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Red blood cell distribution width may predict the prognosis of vestibular neuritis

Eritrosit dağılım genişliği vestibüler nöritin prognozunu öngörebilir

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ABSTRACT

Objectives: The study aimed to determine whether red cell distribution width (RDW), as well as other inflammatory markers of complete blood count, have any predictive value for the etiology, diagnosis, and prognosis of vestibular neuritis (VN).

Patients and Methods: Forty-two VN patients (28 females, 14 males; mean age: 46.7±11.0 years; range, 20 to 75 years) and 50 controls (32 females, 18 males; mean age: 44.4±6.0 years; range, 22 to 55 years) were included in the retrospective study between May 2016 and May 2018. Red cell distribution width and neutrophil, lymphocyte, platelet, and monocyte levels were documented from the hemogram records of all patients. Additionally, the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and lymphocyte-monocyte ratio were calculated.

Results: In the VN group, NLR and PLR values were significantly high (p=0.001 and p<0.001, respectively). Red cell distribution width, platelet, lymphocyte, and monocyte levels were significantly high and hemoglobin was significantly low in VN patients with long-lasting spontaneous nystagmus (p<0.001, p=0.026, p=0.033, p=0.047, and p=0.006, respectively).

Conclusion: High RDW and low hemoglobin levels may predict a poor prognosis in adult VN patients. Moreover, a low lymphocyte-monocyte ratio and high NLR and PLR values are supportive findings in the diagnosis of vestibular neuritis.

Keywords: Lymphocyte-monocyte ratio, neutrophil-lymphocyte ratio, red cell distribution width; platelet-lymphocyte ratio, vestibular neuritis.

ÖZ

Amaç: Çalışmada, tam kan sayımında elde edilen diğer enflamatuvar belirteçlerin yanı sıra, kırmızı küre dağılım genişliği (RDW)'nin vestibüler nörit (VN)'in etiyolojisinde, tanısında ve prognozunda öngörü değeri olup olmadığının gösterilmesi amaçlandı.

Hastalar ve Yöntemler: Mayıs 2016 - Mayıs 2018 tarihleri arasında yapılan retrospektif çalışmaya 42 VN hastası (28 kadın, 14 erkek; ort. yaş: 46.7±11.0 yıl; dağılım, 20-75 yıl) ve 50 kontrol (32 kadın, 18 erkek; ort. yaş: 44.4+6.0 yıl; dağılım, 22-55 yıl) dahil edildi. Hastaların tümünün hemogram kayıtlarından eritrosit dağılım genişliği, nötrofil, lenfosit, trombosit ve monosit seviyeleri dökümente edildi. Ayrıca, nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı (PLR) ve lenfosit-monosit oranı hesaplandı.

Bulgular: Vestibüler nörit grubunda, NLR ve PLR değerleri anlamlı olarak yüksek bulundu (sırasıyla, p=0.001 ve p<0.001). Uzamış spontan nistagmusu olan VN grubunda, RDW, trombosit, lenfosit ve monosit seviyeleri istatistiksel olarak yüksek, hemoglobin seviyesi ise düşük idi (sırasıyla, p<0.001, p=0.026, p=0.033, p=0.047 ve p=0.006).

Sonuç: Vestibüler nöritli erişkin hastalarda, yüksek RDW ve düşük hemoglobin seviyeleri kötü prognoz göstergesi olabilir. Ayrıca, lenfosit-monosit oranı değerinin düşük, NLR ve PLR değerlerinin yüksek olması VN tanısında destekleyici bulgulardır.

Anahtar sözcükler: Lenfosit-monosit oranı, nötrofil-lenfosit oranı, eritrosit dağılım genişliği; trombosit-lenfosit oranı, vestibüler nörit.

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After benign paroxysmal positional vertigo and Meniere's syndrome, vestibular neuritis (VN) is the third most common reason for acute peripheral vestibular disorders.[1,2] The etiology of VN remains unknown, as in other otologic diseases, such as Bell's palsy and idiopathic sudden hearing loss. It is related to viral infections, mainly herpes simplex type 1, microvascular ischemia, and, more widely, autoimmunity.[3,4] Vestibular neuritis is clinically diagnosed with sudden and constant vertigo, disbalance, and spontaneous nystagmus without audiological or neurological symptoms.[5] For diagnosis, the most evident clinical sign is spontaneous horizontal nystagmus. However, no specific test exists for VN. Although caloric and video head impulse tests support laboratory tests in VN diagnosis and follow-up, those tests are not affordable or accessible in every clinic.

Today, some values obtained from complete blood counts, such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), are used to evaluate the relationship between systemic inflammation and the prognosis of some diseases, such as cancer, hypertension, diabetes mellitus, coronary heart disease, optic neuritis, facial palsy, and VN.[6-9] To our knowledge, studies on the relationship between VN and inflammatory markers are scarce.[9,10]

Like NLR and PLR, red cell distribution width (RDW) has also been shown as a blood marker elevating inflammation and oxidative stress in the literature. Moreover, since RDW is related to blood cell volume, increasing RDW levels may also affect microcirculation, causing occlusion of the vessels.[11-13] Even high RDW levels may cause occlusion of the vessels supplying the inner ear and play a role in the etiology of VN. The correlation between RDW and other otologic diseases with similar etiology to VN was demonstrated in various studies.[11,14] Although VN's relation to NLR and PLR has previously been demonstrated, no study has yet shown the connection between VN and RDW in adults.[9] Therefore, this study aimed to determine whether RDW, as well as other inflammatory markers of complete blood count, have any predictive value for the etiology, diagnosis, and prognosis of VN.

PATIENTS AND METHODS

In this study, recordings of 42 VN patients (28 females, 14 males; mean age: 46.7+11.0 years; range, 20 to 75 years) diagnosed and followed at our clinic in a tertiary care center and 50 controls (32 females, 18 males; mean age: 44.4+6.0 years; range, 22 to 55 years) who were ready for septoplasty surgery without ear pathology between May 2016 and May 2018 were retrospectively analyzed. The inclusion criteria for the study were as follows: *(i)* sudden and constant vertigo in the last 72 h, *(ii)* disbalance, *(iii)* spontaneous nystagmus (horizontal and torsional with the fast phase towards one side), *(iv)* an absence of audiological and neurological

Table 1
Demographic data and blood analysis of case and control groups

	VN group (n=42)		Control group (n=50)		
	n	Mean+SD	n	Mean+SD	*p*
Age (year)		46.7±11.0		44.4±6.0	0.200*
Sex					0.789[a]
Female	28		32		
Male	14		18		
Hemoglobin (g/dL)		13.47±1.30		14.53±1.43	<0.001*
Platelet (10^3/uL)		265.40±56.57		252.58±55.29	0.276*
Neutrophil (10^3/uL)		5.27±1.63		4.85±2.27	0.316*
Lymphocyte (10^3/uL)		2.12±0.80		2.56±0.69	0.001*
Monocyte (10^3/uL)		0.64±0.69		0.51±0.18	0.500**
Neutrophil-lymphocyte ratio		2.81±1.52		1.97±0.95	0.001**
Platelet-lymphocyte ratio		138.24±49.18		105.23±35.84	<0.001*
Lymphocyte-monocyte		4.22±1.56		5.44±1.92	0.001*
Red cell distribution width		13.59±1.05		13.18±0.70	0.100**

VN: Vestibular neuritis; SD: Standard deviation; * Student t test; a Pearson chi-square test; ** Mann-Whitney U test.

symptoms, and *(v)* a positive head impulse test. The exclusion criteria were as follows: *(i)* the presence of any comorbid disease, such as anemia, diabetes mellitus, or hypertension; *(ii)* repeated vertigo attacks; *(iii)* the presence of chronic otitis media; *(iv)* acute hearing loss; *(v)* abnormal magnetic resonance imaging findings. Before treatment, all patients were assessed by a complete blood count, including RDW, neutrophil, lymphocyte, platelet, and monocyte levels. The study calculated NLR, PLR, and lymphocyte-monocyte ratio (LMR) using the data for all participants.

The patients' clinical course was followed according to symptoms and signs, such as vertigo, dizziness, nausea, vomiting, and nystagmus. In the study, the clinical course of VN was based on the duration of nystagmus obtained during hospitalization using Frenzel goggles. Patients were divided into two groups according to the mean nystagmus duration: those with nystagmus lasting ≤5 days called Group 1 and those with nystagmus lasting >5 days called Group 2.

Statistical analysis

Data were analyzed using SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). The convenience of parameters for the normal range was analyzed using the Shapiro-Wilk test. To compare two groups with normally distributed parameters, Student's t-test was used. Finally, the Mann-Whitney U test was used to compare the two groups with nonnormally distributed parameters. A *p*-value <0.05 was considered statistically significant.

RESULTS

In descriptive analyses, no statistical difference in age or sex was found between the two groups (p=0.20 and p=0.789, respectively; Table 1). In the VN group, hemoglobin levels, lymphocyte levels, and LMR values were lower (p<0.001, p=0.001, and p=0.001, respectively), but NLR and PLR values were significantly higher (p=0.001 and p<0.001, respectively) than in the control group (shown in Figures 1a-c and Table 1).

In the VN group, nystagmus was between one and 13 days (mean: 5.12±2.33 days; median: 5 days). The duration of nystagmus was ≤5 days in 59.5% (n=25; mean age: 48.9±11.3 years) of VN patients, and it was >5 days in the remainder (40.5%, n=17; mean age: 43.4±10.0 years). There was no statistical difference between the ages of the two subgroups (p=0.115, Table 2).

Comparison between the subgroups of the VN group revealed that RDW, platelet, lymphocyte, and monocyte levels were significantly higher, and hemoglobin was significantly lower in those with >5 days of nystagmus (p<0.001, p=0.026, p=0.033, p=0.047, and p=0.006, respectively; Table 2). The difference between the subgroups by RDW is displayed in Figure 2.

DISCUSSION

In this study, we aim to determine whether RDW, as well as other inflammatory markers of complete blood count, have any predictive value for the etiology, diagnosis, and prognosis of VN. The inflammatory markers of complete blood count may be affected in any inflammatory situation. Since the mean platelet volume (MPV) and RDW are related to the volume of

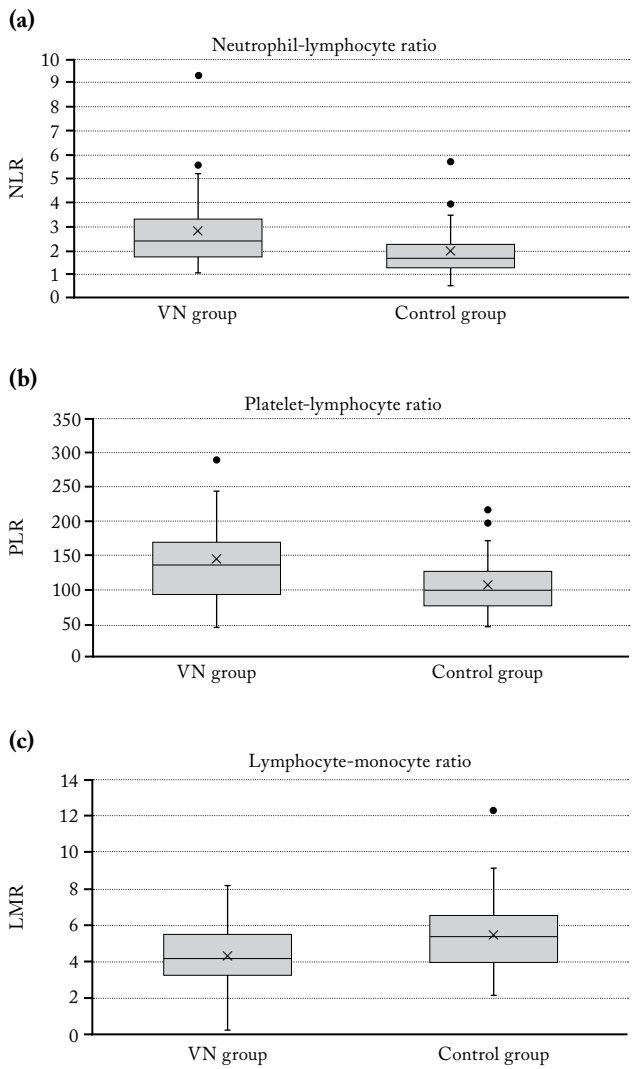

Figure 1. Comparison of NLR, PLR, and LMR between the case and control groups. **(a)** NLR, **(b)** PLR, **(c)** LMR.

VN group: Vestibular neuritis group; NLR: Comparison of neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; LMR: Lymphocyte-monocyte ratio.

Table 2
Demographic data and blood analysis of subgroups of the case group

	Group 1 (n=25) (Nystagmus <5 days)		Group 2 (n=17) (Nystagmus >5 days)		
	n	Mean+SD	n	Mean+SD	*p*
Age (year)		48.9±11.3		43.4±10.0	0.115*
Sex					0.824[a]
Female	17		11		
Male	8		6		
Hemoglobin (g/dL)		13.91±1.19		12.82±1.20	0.006*
Platelet (10^3/uL)		249.60±59.26		288.65±44.37	0.026*
Neutrophil (10^3/uL)		5.29±1.76		5.25±1.46	0.938*
Lymphocyte (10^3/uL)		2.00±0.89		2.29±0.64	0.033**
Monocyte (10^3/uL)		0.50±0.23		0.83±1.04	0.047**
Neutrophil-lymphocyte ratio		3.06±1.77		2.45±1.00	0.206**
Platelet-lymphocyte ratio		139.81±52.32		135.94±45.62	0.805*
Lymphocyte-monocyte		4.36+1.49		4.02±1.66	0.496*
Red cell distribution width		12.96±0.37		14.51±1.07	<0.001**

VN: Vestibular neuritis; SD: Standard deviation; * Student t test; a Pearson chi-square test; ** Mann-Whitney U test.

the cells, they may cause occlusion of the microvessels such as the labyrinthine artery supplying the inner ear.[10,13,15] Sahin et al.[10] studied the MPV in VN and concluded that a high level of MPV might play a role in vascular thrombosis, causing VN. Similar to MPV, a high level of RDW may cause an increase in blood viscosity, impair blood flow, and occlude the microvessels.[15] Therefore, we studied RDW, besides the other inflammatory markers, in VN and whether it contributes to the etiology or prognosis.

The current study provides information on the importance of hematological laboratory markers in VN. Two valuable results were obtained. The first result effective for prognosis was that high RDW, platelet, lymphocyte, and monocyte levels were poor, but high hemoglobin levels were strong prognostic factors for VN patients. The second result effective for diagnosis was that lymphocyte levels and LMR values were low, but NLR and PLR values were high in VN patients.

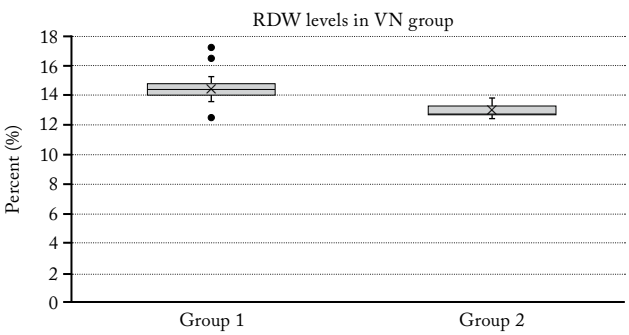

Figure 2. Comparison of RDW levels between the subgroups of vestibular neuritis.
RDW: Red cell distribution width.

The normal levels of the inflammatory markers in complete blood count may be changed by age, sex, and ethnicity.[16-18] In addition to those parameters, anemia may cause an increase in RDW levels.[18] In our study, the VN and control groups did not differ in age and sex. Although the case and control groups did not have anemia, the hemoglobin levels of VN patients were low within normal limits. Moreover, patients with spontaneous nystagmus lasting more than five days had lower hemoglobin levels than the other VN patients. Therefore, low hemoglobin levels may be a poor prognostic factor for VN. In other words, high hemoglobin levels may be a strong prognostic factor for VN.

A few studies have found a relationship between VN and inflammatory markers obtained from a complete blood count.[9,10,19] Chung et al.[9] studied the significance of NLR and PLR in VN in adult patients, but they did not explore the relationship between RDW and VN. The authors grouped patients according to the duration of spontaneous nystagmus. They found that

NLR and PLR were high in patients with nystagmus over five days; thus, NLR and PLR were reliable parameters for predicting VN prognosis.[9] In another study, Sahin et al.[10] showed an increment in MPV, as well as NLR and PLR, in VN patients. They claimed that MPV may play a role in the etiology of VN, causing vascular thrombosis. They also evaluated the correlation between the length of hospitalization and NLR and PLR, but they could not find any correlation. In a study involving a pediatric group, Jeong et al.[19] studied the predictive value of inflammatory markers (neutrophil, lymphocyte, RDW, and MPV) in VN patients. They checked the severity of the disease using two questionnaires, namely the Pediatric Vestibular Symptom Questionnaire and the Dizziness Handicap Inventory, and divided groups according to the duration of spontaneous nystagmus. They declared that NLR and PLR were efficient indicators for pediatric VN patients but had no relation to RDW or MPV. Our study sought a correlation between the inflammatory markers, complete blood count, and VN in adult patients and found that high RDW, platelet, lymphocyte, and monocyte levels were poor, but high hemoglobin levels were strong prognostic factors for VN patients. In addition, lymphocyte levels and LMR values were low, but NLR and PLR values were increased in VN patients. The severity of the disease was determined using the duration of spontaneous nystagmus since it was an objective sign for follow-up of VN. Like Chung et al.,[9] we decided on a cut-off day for the severity of the disease according to the mean value of the duration of spontaneous nystagmus. Since it was found to be 5.12 days, we preferred the cut-off day as five days, and two subgroups were obtained in the VN group.

The correlation between RDW and other otologic diseases with similar etiology of VN was also demonstrated in various studies. Nonoyama et al.[14] studied RDW of idiopathic sudden sensorineural hearing loss patients and showed that RDW levels were significantly higher in unrecovered patients than in recovered ones. Horibe et al.[11] found that unrecovered Bell's palsy patients had higher RDW than the recovered group. Still, Karatoprak and Yılmaz[20] claimed no prognostic effect of RDW on Bell's palsy in a pediatric group. Moreover, high RDW levels have been established as a negative prognostic factor in several diseases, such as coronary heart disease, pancreatitis, and rheumatoid arthritis.[21-23] Since our study showed RDW levels were high in VN patients with long-lasting spontaneous nystagmus, we concluded that high RDW levels may be a poor prognostic factor in VN.

The effect of NLR and PLR on the prognosis of some otologic diseases, such as sudden hearing loss and Bell's palsy, has been widely investigated. High NLR and PLR values were diagnostic and prognostic factors for sudden hearing loss.[14,24] Moreover, high NLR was also a poor prognostic factor for Bell's palsy.[25,26] In several studies on diseases unrelated to otology, such as allergic rhinitis, coronary heart disease, and cancer, high NLR and PLR values were claimed as poor prognostic factors.[27-29] However, according to our study, NLR and PLR were significantly high in VN patients but not different depending on the severity of the disease. Thus, according to our study, NLR and PLR may be diagnostic factors for VN patients and may contribute to the etiology of the disease; however, they are not prognostic factors for VN.

A few studies have also investigated LMR as a prognostic factor in head and neck cancer. In contrast to NLR and PLR, high LMR has been found to be a positive prognostic factor in cancer.[30] In this study, we also investigated the relation between LMR and VN and found that LMR was low in VN patients, but there was no significant relation with the duration of nystagmus. Thus, low LMR may have diagnostic but not prognostic value for VN.

The current study's limitations are the small number of sample size and the retrospective design in a single center. In the literature, a few studies have examined the correlation between inflammatory markers and VN. Therefore, more studies are needed.

In conclusion, high RDW and low hemoglobin levels may predict a poor prognosis in adult VN patients. Moreover, supporting the literature, LMR values were low, but NLR and PLR values were high in VN patients; thus, they may support diagnosis. For the diagnosis and follow-up of VN disease, laboratory tests, including the inflammatory markers of the complete blood count, are inexpensive and accessible in every clinic. Thus, the decision to refer VN patients to tertiary care centers may be easier for outpatient, primary, and secondary care clinics.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Okmeydanı Training and Research Hospital Ethics Committee (date: 19.06.2018, no: 932). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Has mainly contributed to conceptualization, methodology and writing the original draft of the study: A.B.Y.; Has mainly contributed to data curation and investigation of the study: E.A.A.; Has mainly contributed to writing-review and editing of the study: A.E.G.; Has mainly contributed to data analysis and resources of the study: A.A.B.; Has mainly contributed to methodology and editing of the study: H.S.B.; Has mainly contributed to supervision and writing-review of the study: Y.U.

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