DOI: 10.4274/jbuch.galenos.2024.82574
J Dr Behcet Uz Child Hosp 2025;15(1):1-6

Original Article

The Role of Systemic Immune-Inflammation Index and Systemic Inflammation Response Index in the Diagnosis of Bell's Palsy

Bell Palsi Tanısında Sistemik İmmün-İnflamasyon İndeksi ve Sistemik İnflamasyon Yanıt İndeksi'nin Rolü

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ABSTRACT

Objective: Recent studies showed that Systemic Immune-Inflammation Index (SII), Systemic Inflammation Response Index (SIRI) can be used as inflammatory markers. The aim of this study was to determine the prognostic value of SII and SIRI in children with Bell's palsy (BP) disease.

Method: This retrospective study included 107 children diagnosed with BP from 2019 to 2022 in institute and an age- and sex-matched 100 healthy control group. A complete blood count was performed for all participants and hemoglobin, erythrocytes, white blood cell (WBC), absolute neutrophil count (ANC), lymphocytes, and platelet counts were measured. The platelet-lymphocyte ratio, neutrophil-to-lymphocyte ratio (NLR), SII and SIRI values were calculated with the formula.

Results: The male-to-female ratio was 54/53 in patient and 42/58 in the control groups. In estimation of BP, area under the curve was 0.78 for WBC [95% confidence interval (CI): 0.72-0.84, p<0.001], 0.80 for ANC [(95% CI: 0.75-0.86), p<0.001], 0.59 for absolute lymphocyte count [(95% CI: 0.51-0.67), p=0.258], 0.70 for NLR [(95% CI: 0.62-0.77), p<0.001], 0.77 for SII [(95% CI: 0.71-0.84), p<0.001] and for SIRI 0.68 [(95% CI: 0.61-0.76), p=0.001]. When the markers were analyzed according to the most appropriate cut-off values in the prediction of BP, the best markers were determined as WBC, ANC, SII and SIRI (p<0.05).

Conclusion: BP has an inflammatory component. The SII and SIRI value can indicate an inflammatory condition in these patients. It may be used as an indicator marker in BP.

Keywords: Bell's palsy, facial paralysis, Systemic Immune-Inflammation Index, Systemic Inflammation Response Index

ÖZ

Amaç: Son çalışmalar, Sistemik İmmün-İnflamasyon İndeksi (SII), Sistemik İnflamasyon Yanıt İndeksi'nin (SIRI) inflamatuvar belirteçler olarak kullanılabileceğini göstermiştir. Bu çalışmanın amacı, Bell felci hastalığı olan çocuklarda SII ve SIRI'nin prognostik değerini belirlemekti.

Yöntem: Bu retrospektif çalışmaya, 2019-2022 yılları arasında pediatrik acil serviste Bell felci tanısı konulan 107 çocuk ve yaş ve cinsiyete göre eşleştirilmiş 100 sağlıklı kontrol grubu dahil edildi. Tüm katılımcılar için tam kan sayımı yapıldı ve hemoglobin, eritrositler, beyaz kan hücresi (WBC), mutlak nötrofil sayısı (ANC), lenfositler ve trombosit sayıları ölçüldü. Trombosit-lenfosit oranı, nötrofil-lenfosit oranı (NLR), SII ve SIRI değerleri formülle hesaplandı.

Bulgular: Erkek-kadın oranı hasta grubunda 54/53, kontrol grubunda ise 42/58 idi. Bell felcinin tahmininde, eğri altında kalan alan WBC için 0,78 [95% güven aralığı (GA): 0,72-0,84, p<0,001], ANC için 0,80 [(95% GA: 0,75-0,86), p<0,001], mutlak lenfosit sayısı için 0,59 [(95% GA: 0,51-0,67), p=0,258], NLR için 0,70 [(95% GA: 0,62-0,77), p<0,001], SII için 0,77 [(95% GA: 0,71-0,84), p<0,001] ve SIRI için 0,68 [(95% GA: 0,61-0,76), p=0,001] idi. Bell felcinin tahmininde en uygun kesme değerlerine göre belirteçler analiz edildiğinde en iyi belirteçler WBC, ANC, SII ve SIRI olarak belirlendi (p<0,05).

Sonuç: Bell felcinin inflamatuvar bir bileşeni vardır. SII ve SIRI değeri bu hastalarda inflamatuvar bir durumu gösterebilir. Bell felcinde bir gösterge belirteci olarak kullanılabilir.

Anahtar kelimeler: Bell felci, yüz felci, Sistemik İmmün-İnflamasyon İndeksi, Sistemik İnflamasyon Yanıtı İndeksi

Received: 20.09.2024
Accepted: 28.11.2024
Publication Date: 16.04.2025

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Cite as: Öztürk B, Yaradılmış RM, Güneylioğlu MM, Güngör A, Bodur İ, Göktuğ A, Aydın O, Akçaboy M, Atasoy E, Karacan CD, Tuygun N. The role of systemic immune-inflammation index and systemic inflammation response index in the diagnosis of Bell's palsy. J Dr Behcet Uz Child Hosp. 2025;15(1):1-6

INTRODUCTION

Acute peripheral facial paralysis is usually a self-limiting benign disease characterized by paralysis or weakness of the muscles controlled by the facial nerve on one side of the face. Peripheral facial nerve palsy is an uncommon cause of emergency department (ED) access in childhood however, it is a worrying situation for both the clinicians, the child, and the parents. The most common cause is idiopathic which is called Bell's palsy (BP), responsible for 50% to 75% of all cases. Other etiologies include complicated upper respiratory tract infections, herpetic viral infections, and neuroborreliosis[1-4]. Inflammation affecting the facial nerve plays an important role in the pathogenesis of BP. Recent studies have shown that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and mean platelet volume can be used as inflammatory markers in BP[1,5,6].

Systemic immune-inflammation index (SII) is a novel index calculated by multiplying the thrombocyte count with the NLR and it can be used as an indicator of the relationship between the immune system and the inflammatory situation of the patient. Firstly, it was introduced as a prognostic tool to identify the recurrence of hepatocellular carcinoma in 2014[7]. Recent studies demonstrated the prognostic effect of SII in infective endocarditis, coronavirus-19 disease, Guillain-Barré syndrome, and sinus venous thrombosis[8-11] Kınar et al.[12] demonstrated the prognostic value of SII in adult patients with BP in a recent study. The Systemic Inflammation Response Index (SIRI) is calculated with the formula as; neutrophil count x monocyte/lymphocyte count, which can better reflect the host immune and inflammation balance. SIRI was also reported as a prognostic tool in different malignancies[13]. However, the prognostic value of these indices in children with BP remains unclear.

The aim of this study was to determine the prognostic value of SII and SIRI in children with BP disease.

MATERIALS and METHODS

Study Design and Patient Selection

A retrospective study was conducted in institute after the approval of the University of Health Sciences Turkey, Ankara Dr. Sami Ulus Gynaecology and Paediatrics Trainig and Research Hospital Clinical Research Ethics Committee (approval number: E-22/04-319, date: 06.04.2022). The patients' registry system was scanned from January 1, 2019, to May 30, 2022, for the diagnosis of ICD G51.0 and the inclusion criteria were as follows; age between 1 month to 18 years, had complete blood count (CBC) analysis and treated for BP. A diagnosis of BP is made based on clinical presentation-acute facial nerve weakness or paralysis on one side of the face and by ruling out other possible causes of facial paralysis. Patients were excluded if they had congenital fascial paralysis, central fascial paralysis, otitis media, type 1 diabetes mellitus, congenital adrenal hyperplasia, pregnancy, persistent facial paralysis, stroke, cranial neuritis, and Guillain-Barré syndrome. Finally, there were 107 patients with BP included in this study Figure 1.

Age- and sex-matched control group was conducted from the patients that were admitted to the hospital for routine health control and had a routine blood analysis. There was 100 healthy volunteers (58 girls and 42 boys) in the control group.

Evaluation and Treatment

Patient records were scanned, and the age, gender, time from symptom onset to hospital arrival, time to symptom resolution, the House-Brackmann facial nerve grading system. The House-Brackmann Facial Nerve Grading System was first described at the Annual Meeting of the American Academy of Otolaryngology-Head and Neck Surgery in 1985 and is widely used to characterize the clinical assessment of facial paralysis. This scale ranges from grade I to grade VI, with 1 defining normal function and grade VI representing complete paralysis[14].

The dose and the duration of steroid treatment, and the initial CBC results to calculate the SIRI and SII were recorded. The disease recovery was determined from the face-to-face examination records of patients at the control admittance to pediatric neurology, ear-

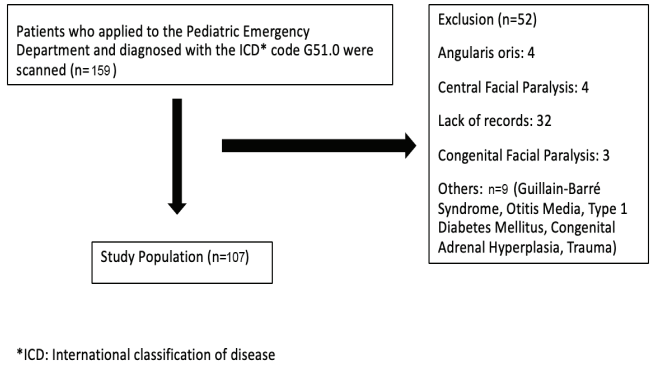

Figure 1. Flow chart of study and inclusion-exclusion criterias

nose-throat, pediatrics, or pediatric EDs. Patients whose symptoms were resolved within the first month were classified as recovery group. We recorded the age, gender, and CBC results of the children in the control group.

Complete blood cell counts were obtained by automatic analysis Advia 2120i (Siemens Healthcare Diagnostics, Eschborn, Germany). The white blood cell (WBC) count, absolute lymphocyte count (ALC), absolute neutrophil count (ANC), NLR, PLR, SII, and SIRI were calculated and recorded.

Statistical Analysis

Statistical analysis of the data obtained in the study was made in IBM SPSS for Windows Version 20.0 package program. Descriptive statistics [percentage, mean, median, standard deviation (SD), range of quarters (IQR)] were used to define the population included in the study. In the comparison of patients and control group, Chi-square or Fisher's exact test and t-test were used for categorical and continuous variables, respectively, and the Mann-Whitney U test was used for variables not suitable for normal distribution. Receiver operating characteristic (ROC) analysis was performed, ROC curves were plotted, and the Youden Index method was used to determine the optimal WBC, ALC, ANC, NLR, SII, and SIRI percent cut-off values to predict BP. The area under the curve (AUC) was calculated to predict BP and compare the performance of each marker. Sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) were calculated for the markers. For all analyses, $p<0.05$ was considered statistically significant.

RESULTS

This study included 107 patients with BP and 100 age- and sex-matched healthy controls. The mean age was 145 ± SD months (2-234 min., max.) in the patient group and 144 ± SD months (54-182 min., max.) in the control group. The male-to-female ratio was 54/53 in the patient group and 42/58 in the control group. The patient and the control groups had similar distributions concerning age and sex (p=0.892). The characteristic features and CBC results of the patients and controls are summarized in Table 1.

The median duration of symptoms in patients with BP was 24 hours (1-192 min., max.). On physical examination, none of the patients had any findings other than facial paralysis. Thirty patients (3 cranial computed tomography and 27 magnetic resonance imagining) underwent further radiological imagining to rule out other causes of fascial paralysis which were all reported as normal. The mean House-Brackmann grade was 3±1 in patients with BP. Of the 107 patients, 91 were treated with 1.02±0.69 mg/kg oral corticosteroids (methylprednisolone). The corticosteroid treatment was tapered and stopped in all patients for mean 8.9±5 days, and no drug-related adverse event was observed.

In estimation of BP, AUC was 0.78 for WBC [95% confidence interval (CI): 0.72-0,84, p<0.001], 0.80 for ANC [(95% CI: 0.75-0,86), p<0.001], 0.59 for ALC [(95% CI: 0.51-0,67), p=0.258], 0.70 for NLR [(95% CI: 0.62-0,77), p<0.001] , 0.77 for SII [(95% CI: 0.71-0,84), p<0.001] and for SIRI 0,68 [(95% CI: 0.61-0,76), p=0.001]. Sensitivity, specificity, PPV, NPV, AUC, and odds ratio (OR) values for each marker are given in Table 2. When the markers were analyzed according to the most appropriate cut-

Table 1. WBC, platelet, ANC, ALC, MPV, NLP, PLR, SII ve SIRI values of participants

	Bell's palsy patients		Control group		p-value
	Median	(Min.-max.)	Median	(Min.-max.)	
WBC (/mm³)	8290	3930-18770	6365	3580-11130	<0.001
Platelet (x10³ cells/mm³)	339	155-683	295	246-552	<0.001
ANC (/mm³)	4450	1670-15090	2895	1430-5670	<0.001
ALC (/mm³)	2630	1590-5950	2495	1450-4590	0.018
MPV(/fl)	8.4	6.1-11.4	10.15	7.2-12.6	<0.001
NLR	1.53	0.62-6.67	1.20	0.51-1.97	<0.001
PLR	120	52.7-558	116.09	40-235.17	0.236
SII (x10⁹/L)	506	140-3338	353	151-793	<0.001
SIRI (x10⁶/L)	933.8	200-517980	585.2	194-1359	<0.001

Mann-Whitney U test, WBC: White blood cell, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, MPV: Mean platelet volume, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, Min.-max.: Minimum- maximum

Table 2. Efficiency of inflammation markers in predicting Bell's palsy							
	AUC (%95)	Cut-off	OR (95%, CI)	Sensivity	Specifity	PPV	NPV
WBC	0.78	7155	7.07 (3.8-13)	73.3	72	73.3	72
ALC	0.60	2670	1.4 (0.8-2.4)	46.7	62	56.3	52.5
ANC	0.81	3495	9.1 (4.8-17.1)	75.2	75	76	74.3
NLR	0.70	1.295	3.4 (1.9-6)	65.7	64	65.7	64
SII	0.78	408	2.6 (1.5-4.6)	73.3	73	74	72.3
SIRI	0.68	646	7.4 (4-13.7)	61.9	62	63.1	60.8

p-value <0.05 statistically significant. WBC: White blood cell, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, AUC: Area under the curve, OR: Odds ratio, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

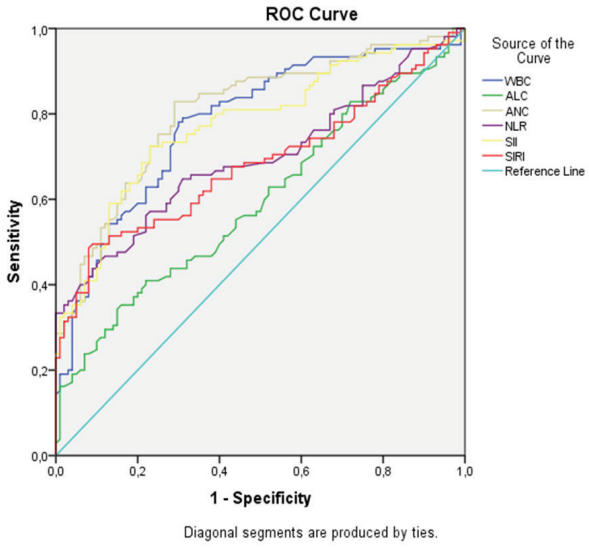

Figure 2. ROC curves of inflammation markers to predict BP

ROC: Receiver operating characteristic, BP: Bell's palsy, WBC: White blood cell, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index

off values in the prediction of BP, the best markers were determined as ANC, SII, and WBC. The ROC curves of the markers for the prediction of BP are shown in Figure 2.

The resolution of the symptoms took less than 1 month in 94 patients (recovery group) while the symptoms persisted in 13 patients after one month (non-recovery group). The mean House-Brackmann grade of these patients in the non-recovery group after one month was 2. There was no difference between the onset of the disease process, the initial House-Brackmann Facial Paralysis Scale, the onset of the treatment period, WBC, PLT, ANC, ALC, NLR, PLR, SII, and SIRI parameters between the recovery and non-recovery patients.

DISCUSSION

This was the first study to evaluate the prognostic value of SII and SIRI in children with BP. This study demonstrated higher SII and SIRI in 107 children with BP compared to the healthy controls. SII is based on platelet counts and NLR (SII is defined as neutrophils x platelets/lymphocytes) and it's a novel inflammation biomarker and can comprehensively reflect the body's inflammatory and immune status[15]. Furthermore, SIRI, which combines the absolute values of neutrophils, monocytes, and lymphocytes (calculated by neutrophil count x monocyte count/lymphocyte count), is a novel inflammatory index and has been widely considered in disease diagnosis and prognosis evaluation in recent years[16]. Based on these findings, we investigated SII and SIRI, a marker that has not yet been studied in children with BP. The cut-off values of SII and SIRI were 408 and 646 respectively and this study demonstrated the prognostic value of SII and SIRI in the pediatric population. Similarly, Kınar et al.[12] reported the prognostic value of SII in adult patients. Compared with SII, the OR ratio of SIRI was higher, and the SIRI is a parameter that is easy to calculate, it can help to identify the patient quickly and make better medical decisions in clinical practice.

Facial nerve palsy is a common disease in children due to congenital or acquired (infectious, neoplastic, traumatic, or idiopathic)[17]. It can affect anyone, regardless of any age and gender. The incidence of peripheral facial nerve palsy in children varies from 5 to 21 in 100,000 annually[18]. The main physical findings of fascial nerve palsy are the inability to fully close the mouth and eye and nasolabial fold on the effected side and causing difficulties in eating and speaking corneal drying and erosion[19]. The diagnosis of BP can made by

physical examination and exclusion of other reasons for facial palsy. In this study, 30 patients needed further imaging to rule out other etiological causes of the disease. The symptoms peak in the first week and then gradually resolve over 3 weeks to 3 months[20]. The first treatment option for pediatric BP is the administration of corticosteroids and for good recovery of facial function, investigators have recommended that physicians initiate steroid therapy within 3 days of symptom onset[21]. Oral prednisolone (1 mg/kg/d) was reported to be highly effective in the treatment of BP in children[22]. The patients in this study were also treated with a similar dose and duration of corticosteroid therapy.

The causes of BP remain unclear, although viral infection, microvascular circulatory impairment, and genetic and immunological diseases have been proposed as possible factors[23]. BP is a diagnosis of exclusion and the initial test required for this is CBC[18]. A CBC provides useful information for evaluating a patient's general state and inflammation status. In this study, the NLR, PLR, SII, and SIRI can be easily calculated from patients' CBC data. The NLR is regarded as a marker of systemic inflammation. It reflects inflammatory status and provides important information about prognosis[24]. Eryilmaz et al.[15] reported that NLR values were higher in children with BP than in the control group and, thus, suggested that NLR is a supportive parameter in the diagnosis of pediatric BP[25]. Similarly, for the prediction of BP, WBC and ANC had the highest AUC and OR in this study. The neutrophil count is the main inflammatory marker, and our study shows a stronger association between increased neutrophils and BP.

The PLR has been used to gauge the risk for microcirculatory thromboembolism. In BP, one group of investigators reported a correlation between high PLR and BP in children[15,26]. Although the platelet count and the PLR was higher in the patients than in the control group, there were no significant difference in this study. Yılmaz et al.[27] reported elevated serum cytokine levels including interleukin-1 (IL-1), IL-6, and tumor necrosis factor-alpha in patients with BP compared to the control group. Accordingly, the authors concluded that BP may more likely be an inflammatory situation than an ischemic disease.

Study Limitations

Limitations of this study include its retrospective design and the small number of patients with BP. Thus, further, multicenter, prospective studies are warranted. The absence of the hearing test due to the conditions of the hospital may be listed as a limitation of this study.

CONCLUSION

In conclusion, pretreatment hematological findings in children with BP provide useful information. Thus, as new and quicker markers with low cost, both the SII and SIRI can be used as diagnostic indicators of BP. More studies are needed to understand the role of SII and SIRI in BP.

Ethics

Ethics Committee Approval: A retrospective study was conducted in institute after the approval of the University of Health Sciences Turkey, Ankara Dr. Sami Ulus Gynaecology and Paediatrics Trainig and Research Hospital Clinical Research Ethics Committee (approval number: E-22/04-319, date: 06.04.2022).

Informed Consent: Retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: M.M.G., A.Gö, M.A., E.A, Concept: B.Ö., A.G., A.Gö, Design: B.Ö., R.M.Y., A.G., A.Gö, Data Collection or Processing: İ.B., M.A., E.A, Analysis or Interpretation: R.M.Y., İ.B., M.A., C.D.K, N.T, Literature Search: R.M.Y., A.G., C.D.K, N.T, Writing: B.Ö., R.M.Y., C.D.K, N.T

Conflict of Interest: The authors have no conflict of interest to declare.

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

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