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Assessment of New Biomarkers Used in the Diagnosis of Acute Appendicitis in Children

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Background: Acute appendicitis (AA) is the most frequent cause of acute abdomen and diagnosis can be difficult in paediatric patients. Our purpose was to examine the initially checked inflammatory markers of paediatric patients operated with a diagnosis of acute appendicitis and to find out the significance of these markers in diagnosis.
Materials and Methods: The study was conducted in a paediatric hospital with patients younger than 18 years of age diagnosed with acute abdomen between May 2017 and December 2018. Patients' inflammatory markers at the time of diagnosis were examined. They were grouped in two as patients who were operated with a diagnosis of AA (Group A) and patients who had abdominal pain but who were clinically followed without operation (Group B).
Results: 103 children diagnosed with acute abdomen were included in our study. 71.8% of the patients were male, while 28.2% were female. Average age of the patients was 9.7±3.4 years. Twenty-four patients had suspicious laboratory and radiological examinations (USG or CT) with abdominal pain were clinically followed and discharged without operation.79 patients were operated. In the comparison of inflammatory markers of patients in Group A and Group B, statistically significant difference was found between WBC, neutrophil count, neutrophil/lymphocyte ratio(NLR), platelet/ lymphocyte ratio (PLR) and CRP ($p<0.05$).
Conclusion: WBC, neutrophil count, NLR, PNR and CRP values, which are examined in complete blood count, are easily accessible and quickly assessable methods that can be used in the diagnosis of AA patients.
Keywords: Abdominal pain; acute appendicitis; paediatric; hemogram

Introduction

Acute appendicitis (AA) is the most frequent cause of acute abdomen among pathologies, which cause abdominal pain in all age groups (1). The diagnosis of AA can be difficult in pediatric patients since it gives atypical symptoms with a rate of 1/3 (2). In making the diagnosis of AA patients, anamnesis, physical examination, increases in blood inflammation parameters and clinical experience play a significant role. Despite these, due to increasing malpractice cases and in order to decrease negative appendectomy rates, physicians make more detailed examinations to distinguish these from other surgical pathologies, and they need additional examinations. Although radiological imaging techniques such as ultrasound (USG) and computerized tomography (CT) are used,

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negative pathology results can be seen in 10-30% of the patients operated (3-5). Perforation can develop as a result of late diagnosis of appendicitis and peritonitis, abscess, sepsis, and ileus can be seen as a result of this (2). For this reason, new researches are needed to prevent complications that may develop as a result of late diagnosis and to decrease morbidity and mortality rates. For this purpose, studies have been conducted which show the association between hematologic and biochemical parameters which are indicators of acute inflammation such as C-reactive protein (CRP), white blood cell count (WBC), Procalsitonin, Pentraxin-3 and AA (3,6,7).

In the study, our purpose was to examine the initially checked hemogram (complete blood count) parameters and CRP values of pediatric patients operated with a diagnosis of acute appendicitis and to find out the significance of these parameters and values in diagnosis.

Materials and Methods

The study was conducted in a tertiary pediatric hospital, which had annually 100.000 patient referrals through a retrospective examination of data after local ethical board approval (Approval number:2019/08) was taken. Patients younger than 18 years of age diagnosed with acute abdomen diagnosis whose information was reached from file and automation records between May 2017 and December 2018 were included in the study. All blood samples were taken by the venous blood system and collected into ethylene diamine tetraacetic acid tubes. Patients' hemogram parameters and biochemical tests at the time of diagnosis and their post-surgery pathology results were examined retrospectively. Patients who were found to have missing data, those who did not have post-surgery pathology results, those who had registered hematological disease, those who were receiving chemotherapy and those who were found to use drugs like steroid which affects blood parameters were not included in the study. Complete blood count device (ABX Pentra DX 120) was used for the measurement of blood parameters. White cell count $\times 10^3$/uL (WBC), neutrophil $\times 10^3$/uL (NEU), lymphocyte $\times 10^3$/Ul (LYM), platelet $\times 10^3$/uL(PLT), red blood cell width (RDW,%), mean platelet volume (MPV), platelet distribution width (PDW), neutrophil/lymphocyte ratio (NLR), platelet/ lymphocyte ratio (PLR), platelet/neutrophil ratio (PNR), platelet distribution width/red blood cell width ratio (PDW/RDW) and CRP values of the patients examined in the study.

The patients were divided into two groups. Hemogram, CRP, and radiological imaging (USG and CT) were ordered for patients who referred with a complaint of abdominal pain, and those who had acute abdominal symptoms. The patients whose tests were compatible with appendicitis were operated. These patients were called Group A. Patients who had right lower quadrant pain in examination results, those who had a suspected acute abdomen, those who did not have high leukocytosis and/or CRP in laboratory examinations, those in whose USG or CT appendix was not visualized were followed and these patients who were not operated were called Group B.

A statistical package program was used for statistical analysis. Descriptive analysis of assessment results was given as numbers and percentage for categorical variables and as mean, standard deviation, min and maximum for numerical variables. Kolmogorov Smirnov test was used to test normality distribution. T-Test was used in normally distributed

parameters for all group comparisons, while Mann Whitney-U Test was used for parameters without normal distribution. Significance level was accepted as p<0,05.

Results

One hundred three patients diagnosed with acute abdomen younger than 18 years of age whose data were reached between May 2017 and December 2018 were included in our study. 71.8% of the patients were male, while 28.2% were female. The average age of the patients was 9.7±3.4 years (min:2 and max:17). Twenty-four of the patients who had suspicious laboratory and radiological examinations (USG or CT) with abdominal pain were clinically followed and discharged without operation. Seventy-nine patients were operated, and AA symptoms were found in surgical pathology results.

In 13 of the patients who were operated, perforated appendicitis symptoms were found. While WBC value of the patients diagnosed with acute abdomen was 13.6±4.7×10^3/uL, mean neutrophil count was 10.6±4.6×10^3/uL, mean lymphocyte count was 1.9±0.8×10^3/uL, mean platelet count was 294.1±81.5×10^3/uL, mean RDW value was 14.4±2, mean MPV value was 8.7±1.7 fL, mean PDW value was 12.6±3.7 fL, mean PLR was 187.1±97.2, mean PNR was 34.3±20.4, mean PDW/RDW was 20.8±6.1, and mean CRP was 3.9±5.7. In the comparison of hemogram parameters and CRP values of the patients in Group A and Group B, a statistically significant difference was found between WBC, neutrophil count, NLR, PNR and CRP values, p<0.05. No statistically significant difference was found between the other parameters, p>0.05 (Table-1).

Table-1. Comparison of biomarker averages of patient groups

Parameters	Grup A (Mean±SD)	Grup B (Mean±SD)	P Value
WBC ×10^3/uL	14,5±4,7	10,8±3,8	0,001
Nötrofil count ×10^3/uL	11,6±4,5	7,6±3,6	<0,001
Lenfosit count ×10^3/uL	1,8±0,8	2,1±0,9	0,108
Platelet count ×10^3/uL	294,2±78,9	293,5±91,4	0,969
RDW,%	14,1±1,9	15±2,1	0,057
MPV fL	8,8±1,7	8,2±1,5	0,146
PDW fL	12,24±3,54	13,84±4	0,064
PNR	29,8±15,4	48,8±27,2	0,003
NLR	8,3±6,2	4,5±3,8	0,005
PLR	194,5±98,6	162,9±90,1	0,164
PDW/RDW	21,1±6	19,7±6,2	0,326
CRP mg/dL	4,4±6,3	2,2±1,8	0,008

Abbreviations. NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio, PNR: Platelet Neutrophil Ratio, RDW: Red Cell Distribution Width, PDW: Platelet Distribution Width, MPV: Mean Platelet Volume, CRP: C-Reactive Protein

When acute and perforated appendicitis were compared, while no statistically significant difference was found between hemogram parameters WBC, neutrophil count, lymphocyte count, NLR and PNR values ($p>0.05$), a statistically significant difference was found in CRP values ($p<0.05$).

Discussion

Appendicitis is a pathology characterized by the inflammation of appendix vermiformis. Although its etiology is not known for sure, it frequently occurs with obstruction of appendix lumen (8). In children whose typical symptoms have not started, atypical abdominal pain referrals cause AA diagnosis to be excluded. AA is an acute abdomen pathology the occurrence possibility of which is higher in male children after the age of 10 (9-11). The patient population in our study is in parallel with the literature.

Finding suitable, easily accessible, and low-cost markers for the early diagnosis of diseases is generally the focus of interest for researchers. Because of the increase in morbidity and mortality caused by delays in diagnosis in patients who refer to emergency services for abdominal pain, a significant number of biochemical diagnostic tests that can be used for early diagnosis have been researched. The complete blood count is the primary examination, which can be easily accessed and quickly assessed in the emergency service. Parameters dependent on each other within the complete blood count such as leukocyte, neutrophil, lymphocyte, NLR, PDW, PLR, PNR have been examined in a high number of studies as inflammatory markers. The focus of studies conducted in recent years is the determination of suitable threshold values for these parameters and the sensitivity and specificity of different threshold values (12).

WBC, neutrophil, RDW, and NLR function as an inflammatory marker. These inflammatory markers have been tested in a significant number of studies, and their diagnostic value has been increasing each day (13, 14). A high number of inflammatory marker studies have been conducted about AA, and such studies are continuing to be conducted today.

Recently, NLR, which is a parameter, has begun to be studied more, and it is a better marker alone for acute appendicitis when compared with CRP, leukocyte, and neutrophil (15, 16). Different threshold values and different performances have been found as a result of these studies. We grouped our patients into two as patients who were hospitalized in a condition of abdominal pain and operated for appendicitis (Group A) and those who were discharged after confirming that they did not have any sign of appendicitis (Group B). We think examining the hemogram parameters, and CRP changes in these groups are more valuable in the definitive diagnosis of appendicitis. In our study, although statistically significant difference was found between WBC, neutrophil count, NLR, PNR and CRP of patients who were operated for AA and those who were not operated and clinically followed ($p<0.05$), no statistically significant difference was found between lymphocyte count, RDW, MPV, PLR and PDW/RDW of these patients ($p>0.05$). This may be useful in differential diagnosis of AA.

In a study, Tanrıkulu et al. found that WBC, MPW, RDW values, and neutrophil rates of patients operated for appendicitis were significantly higher than the control (17, 18). In this study, they concluded that in suspected cases, both MPW and RDW were essential

parameters in terms of AA diagnosis (18). In another study, MPV and RDW values and mean platelet count showed no significant difference between operated and healthy groups (19). In parallel with literature, we found in our study that WBC count, neutrophil count, CRP, PNR, NLR values were statistically significant between the two groups. However, we could not find a statistically significant difference between MPW and RDW values.

In AA studies conducted with inflammatory markers, the standard prediction is that it is vital to assess anamnesis, physical examination, and inflammatory markers together. However, despite all these, radiological imaging should be performed and if the results are speculative, clinical follow should be performed in order not to leave out the diagnosis especially in atypical cases, to prevent mortality rates from increasing, to decrease negative laparotomy rates and to prevent malpractice cases.

As a conclusion, WBC, neutrophil count, NLR, PNR, and CRP values, which are examined in blood samples, are easily accessible and quickly assessable methods that can be used in the diagnosis of AA patients. However, we believe that these parameters alone are not definitive to make AA diagnosis. A good anamnesis, physical examination, suitable radiological imaging following complete blood count and in case of suspected results, hospitalization and clinical follow up are necessary to decrease morbidity and mortality rate as a result of late diagnosis.

Conflict of Interests

None of the authors has a conflict of interest with the present article.

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