

Pre-operative and post-operative changes in values of CRP and hemogram in children with perforated appendicitis

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ABSTRACT

Objective: Since acute appendicitis is a clinical condition that develops after inflammation of the appendix, changes in the markers related to infection are expected in the laboratory tests of these cases. In this study, it was aimed to determine the changes in C-reactive protein (CRP) and hemogram examinations taken before and after surgery in children with perforated appendicitis and even to determine the markers that could indicate appendix perforation.

Material and Methods: This study was conducted in children with perforated appendicitis who were operated on in our pediatric surgery department in 2019. Only patients whose pre-operative and post-operative laboratory tests were performed in our hospital were included in the study. The demographic characteristics, pre-operative and post-operative (CRP, White blood cell [WBC], neutrophil, lymphocyte, mean platelet volume [MPV], and platelets [PLT]) values were analyzed retrospectively.

Results: Only 69 of 141 children with perforated appendicitis who were operated on in 2019 had pre- and post-operative tests performed in our hospital. Of the 69 cases included in our study, 29 were female (40.1%) and 40 were male (59.9%). The median pre-operative values of CRP, WBC, neutrophil, lymphocyte, MPV, and PLT were 4.4 (0.2–21.66) mg/dL, 14.46 (5.27–32.6) 103/mm³, 10.03 (2.6–20.25) 103/mm³, 1.76 (0.17–8.69) 103/mm³, 8.7 (6.99–134) fL, and 280 (134–497) 103/mm³, respectively. The median values of CRP, WBC, Nötrofil, Lenfosit, MPV, and PLT on the 5th post-operative day were 3.8 (0.2–17.7) mg/dL, 11.39 (4.4–36.8) 103/mm³, 8.63 (2.12–22.02) 103/mm³, 1.75 (0.41–6.17) 103/mm³, 8.7(6.5–146) fL, and 286 (146–721) 103/mm³, respectively. The difference of CRP and WBC between pre- and post-operative values was found to be significant based on Wilcoxon Signed Rank Test (Non-parametric) (<0.05).

Conclusion: Moderately high CRP and WBC values are important as an infection marker in the diagnosis of acute appendicitis. Similar to the literature, it has been shown that the CRP level, which was high before the operation, gradually decreased after the operation, but still did not return to normal at discharge. The decrease in CRP and WBC values after surgery is an indication that inflammation has regressed after appendectomy, but it takes time to completely return to normal.

Keywords: Acute appendicitis, child, CRP, hemogram, inflammation, perforated appendicitis.

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INTRODUCTION

Abdominal pain is a common entity in the pediatric population. Although right lower quadrant pain principally brings to mind appendicitis worldwide, the right lower quadrant pain usually remains a diagnostic dilemma for the clinicians in children because many non-surgical conditions also cause right lower quadrant pain and clinically mimic appendicitis.^[1,2]

Acute appendicitis is a clinical condition that developed as a result of inflammation of the vermiform appendix.^[3] If it is a part of the metabolic response as acute inflammation, to determinate the changes of the inflammatory markers associated with appendicitis in children were to verify its.

There is a significant difference between pre-operative and post-operative laboratory findings in appendicitis cases operated. This study was planned to show whether there is a change in hemogram parameters, especially C-reactive protein (CRP) and white blood cell (WBC), which are acute phase reactants, in patients with perforated appendicitis. Therefore, pre- and postoperative changes in markers related to infection will be determined in children with appendicitis. Thus, it will be revealed whether a diagnostic prediction can be made according to CRP and hemogram values in children with acute appendicitis.

In this study, it was aimed to determine the changes in CRP and hemogram values taken before and after surgery in children with perforated appendicitis who were operated on in our pediatric surgery department, and even to determine the markers or markers that could indicate appendix perforation.

MATERIAL AND METHODS

Study Groups

Children with acute appendicitis (who were operated in our hospital in 2019) whose pre-operative and post-operative laboratory analyzes were performed in our hospital were included in this study; patients whose laboratory tests were performed in external centers were not included in the study.

All records of the patients were accessed from the hospital data processing system. The demographic characteristics (age and sex), and preoperatively and postoperatively laboratory values of CRP, WBC, neutrophil, lymphocyte, mean platelet volume (MPV), and platelets (PLT) were analyzed retrospectively.

Collection of Blood Samples

Pre-operative and post-operative 5th day (checked on the day of discharge) hemogram and CRP values were obtained from the hospital data processing soft-ware archive. CRP concentrations were taken from serum and assessed using the turbidimetric method. Values of WBC, neutrophil, lymphocyte, MPV, and PLT were assessed by looking at the whole blood values.

Statistical Analysis

All data were analyzed using SPSS software for Windows (IBM SPSS Statistics 24.0). To compare the differences between the groups, the

Wilcoxon Signed Rank Test (Nonparametric) and Spearman Rank Correlation Coefficient were used statistically. Pre-operative and post-discharge CRP and hemogram results of pediatric patients were presented as median values.

RESULTS

A total of 69 children with perforated appendicitis, 29 girls (40.1%) and 40 boys (59.9%), who were operated in Department of the Pediatric Surgery (Istanbul Zeynep Kamil Maternity and Children's Diseases Training and Research Center, University of Health Sciences) during the 2019, were included to this study due to pre-operative and post-operative laboratory tests had been taken at our hospital. Other 72 cases with perforated appendicitis whose laboratory tests were conducted at external centers were not included in this study. All of them came to the hospital with complaints of abdominal pain. The median age of the surgery was 11 years (2–19 years).

The pre-operative results of blood tests in 69 children were as follows: The median CRP value was 4.4 (0.20–21.66) mg/dL. The median WBC value was 14.46 (5.27–32.6) $10^3/\text{mm}^3$. The median neutrophil value was 10.03 (2.6–20.25) $10^3/\text{mm}^3$. The median lymphocyte value was 1.76 (0.17–8.69) $10^3/\text{mm}^3$. The median MPV value was 8.7 (6.99–134) fL. Pre-operative median PLT value was 310 (134–497) $10^3/\text{mm}^3$.

The post-operative results of blood tests were as follows: The median CRP value was 3.8 (0.2–17.69) mg/dL. The median WBC value was 11.39 (4.4–36.8) $10^3/\text{mm}^3$. The median neutrophil value was 8.63 (2.12–22.02) $10^3/\text{mm}^3$. The median lymphocyte value was 1.75 (0.41–6.17) $10^3/\text{mm}^3$. The median MPV value was 8.7 (6.5–11.6) fL. The median PLT value was 286 (146–721) $10^3/\text{mm}^3$. Pre-operative and post-operative laboratory results were demonstrated in (Table 1).

In the comparison of pre-operative and post-operative values according to Wilcoxon Signed Sequential Nonparametric Test, the differences between pre-operative and post-operative values in CRP, WBC, and PLT were found significant. The differences between pre-operative and post-operative values in lymphocyte and MPV were not significant. The comparison of laboratory values before and after surgery is shown in (Table 2).

In the comparison of pre-operative values according to Spearman Rank Correlation coefficient, there was a weak correlation between pre-operative WBC and CRP, and between pre-operative CRP and neutrophil-to-lymphocyte ratio (NLR) values. There was very poor correlation between pre-operative CRP and PLT values, and between post-operative CRP and PLT values. There was poor correlation between post-operative WBC and CRP values, and between post-operative CRP and NLR values. There was a moderate correlation between pre-operative NLR and PLT values. There was an inverse relationship between pre-operative CRP and PLT/MPV values, and between pre-operative NLR and PLT/MPV values, and between post-operative CRP and PLT/MPV values, and between post-operative NLR and PLT/MPV values. There was a high correlation between post-operative NLR and PLT values. The comparison of pre-operative and post-operative values according to Spearman Rank Correlation coefficient is summarized in (Table 3).

Table 1: Preoperative and postoperative laboratory results were demonstrated

	n	Mean	SD	Median	25%	75%
Pre-WBC	69	14.01	5.83	14.46	8.78	17.74
Pre-PLT	69	281	83	280	229	339
Pre-CRP	64	6.8	6.6	4.4	0.6	11.1
Pre-NEU	69	10.50	5.22	10.03	6.34	13.97
Pre-LY	69	2.06	1.35	1.76	1.30	2.46
Pre-MPV	69	11.5	17.1	8.7	8.0	9.4
Post-WBC	68	12.45	5.98	11.39	8.04	16.88
Post-PLT	68	310	123	286	229	381
Post-CRP	48	16.6	81.6	3.8	0.8	8.9
Post-NEU	68	9.64	5.30	8.63	5.55	14.27
Post-LYM	68	1.94	1.05	1.75	1.12	2.53
Post-MPV	68	11.8	18.7	8.7	8.2	9.3
Pre-NLR	69	7.44	6.00	6.07	3.08	10.46
Pre-PLT	69	181.19	137.46	140.65	114.71	204.49
Pre-PLT/MPV	69	32.1	11.8	31.3	24.3	40.4
Post-NLR	68	7.61	7.96	4.16	2.59	9.48
Post-PLT	68	199.43	115.55	177.61	114.91	261.76
Post-PLT/MPV	68	36.0	18.4	33.2	24.9	45.9

WBC: White blood cell; PLT: Platelets; CRP: C reactive protein; MPV: Mean platelet volume; NLR: Neutrophil-to-lymphocyte ratio.

DISCUSSION

The diagnosis of appendicitis in children was highly troublesome, especially given the difficulty of obtaining a reliable history and clinical examination in young children. Radiological and laboratory evaluations in children are helpful for diagnosis when they support examination findings. Appendicitis is caused by blockage of the lumen of the appendix, mostly from fecal stones, parasites, gallstones, or tumors, or by blockage of inflammatory lymphoid tissues with a viral infection. This blockage leads to increased pressure in the lumen of the appendix, decreased blood flow in the appendix wall, and the growth of bacteria inside the appendix, resulting in inflammation. Inflammation reduces blood flow to the appendix, swelling of the appendix leads to tissue injury and tissue death.^[1–5]

The most common surgical abdominal emergency in children is appendicitis. The clinical, laboratory, and radiological features of appendicitis have been well documented in the previous studies. However, its definitive diagnosis may be elusive in children at the time of initial assessment.^[6] Diagnosis of appendicitis in children is quite difficult, especially in young children, due to the difficulty of getting a reliable history and obtaining a clinical examination. Sometimes radiological and laboratory assessments can also be difficult to interpret. Some studies of the use of WBC and left shifting in the diagnosis of appendicitis in pediatric patients are available, but have not been conclusively proven. It is generally believed that children with appendicitis have high WBC values combined with left shift; most of the data supporting this belief comes from studies in adult appendicitis cases.

The CRP values were high levels before the appendectomy, increased 24 h after surgery generally and gradually decreased 72 h after surgery, and did not reach the normal range in the early period.^[1] Hence, a moderately elevated CRP (6.8 [minimum 0.20-maximum 21.66] mg/dL) and WBC (14.01 [minimum 5.27–maximum 32.6] $10^9/\text{mm}^3$) values were significant as an infection marker for diagnosis in acute appendicitis in our study. The decrease in the post-operative CRP and WBC values was an indication of the regression of inflammation after an appendectomy, but the values did not return to normal completely. It takes time for the increased values to return to normal completely.

In a study by Vaughan-Shaw et al.^[7] among 297 patients, it was shown that CRP, WBC and neutrophil (NC) values were within normal limits in four patients in center A and 13 patients in center B who developed appendicitis. The sensitivities of all three markers were as high as 94% and 92% before surgery in centers A and B, respectively; but were found to be as low as 60% and 64% after surgery. They reported that a single marker could not distinguish between complicated and uncomplicated appendicitis, however, increased NC or CRP >35.5 mg/L values can predict complicated appendicitis. It has been reported that the combination of CRP, WBC, and NC can be used to differentiate between patients with normal appendix, uncomplicated appendicitis, and patients with complicated appendicitis.^[7]

In an another study, 123 patients (62.5%) had uncomplicated acute appendicitis, 20 patients (10%) had complicated acute appendicitis, and while 55 patients (27.5%) had normal appendicitis.^[8] Lab-

Table 2: The comparison of pre-operative and post-operative values were demonstrated

	Pre-operative values				Post-operative values				p
	n	Median	25%	75%	n	Median	25%	75%	
WBC	69	14.46	8.78	17.74	68	11.39	8.04	16.88	0.048
PLT	69	280	229	339	68	286	229	381	0.035
CRP	64	4.4	0.6	11.1	48	3.8	0.8	8.9	0.020
NEU	69	10.03	6.34	13.97	68	8.63	5.55	14.27	0.094
LY	69	1.76	1.30a	2.46	68	1.75	1.12	2.53	0.741
MPV	69	8.7	8.0	9.4	68	8.7	8.2	9.3	0.967
NLR	69	6.07	3.08	10.46	68	4.16	2.59	9.48	0.746
PLT	69	140.65	114.71	204.49	68	177.61	114.91	261.76	0.086
PLT/MPV	69	31.3	24.3	40.4	68	33.2	24.9	45.9	0.129

Wilcoxon signed rank test (Nonparametric); NLR: Neutrophil-to-lymphocyte ratio; WBC: White blood cell; PLT: Platelets; CRP: C reactive protein; MPV: mean platelet volume.

oratory levels of WBC, NC, NLR, red cell distribution width (RDW), and CRP were found to be higher in positive appendectomy patients compared to negative appendectomy patients, while lymphocyte and PLT values were found to be lower. MPV levels were found to be insignificantly different between groups. Compared with uncomplicated acute appendicitis, RDW level was found to be significantly higher in patients with complicated acute appendicitis; however, no significant difference was found between positive and negative appendectomy patients. Sensitivity, specificity, and diagnostic accuracy were shown to be 44.83%, 100%, and 72.415% for WBC count, 72.41%, 81.82%, and 77.115% for neutrophil count, 48.28%, 90.91%, and 69.595% for RDW, and 89.66%, 63.64%, and 76.65% for RDW, respectively.^[8]

The mean pre-operative CRP and leukocyte values were found that the increase in the leukocyte count was an early marker of appendicitis, while the CRP value increased significantly only after appendicitis perforation or abscess formation in another study.^[9] That study had been conducted with 24 cases without appendicitis (Group A), 100 cases with uncomplicated acute appendicitis (Group B), and 100 cases with complicated acute appendicitis (Group C). The CRP and leukocyte values were not in the normal range in Group B (uncomplicated acute appendicitis) and Group C (complicated acute appendicitis); while in Group A (normal appendix), CRP and leukocyte levels were normal.^[9]

In a prospective study, values of WBC and CRP were found to be compatible with each patient’s clinic in 98 patients admitted with lower abdominal pain.^[10] No patients with WBC and CRP, both within the normal range, had acute appendicitis. High WBC and CRP values were weak positive predictors of appendicitis alone or in combination; they were also found to be weak correlated with the development of complications.^[10]

Markar et al.^[11] in a study of 1117 cases in which appendectomies were performed, the median age was 34 years (ranged 16–94 years). According to their results showed that in addition to clinical examination, NLR alone has greater diagnostic accuracy than WBC or CRP.

Table 3: The comparison of pre-operative and post-operative values according to Spearman rank correlation coefficient were demonstrated

	R	p
Before surgery		
WBC and CRP	0.31	0.012
CRP and NLR	0.31	0.012
CRP and PLT	0.15	0.23
CRP and PLT/MPV	-0.09	0.50
NLR and PLT	0.55	<0.001
NLR and PLT/MPV	-0.34	0.005
During discharge		
BK and CRP	0.22	0.13
CRP and NLR	0.26	0.079
CRP and PLT	0.05	0.74
CRP and PLT/MPV	-0.12	0.43
NLR and PLT	0.63	<0.001
NLR and PLT/MPV	-0.23	0.063

Spearman rank correlation; NLR: Neutrophil-to-lymphocyte ratio; WBC: White blood cell; PLT: Platelets; CRP: C reactive protein; MPV: Mean platelet volume.

Blood CRP and WBC values can indicate metabolic response to acute inflammation state and gradual reduction of inflammation. However, some studies have shown inconsistent information about hemogram and CRP values. Although most studies show an association between high WBC and left shift and diagnosis of appen-

ditis, it is reported that the significance of WBC increase and left shift varies greatly. It has been reported that the sensitivities for high WBC counts vary between 50% and 80% and differ in the diagnosis of appendicitis.^[5] Increased WBC or left shift carries high sensitivity in the diagnosis of appendicitis; however, it has the highest specificity if there is a left shift with a high WBC. Therefore, these values have been reported to help the clinician in diagnosing appendicitis or excluding the diagnosis of appendicitis. That study data support a strong association between high WBC and left shift in the diagnosis of appendicitis in children. Although not very conclusive, it can be said that WBC and left shift always assist clinicians in diagnosing and excluding appendicitis.^[5]

Another important question is whether a normal CRP and hemogram values can adequately rule out the diagnosis of appendicitis. High negative predictive values (>90%) have been reported for the normal WBC value, with or without a normal CRP value.^[5] Therefore, instead of a laboratory-driven clinical decision alone, it would be more accurate to conduct a more frequent repeated abdominal examination and analyze laboratory results. About 21% of patients had a normal WBC count and no left shift, all had physical signs suggesting appendicitis.^[5]

In our study, all patients had perforated appendicitis and all patients had physical findings suggestive of the appendicitis. CRP (6.8 [0.20–21.66] mL/dL) and WBC (14.01 [5.27–32.6] $10^3/\text{mm}^3$) values were found moderately high in patients with perforated appendicitis. In addition, CRP and WBC values (which obtained at discharge on the 5th day) did not regress to their normal values. Despite the potential biases of this study, the data obtained from this latest study show that high CRP and WBC values in the diagnosis of complicated appendicitis in pediatric patients presenting to the emergency department with acute non-traumatic abdominal pain are quite useful in diagnosing acute appendicitis. Both high WBC counts and high CRP values were independently associated with appendicitis. Of course, all laboratory results should always be evaluated together with a detailed history and physical examination, so as not to miss patients who developed appendicitis with normal WBC count and CRP counts in 20% of cases.

CONCLUSIONS

It is important to have moderately elevated CRP and WBC values as an infection marker in the diagnosis of acute appendicitis. The decrease in CRP and WBC values after the surgery is an indication that the inflammation has regressed after appendectomy, but it takes time to completely return to normal.

Statement

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Ethics Committee Approval: The Zeynep Kamil Maternity and Children's Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 08.01.2020, number: 02).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Author Contributions: Concept – AC, AE; Design – AC; Supervision – AC; Resource – AC, AE; Materials – AC, AE; Data Collection and/or Processing – AC, AE; Analysis and/or Interpretation – AE, AC; Literature Search – AE, AC; Writing – AE, AC; Critical Reviews – AC.

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REFERENCES

1. Matuszczak E, Tylicka M, Dębek W, Sankiewicz A, Gorodkiewicz E, Hermanowicz A. Concentration of proteasome in the blood plasma of children with acute appendicitis, before and after surgery, and its correlation with CRP. *World J Surg* 2018;42:2259–64.
2. Dunn JCY. Appendicitis. In: Coran AG, Caldamone A, Adzick NS, Krummel TN, Laberge JM, Shamberger R, editors. *Pediatric Surgery*. 7th ed. Philadelphia: Elsevier Saunders; 2012. p.1255–63.
3. Duman L, Cesur Ö, Kumbul Doğuç D, Çelik S, Karabrahimoğlu A, Savaş MÇ. Diagnostic value of serum pentraxin 3 level in children with acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 2020;26:699–704.
4. Bower RJ, Bell MJ, Ternberg JL. Diagnostic value of the white blood count and neutrophil percentage in the evaluation of abdominal pain in children. *Surg Gynecol Obstet* 1981;152:424–6.
5. Wang LT, Prentiss KA, Simon JZ, Doody DP, Ryan DP. The use of white blood cell count and left shift in the diagnosis of appendicitis in children. *Pediatr Emerg Care* 2007;23:69–76.
6. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg* 2013;100:322–9.
7. Vaughan-Shaw PG, Rees JR, Bell E, Hamdan M, Platt T. Normal inflammatory markers in appendicitis: Evidence from two independent cohort studies. *JRSM Short Rep* 2011;2:43.
8. Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. *J Invest Surg* 2018;31:121–9.
9. Grönroos JM, Grönroos P. Leucocyte count and C-reactive protein in the diagnosis of acute appendicitis. *Br J Surg* 1999;86:501–4.
10. Sengupta A, Bax G, Paterson-Brown S. White cell count and C-reactive protein measurement in patients with possible appendicitis. *Ann R Coll Surg Engl* 2009;91:113–5.
11. Markar SR, Karthikesalingam A, Falzon A, Kan Y. The diagnostic value of neutrophil: Lymphocyte ratio in adults with suspected acute appendicitis. *Acta Chir Belg* 2010;110:543–7.