIRI	0.831±0.06	0.717-0.945	78.9	82.1	≥1.3
CRP	0.618±0.03	0.546-0.691	70.2	57.9	>2.8 mg/dl

*p<0.05 indicates statistical significance. Abbreviations: AUC: Area under the curve, SE: Standard error, CI: Confidence interval, Sens: Sensitivity, Spec: Specificity, RBC: Red blood cells, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, CRP: C-reactive protein, MRI: Magnetic resonance imaging

Among the markers, SIRI showed the highest performance. For TN, a SIRI threshold of 0.7 provided 84.2% sensitivity and 82.5% specificity. For white matter abnormalities, a threshold of 1.3 yielded 78.9% sensitivity and 82.1% specificity.

DISCUSSION

To the best of our knowledge, this study is one of the few to investigate the relationship between TN, hematological inflammation parameters, and cranial MRI findings. Additionally, this study is the first to assess the association between SII, SIRI and TN. TN patients had higher leukocyte-based inflammatory indices, and SIRI was found to be an independent predictor. In the TN cohort, inflammatory indices were elevated in patients with white matter abnormalities. Furthermore, SIRI demonstrated superior diagnostic performance compared to other inflammatory markers in predicting both TN and white matter abnormalities.

Previous research has indicated that the progression of TN is induced by inflammatory factors such as tumor necrosis factor, C-C motif chemokine ligand 2 (CCL2), interleukin (IL)-6, and transient receptor potential ankyrin 1 (TRPA1).[19-22] In an experimental model of trigeminal neuropathic pain caused by infraorbital nerve constriction, it was proposed that pain-like behaviors are facilitated by the TRPA1 channel. This is linked to oxidative stress byproducts secreted by monocytes and macrophages concentrated around the site of the nerve injury.[23] Following tissue damage, pro-inflammatory cytokines are expressed by neutrophils, lymphocytes, monocytes and macrophages.[24] This highlights the role of immune cells in the heightened pro-inflammatory cytokine levels observed in TN patients after neurological injury.[10,20] In line with these findings, lymphocyte levels and their subtypes were elevated in TN patients relative to the control group.[14] This finding aligns with the elevated CRP levels in TN patients, which serve as a recognized marker of immune-inflammatory status.[25,26]

Blood parameters are routinely accessible laboratory tests during the initial phase of hospital admission, and they are universally obtained within the first hour.[27] In clinical practice, an easily assessable biomarker could be a crucial predictor for diagnosing central nervous system diseases, assessing prognosis, or identifying high-risk patients. A recent study investigated the role of preoperative inflammatory markers in patients with newly diagnosed glioma, schwannoma, meningioma, pituitary adenoma, or trigeminal neuralgia. The study demonstrated that meningioma and glioma patients had elevated NLR and PLR levels, while TN patients showed levels comparable to the healthy control group.[28] In the existing literature, there are contradictory findings concerning NLR and PLR levels when comparing TN patients with healthy control groups. In a retrospective study conducted in China, newly diagnosed TN patients were reported to have higher NLR and PLR levels than healthy controls.[14] Studies conducted in Turkey have indicated that TN patients show no significant differences in NLR or PLR levels compared to the healthy control group.[15,16] In these studies, the disease duration was either unspecified or focused on patients with chronic disease. Thus, variations among the studies may stem from differences in patient selection.

The current study revealed that newly diagnosed TN patients displayed significantly higher NLR and PLR levels when compared to healthy controls. Furthermore, NLR levels provided superior diagnostic performance over PLR levels in the prediction of TN. These results align with the role of neutrophils and lymphocytes in driving elevated pro-inflammatory cytokine production in TN patients.[24] However, in this cohort, more comprehensive inflammatory indices could better represent the innate immune reaction to nerve damage. SIRI, incorporating monocytes, was identified as an independent predictor of TN and outperformed other inflammatory indices in diagnostic performance. Moreover, the regression model that incorporated SIRI provided a better explanation of the variance in TN than models that including NLR, PLR, or their components. The superior diagnostic performance of SIRI can likely be explained by the involvement of its components in the neuroinflammatory processes triggered by the cytokine-chemokine network, which plays a key role in the pathogenesis of TN.[29,30] Moreover, platelets and platelet-related indices, such as PLR, appear to play a less significant role in the pathogenesis of TN compared to neutrophils or monocytes. This observation aligns with findings from previous studies, which reported no significant differences in platelet levels between TN patients and healthy controls.[14,15] While platelets contribute to the inflammatory milieu by releasing pro-inflammatory mediators like platelet-derived growth factor, their involvement may be less pronounced in the neuroinflammatory processes central to TN.[31] In contrast, neutrophils and monocytes, through their direct roles in cytokine-chemokine signaling and innate immune activation, are likely the primary drivers of inflammation and nerve damage in TN.[31] Consequently, platelet-related indices such as PLR may have limited utility in capturing the complex inflammatory mechanisms underlying TN when compared to indices like NLR or SIRI, which incorporate more dominant immune cell types in the neuroinflammatory response.

Previous research has revealed the presence of white matter abnormalities in TN patients, likely resulting from the effects of chronic pain and peripheral nerve damage.[32-34] Previous studies on TN patients have demonstrated white matter integrity disruption in the right anterior limb and left genu of the internal capsule, the bilateral superior corona radiata, the splenium and body of the corpus callosum, the bilateral posterior corona radiate, and the left posterior thalamic radiation.[35,36] Consistent with these studies, white matter hyperintensities were predominantly located in the frontal and parieto-occipital regions, indicating potential cognitive-emotional or motor function impairment. The exact mechanism underlying the impact of TN on brain white matter integrity has yet to be determined. A previous study found reduced fractional anisotropy in TN patients, linked to increased radial diffusivity, suggesting that demyelination and neuroinflammation might disrupt white matter integrity in these patients.[37] This may explain the higher inflammatory indices observed in TN patients with white matter abnormalities. Studies conducted on other neurological diseases also support the current findings. A study on Parkinson's patients showed that they had lower

fractional anisotropy and higher radial and mean diffusivity compared to healthy control group. The observed reductions in fractional anisotropy and elevations in radial and mean diffusivity were linked to elevated systemic inflammatory markers, including lymphocyte and granulocyte apoptosis.[38] In autopsied brains of monkeys induced with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, an increased infiltration of lymphocyte function-associated antigen 1-positive leukocytes was observed in the substantia nigra.[39] The activation of microglia, facilitated by leukocytes and cytokines, may lead to demyelination and the development of neuritis, ultimately affecting the structural integrity of white matter.[38] On the other hand, pain severity did not correlate with either white matter lesions or inflammatory indices. This finding suggests that in newly diagnosed TN patients, the connection between white matter lesions and neuroinflammatory processes is independent of the mechanisms driving pain intensity.

Limitations

This study has several limitations, including its retrospective design, single-center nature, and relatively small sample size, which may limit the generalizability of the findings. Additionally, the absence of advanced immunological analyses such as cytokine profiling or flow cytometry prevents a more detailed exploration of systemic and neuroinflammatory mechanisms. Furthermore, cranial MRI assessments did not include evaluations of gray matter lesions or cortical thickness, which could provide deeper insights into structural brain changes associated with TN. Future studies with larger, multicenter cohorts and the integration of advanced imaging and immunological techniques are needed to overcome these limitations and better understand the pathophysiology of TN.

CONCLUSION

This study revealed that inflammatory indices were significantly higher in TN patients compared to healthy controls. Furthermore, white matter lesions were associated with elevated inflammation indices, pointing to a potential connection between neuroinflammation and structural alterations in the brain. SIRI demonstrated the highest diagnostic accuracy among inflammatory markers in predicting TN and white matter abnormalities, highlighting its potential utility as both a diagnostic and prognostic screening non-invasive tool for TN.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Üsküdar University Non-interventional Researches Ethics Committee (Date: 27.11.2023, Decision No: 2023-61).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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