



The Role of Neutrophil-Lymphocyte Ratio and Thrombocyte-Lymphocyte Ratio, Systemic Immune Inflammation Index and Systemic Inflammation Response Index in Identifying Risk Factors in Paediatric Patients with Multiple Surgical Treatments for Septic Arthritis: A Single Centre Study

Septik Artrit Nedeniyle Birden Fazla Cerrahi Tedavi Uygulanmış Pedyatrik Hastalardaki Risk Faktörlerini Belirlemede Nötrofil-Lenfosit Oranı ve Trombosit-Lenfosit Oranı ile Sistemik İmmün İnflamasyon İndeksi ve Sistemik İnflamasyon Yanıt İndeksinin Rolü: Tek Merkezli Çalışma

Ahmet Yiğitbay¹(ID), Muhammed Can Ari²(ID), Alev Kural³(ID), Ersin Erçin^{3,4}(ID), Cemal Kural³(ID)

¹ Clinic of Orthopedics and Traumatology, Siverek State Hospital, Şanlıurfa, Türkiye

² Clinic of Orthopedics and Traumatology, Çermik State Hospital, Diyarbakır, Türkiye

³ Clinic of Orthopedics and Traumatology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Türkiye

⁴ Centre for Innovation in Medical Education (CIMED), Ottawa University Faculty of Medicine, Ottawa, Canada

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Abstract

Objective: Our study aimed to determine the effect of neutrophil-to-lymphocyte ratio, thrombocyte-to-lymphocyte ratio, systemic immune inflammation index (SII), and systemic inflammation response index (SIRI) in determining risk factors in pediatric patients who had undergone more than one surgical treatment for septic arthritis.

Material and Methods: The study included patients younger than 16 years of age who were surgically treated for septic arthritis between 2018 and 2022. Blood neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), platelet count x neutrophil count/lymphocyte count ratio (SII), and monocyte count x neutrophil count/lymphocyte count ratio (SIRI) were calculated at admission.

Results: Mean age of the 25 patients (10 males, 40%; 15 females, 60%) included in the study was (6.24 ± 4.51) years. The number of patients

Öz

Giriş: Bu çalışmanın amacı septik artrit nedeniyle birden fazla cerrahi tedavi uygulanmış pediyatrik hastalardaki risk faktörlerini belirlemede nötrofil-lenfosit oranı ve trombosit-lenfosit oranı ile sistemik immün inflamasyon indeksi (SII) ve sistemik inflamasyon yanıt indeksinin (SIRI) etkisini belirlemektir.

Gereç ve Yöntemler: Çalışmaya 2018-2022 tarihleri arasında septik artrit nedeniyle cerrahi olarak tedavi edilmiş 16 yaşından küçük hastalar dahil edildi. Hastaların başvuru anındaki kan nötrofil/lenfosit oranı (NLO), trombosit/lenfosit oranı (TLO), trombosit sayısı x nötrofil sayısı/lenfosit sayısı oranı (SII) ve monosit sayısı x nötrofil sayısı/lenfosit sayısı oranı (SIRI) hesaplandı.

Bulgular: Çalışmaya dahil edilen 25 hastanın (10 erkek, %40; 15 kız, %60) ortalama yaşı (6.24 ± 4.51) idi. Kalça ekleminden opere edilen

Correspondence Address/Yazışma Adresi

Ahmet Yiğitbay

Clinic of Orthopedics and Traumatology,
Siverek State Hospital,
Şanlıurfa, Türkiye

E-mail: ahmetyigitbay@gmail.com

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operated on the hip joint was 6 (24%), and the number of patients operated on the knee joint was 19 (76%). When the type of operation was analyzed, arthroscopic debridement was performed in seven patients (28%) and open debridement in 18 patients (72%) in the first surgical treatment. The number of patients who underwent a second operation was 3 (12%).

Conclusion: When comparing mean values of NLR, PLR, SII, and SIRI between patients who underwent multiple surgeries due to septic arthritis and those who had only one surgery, no statistically significant differences were found. Mean C-reactive protein (CRP) levels in patients who had undergone a second surgery were lower than those who had not. However, no significant differences were detected when examining the impact of CRP levels on the necessity of a second surgery.

Keywords: Arthritis, infectious, platelet count, lymphocyte count, neutrophils

Introduction

Septic arthritis is an orthopedic emergency most commonly observed in children between the ages of two and six. The incidence has been reported to be 4-10/100.000 (1). Knee and hip joints are among the most commonly involved joints, but the involvement of other joints may be observed rarely. Hematogenous route or direct injection is the most common route of transmission. In septic arthritis, it is essential that the diagnosis is made as soon as possible and treatment is started early. Complications are inevitable in patients with late diagnosis. The diagnosis is easily made in many patients with anamnesis, physical examination, and joint puncture. Blood laboratory values and microbiological analysis of joint aspiration fluid are important in differential diagnosis. In response to the microorganism reaching the joint, inflammatory responses are observed in the joint region, and acute phase reactants increase. The resulting bacterial toxins can cause joint damage in at least eight hours. Therefore, early intervention is critical to prevent future morbidities (2).

There are very few studies on the role of biochemical parameters in evaluating the severity and prognosis of the disease in treating pediatric septic arthritis. Kocher criteria are among the most important parameters used in the differential diagnosis of septic arthritis (3). C-reactive protein (CRP) value is among the most frequently used parameters in evaluating septic arthritis. Recently, neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) have been used by many different departments as a systemic inflammatory marker (4-6). Varady et al. have reported that NLR can be easily used to help clinicians diagnose and treat septic arthritis (7). Again, Bayram et al. have reported that NLR may be helpful in terms of confirming the diagnosis of septic arthritis with optimum diagnosis in clinical practice (8). Systemic inflammation index (SII) and systemic inflammation response index (SIRI) are also used in the evaluation of inflammatory responses by many different branches, such as NLR and PLR (9-11). Tang et al. have reported that SII may be a valuable and useful inflammatory

marker that can be used to predict the risk of osteoporosis (9). Again, Liu et al. have reported that SII is a new, valuable, and useful inflammatory marker that can predict the risk of rheumatoid arthritis in adults (10).

Sonuç: Septik artrit nedeniyle birden fazla ameliyat olan hastaların NLO, TLO, SII ve SIRI ortalama değerleri, bir defa ameliyat olan hastalarla karşılaştırıldığında istatistiksel olarak anlamlı bir farklılık saptanmadı. İkinci defa ameliyat olan hastaların C-reaktif protein (CRP) ortalaması, olmayanlara göre daha düşük saptandı. Ancak CRP değerinin ikinci ameliyatı etkileme oranı incelendiğinde herhangi bir anlamlı farklılık saptanmadı.

Anahtar Kelimeler: Artrit, enfeksiyon, trombosit sayısı, lenfosit sayısı, nötrofil

Materials and Methods

After obtaining ethics committee approval for this retrospective study, patients younger than 16 years who had undergone surgical treatment for septic arthritis between 2018 and 2022 were included. Those with immunosuppressive disease and those who started antibiotic treatment in an external center before surgical treatment were excluded from the study. A total of 25 patients were included in the study. Pre-operative biochemistry values of these patients were scanned retrospectively. Blood NLR, PLR, platelet count x neutrophil count/lymphocyte count ratio (SII), and monocyte count x neutrophil count/lymphocyte count ratio (SIRI) were calculated from these data.

After the diagnosis was made in the emergency department, appropriate empirical antibiotic treatment was initiated, and the patients were taken to emergency surgery for surgical debridement within 24 hours. Joint debridement was performed open or closed according to the patient's age and joint size. Patients with no clinical improvement in the first seven postoperative days and persistent effusion in the joint were operated on again. Open debridement was performed in all patients operated for the second time. Appropriate antibiotic treatment was rearranged according to Gram staining and culture results. Postoperatively, blood cultures were not deemed necessary due to significant clinical and laboratory improvement in patients. Blood cultures were taken from patients who did not show regression in clinical

symptoms. However, the results of the blood cultures were not included in the study.

Statistical Analysis

SPSS version 17.0 software was used for data analysis. Histogram plots and the Kolmogorov-Smirnov test analyzed the variables' conformity to a normal distribution. Mean, standard deviation, median, and minimum-maximum values were used for descriptive analyses. In 2 x 2 eyes, Pearson's chi-squared test was used. Mann-Whitney U test evaluated non-normally distributed (non-parametric) variables between the groups. P-values below 0.05 were considered statistically significant results.

Results

Mean age of the 25 patients (10 males, 40%; 15 females, 60%) included in the study was 6 (6.24 ± 4.51) years. The number of patients operated on from the hip joint was 6 (24%) and 19 (76%) from the knee joint. No other joints other than the knee and hip joints were involved in septic arthritis. The number of patients operated on the right side was 12 (48%), and the number of patients operated on the left side was 13 (52%). Bilateral involvement was not detected. The number of patients with hematogenous infection was 20 (80%), and the number of patients with inoculation infection was 5 (20.00%).

When the type of surgery was analyzed, arthroscopic debridement was performed in seven patients (28.00%) and open debridement in 18 patients (72%) in the first surgical treatment. In 22 (88%) patients, no microorganism could be produced from the joint fluid taken in the emergency department. *Staphylococcus aureus* was grown in two patients (8%) and *Escherichia coli* in one patient (4%). In 22 patients (84%), no microorganism was grown from the deep tissue samples taken during surgery. According to the results of intraoperative deep tissue cultures obtained from other patients, *S. aureus* was grown in three patients (12%), and *Candida* was grown in two patients (8%). Mean duration of hospitalization was (24.6 ± 13.06) days. The number of patients who underwent a second operation was 3 (12%), while those who did not was 22 (88%) (Table 1).

Mean values of white blood count (WBC), neutrophil %, lymphocyte %, CRP, NLR, PLR, SII, and SIRI taken at the time of the first presentation to the emergency department are shown in Table 2. Mean WBC (10.71 ± 3.41), mean neutrophil % (56.43 ± 20.39), mean lymphocyte % (31.66 ± 17.97), mean CRP (264.12 ± 1016.66), mean NLR (2.42 ± 1.89), mean PLR (126.4 ± 59.95), mean SII (918.26 ± 724.35) and mean SIRI (2.72 ± 2.1) were found (Table 2).

Table 1. Demographic characteristics and culture results of the patients

		n	%
Sex	Male	15	(60.00)
	Female	10	(40.00)
Age ¹		6.24 ± 4.51	5 (1-16)
Side	Right	12	(48.00)
	Left	13	(52.00)
Joint region	Hip	6	(24.00)
	Knee	19	(76.00)
Causes of infection	Haematogenous	20	(80.00)
	Direct transmission	5	(20.00)
Type of surgery	Atroscopic	7	(28.00)
	Open	18	(72.00)
Pre-op reproducing organism	No reproduction	22	(88.00)
	<i>S. aureus</i>	2	(8.00)
	<i>E. coli</i>	1	(4.00)
Per-op reproducing organism	No reproduction	21	(84.00)
	<i>S. aureus</i>	3	(12.00)
	<i>Candida</i>	1	(4.00)
Duration of hospitalization (days) ¹		24.6 ± 13.06	22 (6-51)
Second operation	No	22	(88.00)
	Yes	3	(12.00)

¹Chi-square test, Mann-Whitney U test.

n is replaced by mean $\pm$ SD and % is replaced by median.

S. aureus: *Staphylococcus aureus*, *E. coli*: *Escherichia coli*.

Table 2. Biochemical parameters in the blood of the patients at the time of first admission

	Mean $\pm$ SD	Median (min-max)
WBC	10.71 $\pm$ 3.41	10.4 (3.9-17.8)
Neutrophil %	56.43 $\pm$ 20.39	58 (11-84.7)
Lymphocyte %	31.66 $\pm$ 17.97	28.3 (9.4-78)
CRP	264.12 $\pm$ 1016.66	40 (0-5134)
NLR	2.42 $\pm$ 1.89	2.07 (0.14-8.9)
PLR	126.4 $\pm$ 59.95	120 (26.7-311)
SII	918.26 $\pm$ 724.35	828 (11.4-3017)
SIRI	2.72 $\pm$ 2.1	2.57 (0.03-8.9)

SD: Standard deviation, WBC: White blood count, CRP: C-reactive protein, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic immune response index.

Sex, age, side, joint site, cause of infection and first operation status of the patients were compared according to the second operation. No significant difference was found in this comparison (Table 3).

Mean values of blood WBC, neutrophil %, lymphocyte %, CRP, NLR, PLR, SII, and SIRI according to the status of the second operation are given in Table 4. No statistically significant differences were found when comparing the mean values of NLR, PLR, SII, and SIRI between patients who underwent a second surgery and those who had only one surgery ($p=0.397$, $p=0.545$, $p=0.304$, $p=0.303$). Accordingly, mean CRP values of the patients who had a second operation (118.53 ± 62.41) were found to be lower than those who did not (320.74 ± 1202.38) ($p=0.006$). However, no significant difference was found when the rate of CRP value affecting the second operation was analyzed (Table 5).

Table 3. Comparison of demographic data according to the second operation status of the patients

		Second Operation				p
		No		Yes		
		n	%	n	%	
Sex	Male	10	(55.56)	5	(71.43)	0.467
	Female	8	(44.44)	2	(28.57)	
Age ¹		6 ± 4.1	5 (1-15)	6.86 ± 5.76	8 (1-16)	0.976
Side	Right	8	(44.44)	4	(57.14)	0.568
	Left	10	(55.56)	3	(42.86)	
Joint region	Hip	3	(16.67)	3	(42.86)	0.169
	Knee	15	(83.33)	4	(57.14)	
Causes of infection	Haematogenous	14	(77.78)	6	(85.71)	0.656
	Direct transmission	4	(22.22)	1	(14.29)	
First operation	Atroscopic	6	(33.33)	1	(14.29)	0.341
	Open	12	(66.67)	6	(85.71)	

¹Chi-square test, Mann-Whitney U test.
n is replaced by mean ± SD and % is replaced by median.

Table 4. Comparison of blood parameters according to the second operation status of the patients

	Second Operation				p
	No		Yes		
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
WBC	10.65 ± 3.72	10.5 (3.9-17.8)	10.89 ± 2.7	10.4 (7.5-15.2)	0.904
Neutrophil %	56.86 ± 21.16	59.55 (11-84.7)	55.32 ± 19.81	52.7 (25.6-76.4)	0.672
Lymphocyte %	31.41 ± 19.39	27.65 (9.4-78)	32.3 ± 14.99	31 (16.2-54.7)	0.672
CRP	320.74 ± 1202.38	25 (0-5134)	118.53 ± 62.41	109 (61.7-212)	0.006
NLR	2.63 ± 2.05	2.19 (0.14-8.9)	1.91 ± 1.39	1.67 (0.47-4.61)	0.397
PLR	131.01 ± 64.29	125 (26.7-311)	114.57 ± 49.35	120 (51.5-193)	0.545
SII	998.8 ± 757.51	870 (11.4-3017)	711.14 ± 635.16	398 (190-1705)	0.304
SIRI	2.97 ± 2.14	2.76 (0.03-8.9)	2.1 ± 2.01	1.4 (0.28-5.91)	0.303
Mann-Whitney U test. SD: Standard deviation, WBC: White blood count, CRP: C-reactive protein, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic immune response index.					

Table 5. Analysis of the effect of CRP value on the second operation

	B	SE	Sig.	EXP (B)	95% CI for EXP (B)	
					Lower	Upper
CRP	0.000	0.001	0.677	1.000	0.998	1.001

Regression analysis.

CRP: C-reactive protein, B: Beta co-efficient, SE: Standard error, Sig.: Significance, EXP (B): Exponentiation of the B co-efficient, CI: Confidence interval.

Discussion

Septic arthritis is one of the orthopedic emergencies in the pediatric age group, with different incidences in different regions. If the diagnosis of septic arthritis is made immediately and treatment is started as soon as possible, the results are promising. However, in case of delay in diagnosis and treatment, joint destruction and physiological arrest are inevitable. While complications related to septic arthritis were observed with a rate of 50% in the past, it has been observed that this rate has decreased to 10% recently (12). Blood biochemistry values have an essential place in the diagnosis of septic arthritis. Significantly, CRP increases within hours and is used for treatment follow-up (13). In addition, CRP is frequently used in the differential diagnosis of septic arthritis and transient synovitis (14). No relation has been found between CRP elevation and the severity of septic arthritis. Olandres et al. have reported that a CRP value ≥ 20 mg/L and an effusion ≥ 7 mm in the hip joint on ultrasound has high specificity and sensitivity in diagnosing pediatric hip septic arthritis (15). In addition, Singhal et al. have reported that the probability of septic arthritis is 74% in the presence of a CRP value > 20 mg/L and inability to load (14). The present study found that the CRP value was lower in patients who underwent surgery for the second time. However, although a correlation was found between low CRP and having a second operation, it is impossible to establish a causal link with such observational studies.

Both NLR and PLR have recently become popular in detecting systemic inflammation (4-11). Bayram et al. have suggested in a study that NLR could be used to diagnose septic arthritis (8). Schab et al. have reported that high NLR value in adults may positively correlate with 90-day mortality (16). In a study by Tekin et al., it has been reported that NLR and PLR are essential markers of one-year mortality in patients over 60 with hip fractures (17). Emektar et al. have reported that NLR and PLR values were associated with increased mortality after geriatric hip fractures. Still, these values are not reliable enough for clinical use, considering their specificity (18). In a study conducted by Ergin et al., it has been reported that a NLR higher than 4.3 in the blood taken at the time of presentation due to septic arthritis could predict CRP values above 20 mg/L in the second week with a good sensitivity and specificity rate. They have also stated that it should be taken into consideration that CRP may remain high and nor-

malize later in these patients (19). Aktar et al., in a study that included 64 patients with Brucella arthritis, have compared NLR and PLR values with control groups. They have found that NLR and PLR were indirect inflammation markers that could be observed as abnormally increased in children with Brucella arthritis (20). SII and SIRI have recently been used by many different clinics like NLR and PLR, and their effects on mortality and morbidity in patients have been analyzed (9-11). A study by Fois et al. has reported that SII could predict in-hospital mortality and early risk classification in COVID-19 patients (21). However, since there are few studies on the role of SII and SIRI in diagnosing and treating septic arthritis, it needs to be corrected to make any prediction for now.

It is essential to conduct a multicentre study to use NLR, PLR, SII, and SIRI values in the treatment of pediatric septic arthritis to determine their prognostic significance and to determine them as risk factors in patients operated on for the second time due to septic arthritis. The limiting factors of this study include the small number of patients, the fact that it was a single-center study, the change in blood inflammatory markers depending on the delay between the onset of the patient's complaints and the time of presentation, and the effect of the causative pathogen on inflammatory processes.

Conclusion

Biochemical markers play an important role in monitoring the treatment processes and clinical recovery of patients who have undergone surgery for septic arthritis. NLR, PLR, SII, and SIRI values have recently emerged as popular new markers for identifying inflammatory processes. The results of this study showed no statistically significant differences in NLR, PLR, SII, and SIRI values between patients who underwent multiple surgeries for septic arthritis in the pediatric age group and those who had only one surgery. However, these markers can be helpful as a simple, rapid, and inexpensive method for diagnosing pediatric septic arthritis and identifying risk factors in patients who do not respond to treatment.

Ethics Committee Approval: Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital (Decision no: 2023-10-04, Date: 22.05.2023).

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