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Is the Systemic Immune-Inflammation Index Associated with the Prognosis and Severity of Bell's Palsy?

Sistemik İmmün-İnflamasyon İndeksi, Bell Palsinin Prognozu ve Şiddeti ile İlişkili mi?

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ABSTRACT

Objective: To investigate the effect of newly defined systemic immune-inflammation index levels on the diagnosis, prognosis, and severity of Bell's palsy.

Materials and Methods: The study group was formed from patients diagnosed with Bell's palsy. Calculated ratios with the data obtained from the complete blood count examinations taken before the treatment were statistically investigated for the diagnosis, prognosis, and severity of the disease.

Results: We did not determine any statistically significant correlation between the determined facial paralysis stages and the investigated ratios. Similarly, there was no correlation between the first and sixth-month recovery rates of the study group and the investigated parameters ($p>0.05$). In addition, differences in parameters between the control and study groups were not statistically significant.

Conclusions: The results of the presented study contain differences from the current literature. In addition, it provides new information about the effect of the systemic immune-inflammation index on the prognosis of Bell's palsy. Considering the outcomes of research on hematological parameters is important, as various factors can impact them.

Keywords: Bell's palsy, ınflammation, lymphocytes, neutrophils, platelets

ÖZ

Amaç: Yeni tanımlanan sistemik immün-inflamasyon indeksi seviyelerinin Bell paralizisinin tanı, prognoz ve şiddeti üzerindeki etkisini araştırmak.

Materyal ve Metot: Çalışma grubu, Bell paralizisi tanısı konan hastalardan oluşturuldu. Tedavi öncesi alınan tam kan sayımı verileri ile hesaplanan oranlar, hastalığın tanı, prognoz ve şiddeti açısından istatistiksel olarak incelendi.

Bulgular: Belirlenen fasial paralizi evreleri ile araştırılan oranlar arasında istatistiksel olarak anlamlı bir korelasyon tespit edilmedi. Benzer şekilde, çalışma grubunun birinci ve altıncı ay iyileşme oranları ile incelenen parametreler arasında bir ilişki bulunmadı ($p>0,05$). Ayrıca, kontrol ve çalışma grubu arasındaki parametre farklılıkları da istatistiksel olarak anlamlı değildi.

Sonuç: Sunulan çalışmanın sonuçları mevcut literatürden farklılıklar içermektedir. Ayrıca, sistemik immün-inflamasyon indeksinin Bell paralizisinin prognozu üzerindeki etkisi hakkında yeni bilgiler sağlamaktadır. Bu hematolojik parametreler üzerinde yapılan araştırma sonuçlarının çeşitli faktörlerden etkilenebileceği göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Bell palsi, inflamasyon, lenfositler, nötrofiller, trombositler

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INTRODUCTION

Bell's palsy is the most common type of acute onset peripheral facial paralysis, and the patients' symptoms can vary from mild to severe according to the degree of neural damage and the localization of the lesion. To diagnose Bell's palsy, it's essential to exclude other causes of peripheral facial paralysis. While the exact etiology of the disease remains unclear, it is understood that inflammation plays a crucial role in the physiopathological process. Inflammatory reactions against the myelin sheath of the peripheral nerves are suggested as a pathogenetic reason by many authors.[1] The efficacy of corticosteroids in the treatment also supports this theory.[2]

Parameters derived from complete blood count data, such as neutrophil-lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR), are commonly studied in the current literature for if they can be used to predict the prognosis of diseases associated with chronic inflammation.[3,4] A new hematologic parameter named systemic Immune-inflammatory Index (SII) calculated with platelet, neutrophil, and lymphocyte counts have also been studied on this subject and concluded that the SII could be beneficial in patients with sudden hearing loss and Bell's palsy.[5,6]

The present study aimed to examine the relationship between the rate of SII and the prognosis of Bell's palsy by evaluating the recovery results after Bell's palsy treatment and investigating the relationship between disease severity and SII. Both of the objectives are investigated for the first time in the literature.

MATERIALS AND METHODS

Ethical Status of the Study: Our study was approved by the Sakarya University Ethical Committee (Date: 12.02.2021; Decision No: 84). The research protocol was created by the ethical principles established by the Declaration of Helsinki and laws and regulations in our country.

Study group: Patients who applied to our clinic with the complaint of peripheral facial paralysis and were diagnosed with Bell's palsy, treated, and followed up between January 2015 and January 2021 were included in the study. A control group was formed from a total of 125 healthy volunteers with demographically similar characteristics. Each participant was informed about the study, and consent forms were duly signed and obtained.

Pathologies in the middle ear, mastoid bone and parotid region, history of otitis media, skin rash, arthralgia, history of trauma, history of surgery and drug use, neurological diseases and serologically detected microbial conditions, high-risk cardiac group (myocardial infarction, valve disease, decompensated heart failure), acute viral or bacterial infection, autoimmune disease, hypertension, diabetes mellitus, hematological malignancy (lymphoproliferative, myeloproliferative diseases, sickle cell anemia, coagulopathies) and patients with malignities were accepted as exclusion criteria. The brain stem, cerebellopontine corner, ear, and parotid lesions were excluded by performing MRI and audiological examinations on each patient participating in the study. The patients' facial palsy grades were staged by using the House-Brackmann classification scale.

Blood Cell Analysis and Clinical Ratios: Peripheral venous blood samples were evaluated by using Cell-Dyn 3700 SL (Abbott Diagnostics, Chicago, Illinois, USA) automated hematology analyzer device before treatment. Neutrophil, lymphocyte, and thrombocyte counts were recorded. By using these data, the SII was calculated by multiplying the platelet count by the neutrophil count and dividing them by the lymphocyte count. NLR and PLR were calculated as described in the literature. The first and sixth-month facial paralysis degrees of the patients treated with systemic methylprednisolone (1mg/kg) were determined. Patients with full recovery were statistically compared with the group of patients with partial or no recovery.

Statistical Method: Statistical evaluation was conducted using the IBM SPSS version 20.0 statistical software program for Windows (IBM Corporation, Armonk, New York, United States of America). Continuous variables were presented as mean ± standard deviation, and categorical variables as percentages. The Kolmogorov-Smirnov test determined normality, guiding the selection of non-parametric tests for other analyses. Mann-Whitney U test and Kruskal Wallis test were used for pairwise comparisons, P values less than 0.05 were considered statistically significant.

RESULTS

Between January 2015 and January 2021, a total of 223 patients with peripheral-type facial paralysis were admitted to our clinic. Twenty-nine of these patients were excluded due to a lack of data. The diagnosis of Bell's palsy was excluded because five patients had an additional neurological disease, and one patient had a cerebellopontine angle tumor. It was decided to exclude from the study sixty patients because of comorbidities and six patients because of pregnancy. At the end of this process, 122 Bell's palsy patients who met the inclusion criteria were included in the study. The mean age of the study group was 37.8±16.2 years, while that of the control group was 38.8±16.3. The male-to-female ratio was 65/57 in the study group and 66/59 in the control group. When the groups were compared in terms of

gender and age with Ki-square and Mann-Whitney U tests, no difference was observed with either analysis for age and gender (p=0.940; p= 0.534). When the patients were classified according to the severity of facial paralysis, 13.9% of them were grade 2, 41% were grade 3, 36.1% were grade 4, 7.4% were grade 5, and 1.6% were grade 6 patients (Figure 1). All of the patients were treated with 1mg/kg/day oral methylprednisolone. This treatment regime was terminated by reducing the dose by halving at 3-day intervals.

At the end of the first month, 71.2% of the patients had a full recovery by decreasing to House-Brackmann grade 1, 26.2% of the patients had partial recovery, and the rest of the patients had no recovery 2.6%. No statistically significant difference was observed in terms of NLR, PLR, and SII rates for the first month's recovery results (p=0.524; 0.388; 0.394) (Table 1).

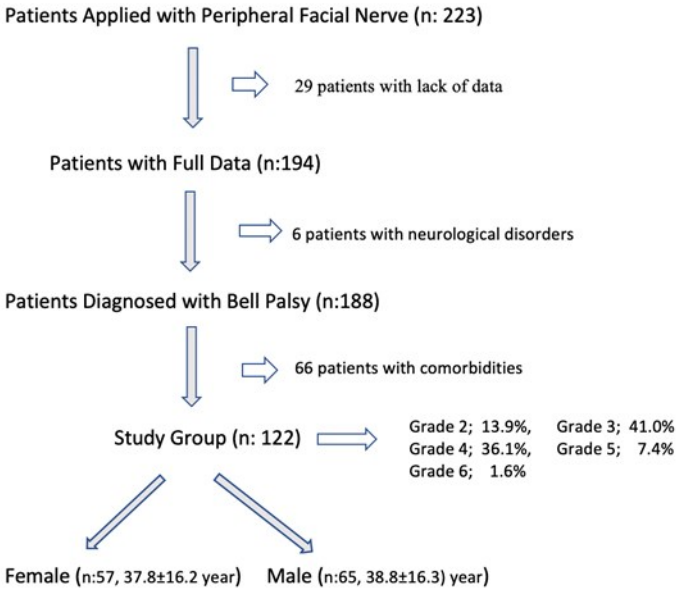

Figure 1. Creation of the study group.

Table 1. Comparison of the parameters in terms of the first month's recovery rates.

	Patients with full recovery (71.2%)			Patients with partial (26.2%) / no recovery (2.6%)			p-value
	25th percentile	Median	75th percentile	25th percentile	Median	75th percentile	
Neutrophil	2.35	4.36	5.29	3.51	5.27	6.57	0.100
Lymphocyte	1.62	2.55	3.24	1.92	2.47	3.38	0.604
Platelet	210	238	295	206	274	314	0.469
NLR	1.19	1.61	2.44	1.2	2.02	2.61	0.524
PLR	73.5	102	147	75.6	92.1	117.1	0.388
SII	273.94	394.56	615.53	316.18	528.30	666.47	0.394

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic Immune-Inflammatory Index.

In the sixth-month evaluation, 90.2% of the patients had fully recovered, achieving a House-Brackmann grade of 1. While partial improvement was observed in 8.2% of the patients, there was no improvement in 1.6% of them. In the sixth month results, there was no statistically significant difference between the groups formed according to treatment response in the comparison of investigated parameters like the first month's results (p=0.770; 0.288; 0.857) (Table 2).

The study group was subgrouped according to the House-Brackman stages and statistically compared in multiple group comparison tests; no statistically significant difference was observed at any of the parameters (p=0.235; 0.241; 0.351) (Table 3).

Comparing the patients in the control and study groups in terms of PLR, NLR, and SII showed no statistically significant difference in any of the parameters (p=0.248; 0.977; 0.360) (Table 4).

Table 2. Comparison of the parameters in terms of the sixth month's recovery rates.

	Patients with full recovery (90.2%)			**Patients with partial (8.2%) / no recovery (1.6%)**			**p-value**
	25th percentile	**Median**	**75th percentile**	**25th percentile**	**Median**	**75th percentile**	
Neutrophil	3.12	4.47	5.61	3.81	4.97	6.81	0.310
Lymphocyte	1.75	2.43	3.32	1.79	2.89	3.62	0.680
Platelet	206.0	242.0	299.2	213.5	244.5	287.0	0.949
NLR	1.21	1.67	2.58	1.38	1.83	2.39	0.770
PLR	75.27	100.54	414.78	61.43	81.95	130.01	0.288
SII	298.30	414.78	635.39	288.00	410.67	600.39	0.857

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic Immune-Inflammatory Index.

Table 3. Comparison of the parameters in terms of initial House-Brackmann stages.

	Grade 2 Median (25-75) n:17	**Grade 3 Median (25-75) n:50**	**Grade 4 Median (25-75) n:44**	**Grade 5-6* Median (25-75) n:11**	**p-value**
NLR	1.42 (0.8-3.1)	1.85 (1.3-2.4)	1.78 (1.2-2.7)	1.35 (0.1-1.7)	0.235
PLR	102.3 (71.4-160.7)	100.5 (76.8-152.3)	104.3 (74.1-136.4)	76.7 (69.4-92.0)	0.241
SII	410.6 (216.3-769.7)	441.4 (299.8-610.3)	456.6 (317.1-669.1)	337.7 (38.4-536.8)	0.351

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic Immune-Inflammatory Index; *: Grades 5 and 6 were combined since grades 6 had only 2 individuals.

Table 4. Comparison of the parameters between the study and control group.

	Study Group			**Control Group**			**p-value**
	25th percentile	Median	75th percentile	25th percentile	Median	75th percentile	
Neutrophil	3.07	3.9	5.35	3.15	4.56	5.68	0.205
Lymphocyte	2.09	2.50	2.85	1.75	2.51	3.33	0.957
Platelet	218.0	254.0	291.0	209.2	242.0	298.2	0.502
NLR	1.25	1.61	2.08	1.24	1.68	2.47	0.248
PLR	81.4	101.9	128.7	74.0	100.4	137.3	0.977
SII	280.33	390.21	554.40	298.30	414.78	621.01	0.360

NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic Immune-Inflammatory Index.

DISCUSSION AND CONCLUSION

Studies examining the etiology of Bell's palsy draw attention to the viral infections, anatomical causes, theories related to ischemia, exposure to cold and immune-inflammatory theories.[7] Regardless of the etiological factors, inflammation, which is the main pathophysiological result, occurs in the facial nerve, and the compression of the nerve in a narrow canal leads to clinical symptoms. So, biomarkers that are related to inflammation have always been a necessity in this regard. A literature review on this subject shows that biological markers that can be associated with both the severity and prognosis of facial paralysis are tried to be determined. In this regard, it has been reported in previous studies that IL-6, IL-8 TNF-a, and CRP levels are higher in Bell's palsy patients than in controls.[8,9]

Another biomarker examined in this regard is the neutrophil-lymphocyte ratio (NLR), which can be easily obtained with complete blood count values, and studied in many diseases with inflammatory etiology, including cardiological and oncological diseases. Similarly, there are many studies examining the relationship between Bell's palsy and NLR. According to a meta-analysis of seven articles, including 791 patients in total, NLR rates were found to be higher in patients with Bell's palsy than in controls.[3] A few studies examining the relationship between NLR rates and prognosis concluded that high NLR values were associated with poor prognosis.[10-12] According to the results of our study, it was observed that there was no difference between the control and Bell's palsy groups in terms of NLR rates. In addition, when the study group was evaluated in terms of recovery rates, no statistically significant difference was observed in the recovery results of both the first month and the sixth month. These results differ from the published literature.

PLR, another indicator of ischemia and inflammation, is among the parameters used to show the inflammation observed in Bell's palsy cases, similar to NLR.[13] When the studies on this subject are examined, in the article written by Atan et al., although PLR was found to be statistically higher in the Bell's palsy group than the control group, no correlation was found with the degree of Bell's palsy.[14] Similarly, in the study of Kim et al., higher PLR values were found when they were compared to the control group, and it was emphasized that high PLR values were associated with poor prognosis. However, there was no correlation between the degree of facial paralysis and PLR.[15] In the study of Kınar et al. and the meta-analysis results of Oya et al., no statistically significant difference was observed between the healthy control group and the Bell's palsy groups in terms of PLR values.[3,6] The results of our study also support the lack of a diagnostic and prognostic correlation between PLR and Bell's palsy.

In recent years, SII has been used as a new biomarker for inflammatory diseases. Most of the studies on this subject have been done with patients diagnosed with malignancies.[16-19] Atasever et al. also examined SII biomarkers in patients diagnosed with laryngeal carcinoma. They reported a statistically significant relationship between SII and lymphovascular invasion.[20] There is only one study in the literature in which Bell's Palsy and SII were studied.[6] In this study, Kınar et al. emphasized that the SII was statistically significantly higher in the Bell's palsy patient group than in the control group, which would make a diagnostic contribution.[6] Similar results were not observed in our study. Although minimally higher values were observed in NLR and SII values compared to the control group, the difference was not statistically significant. In addition, in our study, SII and Bell's palsy severity and treatment response rates were compared statistically for the first time in the literature, and no statistically significant difference was observed.

Considering that many new diseases and conditions can affect the inflammatory parameters mentioned in current studies continue to be identified, many different diseases were determined as exclusion criteria in our study; unfortunately, it is impossible to create groups with completely identical characteristics. This situation constitutes the most critical study limitation, as in similar studies in the literature.

In conclusion, there is no clear consensus on the relationship between the investigated parameters and Bell's palsy. The presented study results also contain differences from the literature both in terms of NLR and PLR and for SII, a new inflammation marker. We think that it will be beneficial to continue to carry out objective studies on this subject.

Ethics Committee Approval: Our study was approved by the Sakarya University Ethics Committee (Date: 12.02.2021, decision no: 84). The study was carried out following the international declaration, guidelines, etc.

Conflict of Interest: No conflict of interest was declared by the authors.

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