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The role of the Inflammatory Biomarkers in the Early Prediction of the Severity of Paediatric Acute Pancreatitis

Pediatrik Akut Pankreatit Şiddetinin Erken Tahmininde İnflamatuar Biyobelirteçlerin Rolü

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Öz

Amaç: Yıllardır erişkin literatürünün gölgesinde kalmış olan pediatrik akut pankreatit çalışmaları, pediatrik şiddet sınıflamasının kabul edilmesinden sonra ivme kazanmıştır. Artık hangi hastalarda ciddi hastalık gelişeceğini erken aşamada hızla öngörebilecek inflamatuar biyobelirteçlerin belirlenmesine ihtiyaç vardır. Bu çalışmanın amacı, sistemik immün-enflamasyon indeksi (SII) ve nötrofil-lenfosit oranı (NLO) gibi inflamatuar biyobelirteçlerin erken prediktör olarak etkinliğini değerlendirmek ve eşik değerler belirlemekti.
Hastalar ve Yöntem: 2019-2022 yılları arasında akut pankreatit tanısı alan 53 çocuğun klinik özellikleri, laboratuvar test sonuçları ve görüntüleme bulguları retrospektif olarak değerlendirildi. Hastalar şiddetine göre "hafif" ve "orta şiddetli-şiddetli" olarak iki gruba ayrıldı. Gruplar inflamatuar belirteçler açısından karşılaştırıldı. Hastalık şiddetini öngören faktörler ROC eğrisi analizi ile incelendi. Anlamlı eşik değerler için duyarlılık, özgüllük, pozitif prediktif değer (PPD) ve negatif prediktif değer (NPD) hesaplandı.
Bulgular: NLO ve SII değerleri "orta şiddetli-şiddetli" grupta "hafif" gruba göre istatistiksel olarak anlamlı derecede yüksekti (tümü için p<0,001). NLO≥3.33 (AUC:0.894, %95 güven aralığı: 0.81-0.979, PPD %89.7, NPD %83.3%) ve SII indeksi≥1225.57(AUC: 0.912, %95 güven aralığı:0.831-0.992, PPD %90.0, NPD %87.0) eşik değerlerinin hastalık şiddetini yüksek duyarlılık ve özgüllükle tahmin edebildiği belirlendi.
Sonuç: NLO ve SII pediatrik akut pankreatitte kötü klinik sonucu erken tahmin edebilir. Mevcut çalışma pediatrik akut pankreatitte bu biyobelirteçlerin prognostik öneminini değerlendiren ilk çalışmadır.

Anahtar Kelimeler: Pediatrik ciddi akut pankreatit, sistemik immün-inflamasyon indeksi, nötrofil-lenfosit oranı

Abstract

Aim: Studies of paediatric acute pancreatitis have remained in the shadow of adult literature for many years, and have only increased following the recent acceptance of the severity classification. There is now a need to determine inflammatory biomarkers which will be able to rapidly predict in the early stage which patients will develop severe disease. This study's purpose was to research the efficacy as early predictors and determine cutoff values for inflammatory biomarkers including the systemic immune-inflammation index (SII), and the neutrophil-lymphocyte ratio (NLR).
Patients and Methods: A retrospective evaluation was made of the clinical characteristics, laboratory test results, and imaging findings of 53 children diagnosed with acute pancreatitis between 2019-2022. The study population were separated into groups as 'mild' and 'moderately severe-severe' according to severity. The groups were compared in respect of inflammatory markers. Factors predicting disease severity were evaluated with ROC curve analysis. For the significant cutoff values, positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity were calculated.
Results: The NLR, and SII values were found to be statistically significantly higher in the "moderately severe-severe" group than in th "mild" group (p<0.001 for all). The cutoff values of NLR≥3.33 (AUC:0.894, 95% CI:0.81-0.979, PPV 89.7%, NPV 83.3%), and SII≥1225.57 (AUC:0.912, 95% CI:0.831-0.992, PPV 90.0%, NPV 87.0%) were determined to be able to predict disease severity with high sensitivity and specificity.
Conclusion: The NLR, and SII are inflammatory biomarkers that can make an early prediction of a poor outcome in paediatric acute pancreatitis. To the best of our knowledge, this is the first study to have evaluated the prognostic importance of these biomarkers, in paediatric acute pancreatitis.

Key words: Paediatric severe acute pancreatitis, systemic immune-inflammation index, neutrophil-lymphocyte ratio

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INTRODUCTION

In recent times, the incidence of pediatric acute pancreatitis (AP) has increased and approached the incidence level reported in the adult age group (1). In the majority of the pediatric age group, the clinical outcome is good. However, together with the increasing incidence, pediatricians are now encountering increasingly more severe disease accompanied by local and/or systemic complications and organ failure (2). Early estimation of the serious disease picture may enable early detection of patients who need referral to the pediatric gastroenterology clinic or intensive care unit. Thus, patients can reach the appropriate treatment conditions in the appropriate center at an early time and the clinical outcome of the patients can be improved (3). Although there are many classifications and scoring systems in adult literature, the search is ongoing for reliable biomarkers that could be easily applied and provide rapid results, which would be able to make an early prediction of cases that would develop severe AP (4,5).

For many years, pediatric studies on the prediction of acute pancreatitis severity have been inadequate. Because, until the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Pancreas Committee announced the acute pancreatitis severity classification in 2017, there was no universally accepted severity classification for children with AP (2). After the acceptance of this classification, pediatric acute pancreatitis studies gained momentum. In recent years, studies on biomarkers that can predict children who will develop severe AP at an early stage have been continuing. In some of these studies, the predictors evaluated have not been inflammatory biomarkers (6,7). However, AP is a sterile inflammatory disease and a poor prognosis is associated with an uncontrolled systemic inflammatory response (8). Although the predictors recommended in several pediatric studies that have evaluated inflammatory biomarkers support the role of uncontrolled systemic inflammation in severe disease, they do not have the properties of an optimal predictor (9,10). Because, the ideal predictive marker should be low-cost, readily available, easy to apply, and provide results in a short time (11).

The neutrophil-lymphocyte ratio (NLR) and the monocyte-lymphoctye ratio (MLR) are inflammatory indexes that integrate two cell types. They have been defined as inflammatory prognostic biomarkers in some malignant and inflammatory diseases (including acute pancreatitis) in adults (4,5).

The systemic immune-inflammation index (SII), which integrates the neutrophil, thrombocyte, and lymphocyte counts, is a new predictor that reflects the balance between immune and inflammatory statuses. It was first described in 2014 in patients with hepatcellular carcinoma (12). In 2021, it was used for the first time in adult AP patients and was reported to be a better predictor than NLR in the early prediction of the development of severe disease (13).

The NLR, MLR, and SII are ideal biomarkers which can be computed from the laboratory parameters obtained at the time of presentation, are easily accessible, and low cost. No previous study has evaluated the efficacy of these inflammatory biomarkers as early predictors of the development of severe AP in children.

The goal of study was to investigate the utility of inflammatory biomarkers such as NLR, MLR, and SII as early predictors of a severe disease status in pediatric AP, and to determine the cutoff values that can be used for this purpose.

PATIENTS AND METHODS

The study included patients aged <18 years who were treated as inpatients for a diagnosis of AP in Meram Faculty of Medicine Hospital at Necmettin Erbakan University between 2019 and 2022. Ethical approval was obtained from the Ethics Committee of Necmettin Erbakan University Meram Faculty of Medicine (code number:2022/3875).

The patients included in the study were those defined as AP with at least two of the criteria of abdominal pain consistent with AP, imaging findings, and plasma levels of pancreatic enzymes more than three-fold higher than the normal upper limit, as recommended by the International Study Group Of Pediatric Pancreatitis: In Search For A Cure consortium (14).

AP severity was determined according to the 2017 NASPGHAN criteria. To apply this classification, the criteria required are the presence and continuation period of organ dysfunction, and the presence of local and systemic complications (Figure 1) (2). In accordance with the NASPGHAN recommendation, the recommendations of the International Pediatric Sepsis Consensus were used to define organ dysfunction (15).

Similar to the procedures applied in previous adult and pediatric literature, the patients were separated into two groups of “mild AP” (MAP) and “moderately severe-severe AP” (MS-SAP) to differentiate mild

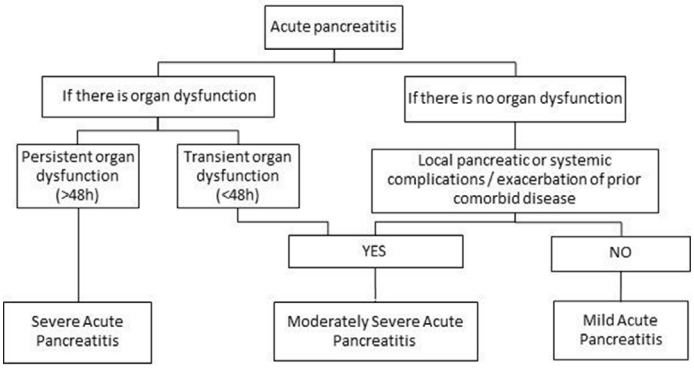

Figure 1. Paediatric acute pancreatitis severity classification of the North American Society for Paediatric Gastroenterology, Hepatology and Nutrition Pancreas Committee

cases from non-mild cases. Patients with moderately severe AP and those with severe AP were combined in one group. For patients with acute recurrent pancreatitis, only the findings of the first pancreatitis attack were included in the analyses. Patients were not included in the study if they had an inflammatory disease that could affect the full blood count parameters (malignancy, FMF, Henoch-Schönlein purpura, etc), or if the data from the first day of the disease were incomplete (Figure 2).

Data were retrieved from the patient records of the demographic characteristics, vital signs, etiology, comorbidities, laboratory test results on first presentation (white-blood cells, neutrophil, lymphocyte and monocyte absolute counts, C-reactive protein, liver enzymes, serum creatinine, glucose, calcium, amylase and lipase), and imaging findings.

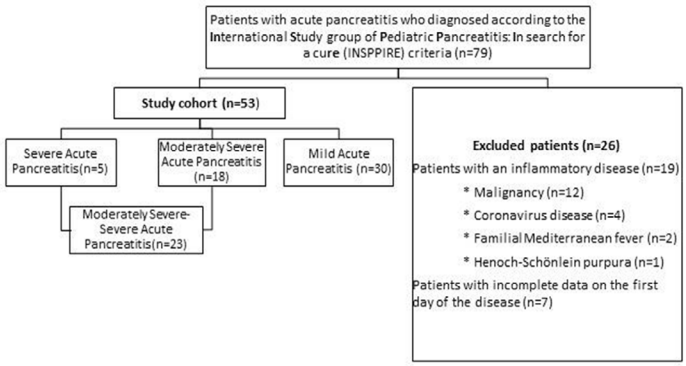

Figure 2. Flow chart of study and inclusion- exclusion criterias

The neutrophil and lymphocyte counts were used to calculate the NLR, and the absolute monocyte and lymphocyte counts to calculate the MLR. The SII was computed with the formula –"neutrophil count x platelet count/lymphocyte count".

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS vn. 20.0 software (IBM Corpn., Armonk, NY, USA). Numerical data were presented as median (Q1-Q3) values, and categorical variables as number (n) and percentage (%). Conformity of the variables to normal distribution was assessed with the Shapiro Wilk test. In the comparisons of categorical variables and frequencies, the Chi-square test was applied. In the comparisons of two groups, the Mann Whitney U-test was applied. To determine relationships between variables, Spearman correlation analysis was used. The decision -making characteristics of the laboratory parameters in the prediction of disease severity were examined with Receiver Operating Characteristics (ROC) curve analysis. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for cutoff values. Type I error level was interpreted as significant at <5%. 95% confidence intervals were given for Area Under Curve (AUC).

RESULTS

Evaluation was made of 53 patients who met the study criteria, comprising 25 (47.2%) females and 28 (52.8%) males with a median age of 156 months (range, 6-204 months). Comorbidities were present in 10 (18.9%) patients; meningomyelocele in 1 (1.9%), congenital metabolic disease in 2 (3.8%), type 1 diabetes mellitus in 2 (3.8%), nephrolithiasis in 1 (1.9%), cerebral palsy in 1 (1.9%), chronic renal failure in 1 (1.9%), hyperlipidemia in 1 (1.9%), and thalassemia intermedia in 1 (1.9%). The MAP group included 30 (56.6%) patients and the MS-SAP group, 23 (43.4%) patients, comprising 18 (34%) with MSAP and 5 (9.4%) with SAP. No significant difference was detected between the groups in respect of anthropometric measurements and etiology (Table 1).

When the laboratory test results were compared according to disease severity, the white blood cell count (WBC), NLR, monocyte count, MLR, absolute neutrophil count, amylase value and SII value at the time of presentation were determined to be significantly lower in the MAP group than in the MS-SAP group (p=0.02 for amylase, p<0.001 for each of the others). The absolute lymphocyte count was determined to

Table 1. Distribution of the Anthropometric Measurements and Etiology Findings of the Patients According to the Severity Groups

		MAP (n=30)	MS-SAP (n=23)	*p value
Anthropometry	W-H z score (<5 years)	0.46 (-0.73-1.61)	-0.24 (-1.70-1.25)	0.896
Median (Q1-Q3)	BMI z score (>5 years)	0.55 (-0.91-1.16)	0.73 (-1.25-1.81)	0.230
Etiology	Idiopathic	14 (46.7%)	10 (43.5%)	0.374
N (%)	Biliary Pancreatitis	8 (26.7%)	3 (13.0%)	
	Toxic	2 (6.7%)	0 (0.0%)	
	Metabolic	2 (6.7%)	3 (13.0%)	
	Systemic Disease	3 (10.0%)	2 (8.7%)	
	Infection	1 (3.3%)	3 (13%)	
	Congenital Anatomic Malformation	0 (0.0%)	1 (4.3%)	
	Genetic	0 (0.0%)	1 (4.3%)	

*p<0.05 was accepted as statistically significant. Data are stated frequency (percentage) and median (Q1-Q3) values.
W-H: Weight for height, BMI: Body mass index, MAP: Mild acute pancreatitis, MS-SAP: Moderately severe-Severe acute pancreatitis

be significantly higher in the MAP group than in the MS-SAP group (p=0.028). The distribution of the laboratory findings according to disease severity is shown in Table 2.

Correlations were examined between the laboratory findings and the MAP, MS-SAP groups, and there was seen to be a statistically positive correlation between disease severity and WBC count, absolute neutrophil count, NLR, MLR, and SII value (r=0.556 p<0.001, r=0.662 p<0.001, r=0.677 p<0.001, r=0.661 p<0.001, r=0.707 p<0.001, respectively). A statistically negative correlation was determined between disease severity and absolute lymphocyte count (r=-0.315, p=0.022).

The diagnostic rates of the laboratory parameters according to the severity groups were calculated. WBC count, neutrophil count, NLR, MLR and SII (p<0.001 for all) were found to be at extremely good levels of diagnostic rates ort he prediction of the development of severe AP with high sensitivity and specificity. The AUCs of the parameters were interpreted using the criteria reported by Fischer et al (A test with an AUC >0.9, 0.7 to 0.9, and 0.5 to 0.7 indicate high, moderate, and low accuracy, respectively) (16). The AUC values in predicting poor clinical outcomes were 0.912 (95% confidence interval [CI]:0.831-0.992) for SII, 0.894 (95% CI:0.81-0.979) for NLR, 0.885 (95% CI:0.799-

Table 2. Distribution of the Laboratory Findings of the Patients According to the Severity Groups

	MAP (n=30)	MS-SAP (n=23)	*p value
White-blood cells (/mm^3)	7650 (6265-9502)	12400 (11320-16130)	<0.001*
Absolute neutrophil count (/mm^3)	4435 (3045-5942)	10590 (7700-13100)	<0.001*
Absolute lymphocyte count (/mm^3)	2235 (1682-2725)	1700 (1000-2430)	0.028*
Neutrophil/lymphocyte ratio	2.04 (1.38-2.94)	5 (3.46-15.4)	<0.001*
Monocyte count (/mm^3)	490 (300-742)	800 (660-1000)	<0.001*
Monocyte/ lymphocyte ratio	0.20 (0.16-0.32)	0.43 (0.32-0.89)	<0.001*
Eosinophil count (/mm^3)	85 (27.5-140)	30 (0-70)	0.133
Eosinophil/lymphocyte ratio	0.03 (0.01-0.05)	0.01 (0-0.03)	0.963
Basophil count (/mm^3)	20 (3.25-40)	10 (1-30)	0.268
Sedimentation rate(mg/s)	13 (5-22)	14 (8-28)	0.916
Creatinine (mg/dL)	0.62 (0.46-0.75)	0.52 (0.43-0.67)	0.586
Albumin (g/L)	4.6 (4.1-4.82)	4.45 (4.07-4.8)	0.387
Aspartate aminotransferase (U/L)	26 (19-50)	29 (23-38)	0.621
Alanine aminotransferase (U/L)	18 (10-57)	14 (10-66)	0.836
Gamma glutamil transferase (U/L)	16 (10-107)	15 (11.75-44.5)	0.985
Amylase (U/L)	305 (184-487)	640 (237-1340)	0.02*
Lipase (U/L)	475 (258-817)	926(261-2673)	0.069
C-reactive protein (mg/L)	2.5 (1-8.2)	12 (1-46)	0.056
Systemic immune-inflammation index	516.32(380.62-796.30)	1894.73(1301.53-3284.89)	<0.001*

*p<0.05 accepted as statistically significant, Data are stated as median (Q1-Q3) values. Comparisons between groups were made using the Mann-Whitney U-test.
MAP; mild acute pancreatitis, SAP; severe acute pancreatitis

Table 3. ROC curve analysis results according to disease severity

Risk factor	AUC* (95% CI**)	Cut off	p value***	Sensitivity	Specificity	PPV	NPV
WBC (/mm^3)	0.824(0,698-0.949)	10350	<0.001	82.6%	82.1%	85.7%	76.0%
NLR	0.894(0.81-0.979)	3.33	<0.001	87.0%	85.7%	89.7%	83.3%
MLR	0.885(0.799-0.97)	0.3292	<0.001	73.9%	75.0%	79.3%	70.8%
ANS (/mm^3)	0.886(0.779-0.992)	7095	<0.001	87.0%	89.3%	90.0%	87.0%
SII	0.912(0.831-0.992)	1225.57	<0.001	87.0%	89.0%	90.0%	87.0%

*Area under curve **Confidence interval *** p<0.05 accepted as statistically significant
WBC:White blood cells, NLR:Neutrophil lymphocyte ratio, MLR:Monocyte lymphocyte ratio, ANS:Absolute neutrophil count, SII: Systemic immune-inflammation index

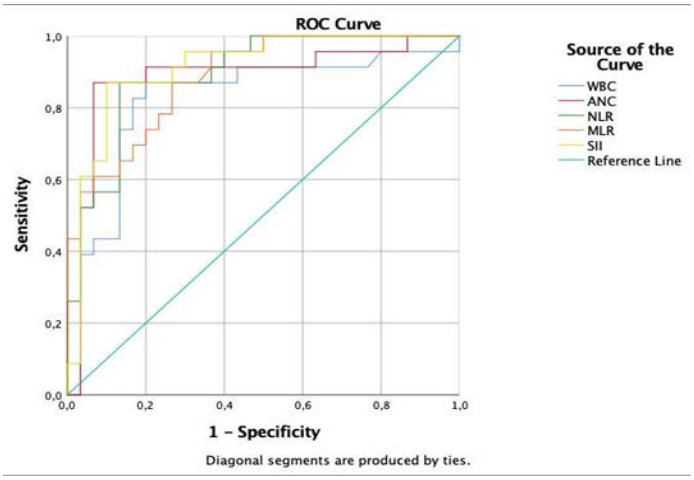

Figure 3. Graph showing the curve obtained with ROC analysis of WBC, absolute neutrophil count, NLR, MLR, and SII values

0.97) for MLR, 0.824 (95% CI:0,698-0.949) for WBC, and 0.886 (95% CI:0.779-0.992) for ANS. The AUC values of parameters indicated high accuracy for SII, and moderate accuracy for others. The results of the ROC curve analysis from which the cutoff values of the laboratory parameters according to disease severity, the area under the curve (AUC) values, and the positive and negative predictive values were calculated, are shown in Table 3 and Fig 3.

DISCUSSION

The results of this study demonstrated that NLR, and SII were significant markers in the development of severe disease in children with AP, and could predict the development of SAP. The diagnostic rates of all the indexes had high sensitivity and specificity in the prediction of SAP, with the SII value having the highest sensitivity and specificity, and the cutoff value for each index was determined. These findings can be explained by the principle of excessive systemic inflammation related to the uncontrolled adaptive and innate immune response in the pathogenesis of AP.

The results showed that at the time of diagnosis, the WBC count, absolute neutrophil count, monocyte count, and amylase value were significantly higher and the absolute lymphocyte count was significantly lower in the MS-SAP group. The increase in neutrophil and monocyte counts and decrease in lymphocyte count have been associated with SAP pathogenesis in previous studies (17).

In the current study, there was determined to be a significant positive correlation between WBC count, absolute neutrophil count and disease severity, and a significant negative correlation between absolute lymphocyte count and disease severity. At a cutoff value of 10350/mm^3 for WBC count and 7095/mm^3 for absolute neutrophil count, the development of MS-SAP could be predicted with high sensitivity and specificity. Although serum WBC count is a component of some adult AP scoring systems, the results reported related to AP prognosis are variable. Silva -Vaz et al. Reported that a cutoff value of ≥14880 mm^3 for WBC count on presentation was a good prognostic tool (3). In a multicentre study by Farkas et al., it was confirmed that WBC count was not sufficient ort he prediction of disease severity (18). Absolute WBC count is the combination of the cells in circulation such as neutrophils and lymphocytes. In a patient with no evident lymphopenia, the WBC count may be high associated with an increase in neutrophil count, and if lymphopenia is very evident, there may be no increase in WBC count (10). Moreover, the distribution of peripheral blood cells and the norms of WBC count can vary according to age in childhood (19). In this study, no statistically significant difference was found between the age distribution in the MAP and MS-SAP groups. Ratios such as NLR and MLR with a composition of two cell types are more stable than WBC and subtype counts and do not have the mentioned disadvantages (5). The cutoff value of 3.33 for NLR determined in this study was found to have extremely

high sensitivity and specificity in the prediction of MS-SAP development. For adults with AP, NLR was first reported by Azab et al. To be valuable in predicting severe disease with a cutoff value of 4.7 (5). These findings were later supported by Jeon et al. With a cutoff value of 4.76 (8). In another study of adults with pancreatitis evaluating the efficacy of ratios obtained from peripheral blood cells, Akoglu et al. Reported that NLR was the best predictor with a cutoff vslue of 5.1. MLR was seen to be statistically significantly different in patients with MS-SAP compared to MAP, but it was not recommended for use as it did not have high sensitivity and specificity (20). In the current study, although the sensitivity and specificity of the cutoff value of 0.32 for MLR was lower than the other biomarkers in the prediction of MS-SAP, it was still extremely high. Although the value of ratios such as NLR and MLR has been shown in inflammatory diseases in the pediatric ort he e, there is no study of children with acute pancreatitis, with which the current study results could be compared. In this study it was determined that both NLR and MLR could be used as independent biomarkers with sufficient sensitivity and specificity in the prediction of the development of MS-SAP. However, the diagnostic rates of NLR were higher than those of MLR.

SII had the highest reliability , in the current study. With a cutoff value of ≥1225.57, SII had extremely good diagnostic rates of the prediction of MS-SAP development. Since SII is the synthesis of 3 cell types involved in the pathogenesis of acute pancreatitis, it is more reliable than rates integrating fewer cell types. The SII was first reported by Zhang et al. İn 2021 to be a poor prognostic marker in adults with acute pancreatitis (21). Subsequently, Liu et al. Reported that the SII could be an early predictor of severe disease with a cutoff value of ≥2207.53 (13). There are few studies of adult patients related to whether or not SII can predict SAP development in acute pancreatitis, and no report could be found of pediatric AP. In several very recent pediatric studies, it has been emphasised that the SII reflects the immune-inflammatory balance. Winker et al. Reported that a decrease in SII in pediatric cancer patients was seen with the anti-inflammatory effect of exercise (22). Guneylioglu et al. Reported that a cutoff value of ≥ 2609 for SII was useful in differentiating children with empyema from those with parapneumonic effusions (23). In another study of infants (1-4 months) with fever of unknown focus, a cutoff value of ≥438.44 could predict the risk of severe bacterial infection (24).

There is no other study showing that the SII can be used to make an early prediction of the development of severe disease in children with AP. The determination of severity within the first 48 hours will be able to improve clinical results by accelerating referral to an appropriate centre, the provision of intensive care support and the appropriate treatment approach (3). However, there are several recent studies related to laboratory parameters which can predict severe disease early in children with AP. Vitale et al. Showed that an increase in BUN could predict SAP development in the early stage (6). Farell et al. Also reported that BUN and albumin values were an independent marker for SAP development (7). However, when the immune-inflammatory pathwways in the pathogenesis of SAP are taken into consideration, it is necessary to evaluate whether inflammatory markers are reliable predictors or not. In a prospective study by Vitale et al. Evaluating biomarkers which could make early predictions of the risk of SAP development in children with AP, it was shown that the matrix metalloproteinase-9 (MMP-9) and tissue inhibitors of metalloproteinase-1 (TIMP-1) levels were significantly higher in SAP patients than in the MAP group (9). In another study, Farell et al. Examined whether interleukin 6 (IL-6) and monocyte chemotactic protein-1 (MCP-1) could differentiate MAP and SAP pediatric patients, and reported that they could predict progression to SAP (10). With these studies, Vitale and Farell emphasised the inflammatory pathways in the early prediction of SAP risk. Ideally, a predictive marker should be low cost, easily accessible and applicable and provide results in the early period (11). Biomarkers such as MMP-9, TIMP-1, and MCP-1 may not be available everywhere and may not provide rapid results. NLR and SII are significant independent variables which can predict MS-SAP development in the early period and can be calculated from the laboratory data obtained on first presentation. Thus, they are ideal biomarkers which can be accessed easily and can provide results in the early period. They can reliably predict the risk of MS-SAP development in children in the early period and can be helpful in improving clinical outcomes. Therefore, NLR (with a cutoff value of ≥3.3) and SII (with a cutoff value of ≥1225.57) can be used with high sensitivity and specificity to predict severe disease that may develop in any patient at the time of presentation.

An important limitation of this study was that there are conflicting reports of the evaluation of WBC and

ANC and cutoff values in the pediatric age group. For example, cutoff values of 10350/mm^3 for WBC or 7095/mm^3 for absolute neutrophil count may not be valid for all age groups. Although high sensitivity and specificity was shown for these parameters in this cohort with no significant difference in the age distributions of the MAP and MS-SAP groups, they cannot be generalised to all age groups. Therefore, because of these above-mentioned disadvantages, WBC and neutrophil count cannot be recommended as parameters ort he prediction of disease severity in childhood. However, these disadvantages are not relevant to the NLR, MLR, and SII, which integrate more than one cell type, and the evaluation of which was the main aim of this study. Other limitations of the study could be said to be the retrospective design, that the biomarkers were only evaluated at the time of presentation, and that the ort he of the disease course were not evaluated. However, the main aim of the study was to detect inflammatory biomarkers that could predict disease severity at the time of presentation. Although the study content served this purpose, there is a need for further prospective controlled studies with larger samples to evaluate patients with high NLR and SII values on presentation. Nevertheless, as the first study on this subject in a pediatric patient group, it can be considered that this study will be of guidance for future prospective studies.

CONCLUSION

NLR and SII are reliable biomarkers ort he early estimation of the development of severe disease in children with acute pancreatitis. As this is the first study conducted on children, there is a need for further large-scale, randomised, controlled studies.

Conflict of interest: *Authors declare that there is no conflict of interest between the authors of the article.*

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