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The place of delta neutrophil index (immature granulocyte) and hematological markers in diagnosing pediatric acute appendicitis

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Abstract

Aim: It is aimed to reveal the importance of markers such as inflammation markers, c-reactive protein, complete blood count parameters (white blood cell, neutrophil lymphocyte ratio, platelet lymphocyte ratio), delta neutrophil index (immature granulocyte), which play a role in acute appendicitis pathology and progression, in the diagnosis of pediatric acute appendicitis, and the relationship between these markers.

Materials and Methods: 47 patients who applied to Kahramanmaraş Sütçü İmam University Medical Faculty Hospital between 01.01.2019 and 31.08.2022 due to acute appendicitis were included in the study. Demographic and medical information of the patients were obtained by examining the hospital automation system.

Results: In the diagnosis of acute appendicitis in pediatric patients, delta neutrophil index, neutrophil lymphocyte ratio and platelet lymphocyte ratio, which are inflammatory markers, were found to be statistically significantly higher. It was stated that delta neutrophil index, white blood cell, neutrophil lymphocyte ratio and platelet lymphocyte ratio measurement are easily accessible blood parameters without requiring additional cost to the health system, as they are worked automatically within the parameters of the complete blood count.

Conclusion: We recommend the use of delta neutrophil index, neutrophil lymphocyte ratio and platelet lymphocyte ratio values along with physical examination, imaging studies, and laboratory tests to assist in the diagnosis of pediatric acute appendicitis patients.

Introduction

The most common causes of acute abdomen requiring immediate surgical intervention include acute appendicitis (AA). In the etiology of appendicitis, the most important factor is the obstruction of appendix lumen [1]. During the entire life, incidence of appendicitis is 7%. In the general population, the rate of mortality is less than 1%, however, this rate can reach up to 50% in advanced age. Dangerous complications of AA include necrosis and perforation, which are seen in all cases with AA by 40% [2]. Right lower quadrant pain and increased leukocyte count, which are the most known symptoms of appendicitis, were used for diagnosing appendicitis, however, the sensitivity of these symptoms was found to be low. It has been reported that biochemical markers like white blood cell count (WBC) and c-reactive protein (CRP) are potential predictors for diagnosing appendicitis [3, 4, 5, 6]. Markers like Alvarado

score and neutrophil lymphocyte ratio (NLR) were also used for diagnosing appendicitis. However, in the diagnosis of appendicitis, the false positive rate is still around 15% [7, 8]. The inflammatory markers inflammatory markers, which are examined in routine blood tests in the diagnosis of acute appendicitis and can be found in every hospital, will increase the accuracy of diagnosis. CRP and complete blood count tests are used to evaluate the inflammatory process in the pathology and progression of pediatric acute appendicitis. WBC, neutrophil, lymphocyte, platelet (PLT) and mean platelet volume (MPV) values, which are among the complete blood count parameters, and the ratios of these values to each other are used as inflammatory markers. NLR and platelet lymphocyte ratio (PLR) are some of the most important of these markers.

Delta neutrophil index (immature granulocytes-IG) is also an inflammatory marker that can be examined in routine hemogram examination recently [9, 10, 11, 12]. Delta neutrophil index is a marker showing immature granulocytes in the peripheral circulation. There are studies demon-

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strating that IG is generally increased in inflammatory conditions [10, 11, 12]. There is an increase in the immature/total granulocyte ratio or neutrophil band count caused by infection, stress, and systemic inflammation, and consequently, IG can be used as a criterion of the presence of immature granulocytes and as an indicator of a leftward granulocyte shift. IG are observed in peripheral blood as immature polymorphonuclear cells due to the bone marrow's activation. While their number can be identified directly by examination, it can be provided without additional cost within the complete blood count parameters in addition to technological developments. The increases in the number of immature granulocytes particularly suggest the activation of bone marrow and may provide information about inflammation and sepsis without observing leukocytosis. To this end, inflammatory events such as adult acute appendicitis, sepsis, and acute pancreatitis were also investigated. The change in WBC levels and CRP levels was shown to be significant to evaluate the success of medical treatment. However, examining CRP as a separate parameter from the complete blood count leads to an additional cost. IG, NLR, PLR measurements are easily accessible blood parameters that do not require additional costs to the health system since they are automatically studied within the complete blood count parameters [10, 11, 12, 13].

The purpose of this study was to reveal the importance of markers like inflammation markers, CRP, PCT, complete blood count parameters (WBC, NLR, PLR), delta neutrophil index, that play a role in the pathology and progression of AA, in the diagnosis of pediatric acute appendicitis, and the relationship between these markers.

Materials and Methods

The anamnesis of 47 patients admitted to Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital Emergency Department between 01.01.2019 and 31.08.2022 due to acute appendicitis was taken by the researcher, they were examined, the findings were recorded, and patient data were obtained by examining their files via the automation system. Demographic data, blood values and radiological imaging results of the patients were examined. The Kolmogorov Smirnov test was performed to evaluate the normal distribution of the data. The required tests were performed by using the SPSS 20.0 package program for statistical evaluation. Numbers and percentages were used to express categorical variables. The measurement based continuous variables were expressed as median (minimum-maximum) and mean±standard deviation by checking whether they fitted the normal distribution. The Spearman correlation test was performed to evaluate the correlation between variables. It was considered that p<0.05 was statistically significant.

Ethics committee approval of our study was obtained from the ethics committee of Kahramanmaras Sutcu Imam University Faculty of Medicine (session number: 2022/23, decision number: 07, date: 06.09.2022).

Results

The ages of the patients who presented to the emergency department due to appendicitis were between 2 and 17,

with a median age of 10.0. 34 (72.3%) of the admitted patients were male (Table 1).

The WBC values of the patients were found to be 16460.2±4961.1 mm3/L, and the ratio of patients with WBC values above normal was 85.1% (n=40). While neutrophil counts were found to be 13418.5±4745.4 mm3/L, the ratio of patients with neutrophil counts above normal was 85.1% (n=40). The lymphocyte counts were between 640 and 4450 mm3/L, with a median value of 1310 mm3/L. While lymphocyte values of 59.6% (n=28) of the patients were within the normal range, 17 patients (36.2%) and 2 patients (4.3%) had lower lymphocyte levels and higher lymphocyte levels, respectively. While the median platelet value was found to be 295000 mm^3/L, platelet values ranged between 178000 and 609000 mm3/L, and the ratio of patients with platelet counts above normal was 87.2% (n=41). The delta neutrophil index of the patients ranged from 10 to 760 mm3/L with a median value of 80. The delta neutrophil percentages varied between 0.2% and 3.8%, and the median value was found to be 0.5%. While the delta neutrophil index count was found to be high in 85.1% (n=85.1) of the patients, the value in 7 patients was found to be within the normal range. The number of the patients who had high delta neutrophil percentages was 15 (31.9%) and the number of patients with normal delta neutrophil percentages was 32 (68.1%) (Table 1).

The CRP values of the patients ranged from 1.43 to 477 mg/L, and the median value was found to be 77 mg/L. While the CRP values of 7 patients (14.9%) were within normal limits, the CRP values of 40 patients (85.1%) were higher than normal. Calcium values were between 7 and 10.1 mg/dL, and the median value was found to be 9.1 mg/dL. The mean sodium values of the patients were 137.2±3.5 mmol/L. The median potassium value was 4.0 mmol/L and ranged from 3.7 to 5.4. The diameter of appendix measured by ultrasonography or tomography ranged from 6 to 20 millimeters (mm), with a median value of 10.0 mm (Table 1).

The NLR values of the patients were between 1.66 and 24.48, with a median value of 9.13 and a mean value of 10.6±6.4. The PLR values of the patients were between 80.2 and 617.1, with a median of 205.1 and a mean of 246.4±17.6 (Table 1).

While there was a high negative correlation between patients' age and platelet counts (p<0.01, r=-0.733), a weak negative correlation was found with delta neutrophil index counts (p<0.05, r=-0345) and a weak negative correlation was found with delta neutrophil percentages (p<0.01, r=-0.405) (Table 2). These values decreased as the age of the patients increased. No significant correlation was found between the other data we included in the correlation analysis and the patients' age. A weak positive correlation was found between the patients' WBC values and platelet counts (r=0.292) and the delta neutrophil index counts (r=0.293) (p<0.05), and there was a weak positive correlation with the NLR values (p<0.01) (Table 2). These values increased as the WBC counts of the patients increased. It was found that there was a positive and moderate correlation between the neutrophil counts and NLR values of the patients (r=0.573, p<0.01), and NLR values increased as the neutrophil counts increased.

Table 1. Hemogram and biochemical values of pediatric acute appendicitis patients.

Variable	Variable Value	
	Mean±Standard Deviation	Median (Least-Largest value)
Age	10.6±4.4	10.0 (2-17)
White blood cell (WBC) (mm^3/L)	16460.2±4961.1	16000 (4320-29490)
Neutrophil (mm^3/L)	13418.5±4745.4	13230 (2280-24740)
Lymphocyte (mm^3/L)	1649.7±936.3	1310 (640-4450)
Platelets (mm^3/L)	327085.1±99398.8	295000 (178000-609000)
Delta Neutrophil Index Number (IG) (mm^3/L)	117.8±123.6	800.0 (10-7600)
Delta Neutrophil Percentage (IG) %	0.73±0.68	0.50 (0.20-3.80)
C-reactive protein (CRP) (mg/L)	88.8±112.3	77.0 (1.43-477.0)
Calcium (mg/dL)	9.3±0.6	9.1 (7.0-10.1)
Sodium (mmol/L)	137.2±3.5	138.0 (127.0-144.0)
Potassium (mmol/L)	4.2±0.4	4.0 (3.7-5.4)
Appendix diameter (mm)	9.8±2.7	10.0 (6-20)
Neutrophil lymphocyte ratio (NLR) (%)	10.6±6.4	9.1 (1.6-24.4)
Platelet lymphocyte ratio (PLR) (%)	246.4±121.2	205.1(80.2-617.1)

Table 2. Comparison of hemogram and biochemical values of pediatric acute appendicitis patients.

	Age	WBC	Neutrophil Count	Lymphocyte Count	Platelet Count	Delta Neutrophil Index Count	Delta Neutrophil Index Percentage	CRP	Ca	Na	K	Apandix Diameter	NLR	PLR
Age	1													
WBC	-0.163	1												
Neutrophil Count	-0.086	0.960**	1											
Lymphocyte Count	-0.255	0.232	0.015	1										
Platelet Count	-0.733**	0.292*	0.178	0.442**	1									
Delta Neutrophil Index Count	-0.345*	0.293*	0.189	-0.368*	0.465**	1								
Delta Neutrophil Index Percentage	-0.405**	-0.037	-0.119	0.262	0.401**	0.900**	1							
C-Reactive Protein (CRP)	-0.171	-0.183	-0.161	-0.253	0.108	0.133	0.215	1						
Calcium (Ca)	0.057	0.257	0.287	-0.028	-0.117	-0.468**	-0.510**	-0.239	1					
Natrium (Na)	0.115	0.263	0.178	0.455**	0.077	-0.103	-0.284	-0.662**	0.136	1				
Potassium (K)	-0.071	-0.081	-0.069	-0.089	0.145	-0.290*	-0.314*	0.077	0.220	0.134	1			
Apandix Diameter	0.107	-0.017	0.065	-0.217	-0.025	-0.152	-0.157	0.097	0.022	-0.110	-0.048	1		
Neutrophil lymphocyte ratio (NLR)	0.168	0.386**	0.573**	-0.705**	-0.260	-0.164	-0.268	0.082	0.231	-0.219	-0.054	0.200	1	
Platelet lymphocyte ratio (PLR)	-0.210	-0.124	0.031	-0.716**	0.185	-0.116	-0.009	0.358*	-0.018	-0.506**	0.161	0.242	0.611**	1

*: p<0.05. **: p<0.01.

While there was a weak positive correlation between the patients' lymphocyte counts and thrombocyte (r=0.442) and Na (r=0.455) values (p<0.01), a high negative correlation was found between NLR (r=-0.705) and PLR (r=-0.716) values (p<0.01), and a weak negative correlation was found with delta neutrophil index counts (r=-0.368, p<0.05) (Table 2). As the lymphocyte counts increased, platelet and sodium (Na) values increased and NLR, PLR and delta neutrophil index counts decreased. It was determined that there was a weak positive correlation be-

tween the patients' platelet counts and delta neutrophil index counts (r=0.465) and delta neutrophil percentages (r=0.401) (p<0.01) (Table 2), and these values increased as the platelet counts increased. While very high positive correlation was found between the patients' neutrophil index counts and delta neutrophil percentages (r=0.900, p<0.01), there was a weak negative correlation between Calcium (Ca) (r=-0.468, p<0.01) and Potassium (K) values (r=-0.290, p<0.05). There was a moderately negative correlation (r=-0.510, p<0.01) between delta neutrophil percentage values and Ca, but a weak and negative correlation (r=-0.314, p<0.05) was found between K. There was a moderately negative correlation between CRP values and Na values of the patients (r=-0.662, p<0.01), but there was a weak and positive correlation between PLR values (r=0.358, p<0.05). As the CRP values of the patients increased, the Na values decreased and the PLR values increased. There was a moderately positive correlation between the Na values and PLR values of the patients (r=-0.506, p<0.01). There was a moderately positive correlation between the NLR values and PLR values of the patients (r=0.611, p<0.01), and the PLR values increased with the increase in NLR values. It was determined that there was no significant correlation between the patients' appendix diameters measured by imaging methods and the parameters included in the study (Table 2).

Discussion

The most common causes of acute abdomen include acute appendicitis. Ultrasonography and computed tomography are used to diagnose AA and to detect its complications. The lack of computed tomography and ultrasonography in each hospital and radiologists' subjective evaluations in reaching a definitive diagnosis lead to difficulties in diagnosis. Therefore, certain serological markers are used for diagnosing AA. Biochemical markers like WBC, CRP, PCT, NLR, and PLR have been reported as potential predictors for diagnosing AA. Considering the involvement of inflammatory markers in the disease's pathophysiology, studies examining the diagnostic value of inflammatory markers are important.

In the study conducted by Şeyhanlı, hemogram parameters of pediatric patients with and without acute appendicitis were compared. It was determined that there was a statistically significant difference between them and the NLR (p<0.05). It was observed that the NLR was higher in acute appendicitis patients. It was indicated that no statistically significant difference was found between them and the red blood cell width (RDW), platelet mass index (PMI), WBC, and Neutrophil count (p>0.05) [14].

In the study of Özçelik et al., 64.2% and 35.8% of pediatric patients with appendicitis were females and males, respectively. In AA patients, WBC was 13.9±5.6 mm3/L, Neutrophil ratio was 74.4±14.2%, Lymphocyte ratio was 16.4%±10.8%, Platelet count was 311.2±93.7 mm3/L, and C-reactive protein was 37.7±53.8 mg/L [15]. 72.3% of our patients diagnosed with pediatric appendicitis included in this study were male.

In their study, Dulkadir et al. found that the neutrophil/lymphocyte ratio, C reactive protein level, C reactive protein level/albumin value and hematocrit level

were significantly higher in children with AA compared to children without AA [16].

In the study of Doğan et al., it was indicated that the NLR, WBC/MPV, CRP/MPV, PLR and MPV/L values in children with AA were higher in patients who underwent appendectomy compared to abdominal pain observation group (p<0.001). Since it was determined that the NLR, WBC/MPV, CRP/MPV, PLR and MPV/L were higher in patients undergoing appendectomy, it was stated that these parameters would support the diagnosis in deciding the operation or determining the observations of abdominal pain [17].

In the study conducted by Doğan et al., immature granulocyte, WBC count, NLR and MPV values were found to be higher in children with AA compared to the control group. Among inflammatory markers, only IG was statistically significantly different from other markers (p<0.001). The ROC analysis revealed that the sensitivity and specificity of IG were 81.8% and 85.2%, respectively, in patients with AA [9]. The delta neutrophil index count, CRP, NLR, PLR and WBC values were also found to be high in the patients included in our study. In the study conducted by Bozan et al., it was indicated that the IG count and the IG percentage were effective and high in the diagnosis and evaluation of patients with acute appendicitis and were guiding in the follow-up of the treatment of acute appendicitis. In the same study, it was stated that IG measurements were easily accessible blood parameters that did not require additional cost to the health system since they were studied with automatic systems within the complete blood count parameters [10].

In our study, WBC values and neutrophil counts of 85.1% of the patients were found to be high. While lymphocyte values of 59.6% patients were found to be within the normal range, 36.2% of patients had low lymphocyte levels. It was determined that thrombocyte values increased in 87.2% of the patients. The delta neutrophil index count and CRP values were found to be high in 85.1% of the patients. It was determined that NLR and PLR values of the patients were high. As the WBC counts of the patients increased, the platelet counts and delta neutrophil index counts also increased. The NLR values increased as the neutrophil counts of the patients increased. As the platelet counts of the patients increased, delta neutrophil index counts (r=0.465) and delta neutrophil percentages (r=0.401) increased. The patients' PLR values increased as their NLR values increased. The results in our study are similar to those in literature. It was determined that the WBC, CRP, delta neutrophil index count/percentage, NLR and PLR values increased in pediatric appendicitis patients. Delta neutrophil index counts, delta neutrophil percentages, NLR and PLR are important as new markers to be used for diagnosing pediatric acute appendicitis.

Conclusion

Delta neutrophil index, NLR, and PLR, which are inflammatory markers, were found to be statistically significantly high in the diagnosis of AA in pediatric patients. IG, NLR, PLR measurements are easily accessible blood parameters that do not require additional costs to the health system since they are automatically studied with in the complete

blood count parameters. We recommend the use of delta neutrophil index, NLR, and PLR values along with physical examination, imaging studies, and laboratory tests to be helpful in the diagnosis of pediatric patients with AA.

Conflict of interest

There is no conflict of interest between the authors.

Ethical approval

Ethics committee approval of our study was obtained from the ethics committee of Kahramanmaras Sutcu Imam University Faculty of Medicine (session number: 2022/23, decision number: 07, date: 06.09.2022).

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