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# The Correlation of Leukocyte Count and Percentage of Segmented Neutrophils with Pathohistological Findings of Appendix in Children

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## *Abstract*

***Background:*** Appendicitis is the most common indication for an emergency operation in children's age. Although none of the laboratory values has not high sensitivity and specificity for the diagnosis of appendicitis, leukocyte count and the percentage of segmented neutrophils are most commonly used. The aim of this study was to determine whether there is a statistically significant correlation between leukocyte count and the percentage of segmented neutrophils compared to the pathohistological finding of appendix in children.

***Materials and Methods:*** We retrospectively analyzed the data in the period from 1 January 2016 to 31 December 2016. The analysis was made on 211 patients (from the Children's Hospital Zagreb, Croatia). Spearman's correlation coefficient ($r_s$) was calculated. We determined the specificity and sensitivity of leukocyte count and the percentage of segmented neutrophils used in the calculation of Alvorado and Pediatric Appendicitis score.

***Results:*** The results of the research have shown that the correlation between leukocyte count and the pathohistological findings is weak ($r_s = 0.29$, $p = 3.61*10^{-8}$); while there is no correlation between the percentage of segmented neutrophils and pathohistological findings ($r_s = 0.18$, $p = 7.08 *10^{-5}$). The sensitivity of leukocyte count is 93% and the specificity is 30%, while the sensitivity to the percentage of segmented neutrophils is 71% and the specificity is 50%. The Receiver Operating Characteristic (ROC) curve analysis for leukocytes shows area under the curve of 0.648, while for segmented neutrophils of 0.574.

***Conclusion:*** Given the correlation results obtained, the clinical experience of physicians will still have one of the leading roles in diagnosing acute appendicitis in children.

***Key Words:*** Appendicitis, Children, Leukocytes, Segmented neutrophils.

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## 1- INTRODUCTION

Appendicitis is the most common indication for an emergency operation in children's age. In everyday clinical practice diagnosis of appendicitis is usually based on clinical picture, physical examination, laboratory findings and ultrasound examination. Although none of the laboratory values has not high sensitivity and specificity for the diagnosis of appendicitis, leukocyte count and the percentage of segmented neutrophils are most commonly used. The increase in the percentage of segmented neutrophils is strongly associated with appendicitis, as only 3.7% of children without left shift have appendicitis (1).

These two lab markers are the most discriminating factor for appendicitis within 24 hours of the onset of pain. In order to objectively evaluate the clinical findings, in Alvorado score leukocytosis ($\geq 10 * 10^9$ / L) with segmented neutrophils ($\geq$ 75%) carry 3 points while in Pediatric Appendicitis score carry 2 out of 10 points (2, 3). The aim of this study was to determine whether there is a statistically significant correlation between leukocyte count and the percentage of segmented neutrophils compared to the pathohistological finding of appendix in children.

## 2- MATERIALS AND METHODS

In order to ascertain whether there was a statistically significant correlation between leukocyte count and the proportion of segmented neutrophils compared to the pathohistological finding of children whose appendix has been removed, we retrospectively analyzed the data from the Hospital Information System and hospital documentation in the period from 1 January 2016 to 31 December 2016 (from the Children's Hospital Zagreb, Croatia). During this period 243 children were operated with a classic or laparoscopic approach. From the study, 25 patients were excluded due to incomplete documentation, and 7 patients with periappendiceal abscess who subsequently went to elective appendectomy. The analysis was made on 211 patients. All analyzed laboratory findings (leukocyte count, percentage of segmented neutrophils) were made within 12 hours before surgery. The results of the pathohistological analysis are classified into five categories: normal findings, acute appendicitis, acute phlegmonous appendicitis, acute gangrenous appendicitis and acute gangrenous perforated appendicitis. The data obtained is displayed via the scatter diagram in Microsoft Excel. In order to ascertain whether there is a correlation between leukocyte count and the segmented neutrophils in relation to the pathohistological finding, Spearman correlation coefficient is calculated ( $r_s = 1 - 6 \times \sum_{i=1...N} D_i^2 / [\, N(N^2-1) \,]$ ), the result of which is interpreted according to the following value ranges (0 - ± 0.25 ↔ no correlation, ± 0.26 - ± 0.50 ↔ weak correlation, ± 0.51 - ± 0.75 ↔ good correlation, ± 0.76 - ± 1 ↔ excellent correlation). Results were interpreted if they were statistically significant ($p < 0.05$). We determined, based on our results, the specificity and sensitivity of leukocyte count and the percentage of segmented neutrophils used in the calculation of Alvorado and Pediatric Appendicitis score. We calculated area under the curve for leukocytes and segmented neutrophils. The analysis was made in XLSTAT (statistical ***software*** for Microsoft Excel).

## 3- RESULTS

Out of a total of 211 patients (boys - 118 (55.9%); girls - 93 (44.1%)), the youngest operated patient was 2 years and 3 months, while the oldest was 17 years and 9 months. The average age was 11 years and 5 months. The results of the pathohistological analysis were as follows:

normal finding - 30, acute appendicitis - 47, acute phlegmonous appendicitis - 79, acute gangrenous appendicitis - 43, acute gangrenous perforated appendicitis - 12. In the scatter diagrams (**Figure.1, Figure.2**), results of leukocyte count and the percentage of segmented neutrophils relative to the pathohistological finding are shown. One hundred and ninety (90%) patients had a leukocyte count greater than $10*10^9$/L, while 144 patients (68.2%) had a percentage of segmented neutrophils greater than 75%. The results are presented in the contingency tables (**Table.1**, **Table.2**), with sensitivity for leukocyte count of 93% and specificity of 30%, while sensitivity for percentage of segmented neutrophils is 71% and specificity of 50% (**Figure.3, Figure.4**).

The Receiver operating characteristic (ROC) curve analysis for leukocyte count shows area under the curve of 0.648, while for segmented neutrophils of 0.574 (**Figure.5, Figure.6**).

By adding the leukocyte and pathohistological findings data into the Spearman coefficient correlation formula, $r_s = 0.29$ ($p = 3.61*10^{-8}$) is obtained. For leukocytes, the correlation is weak. By adding the data for the segmented neutrophils into the formula for the Spearman coefficient of correlation, $r_s = 0.18$ ($p = 7.08*10^{-5}$) is obtained. Correlation between the percentage of segmented neutrophils and pathohistological findings does not exist.

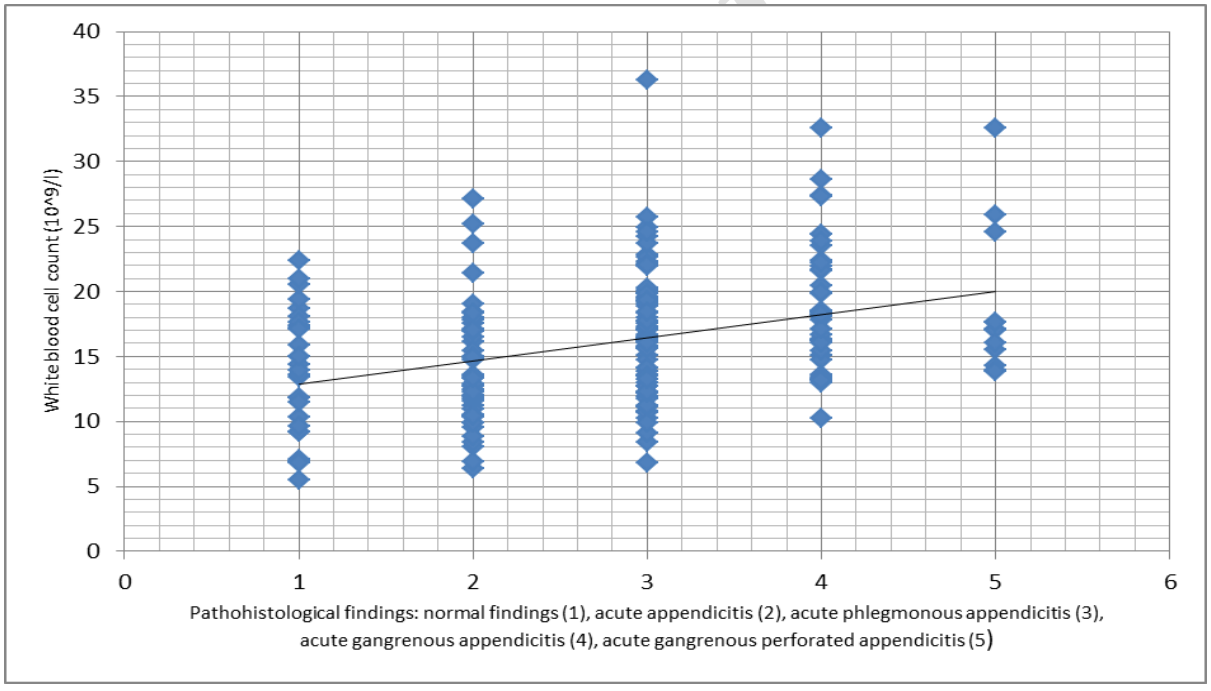


**Fig.1**: Scatter plot: relationship between pathohistological finding and leukocyte count.

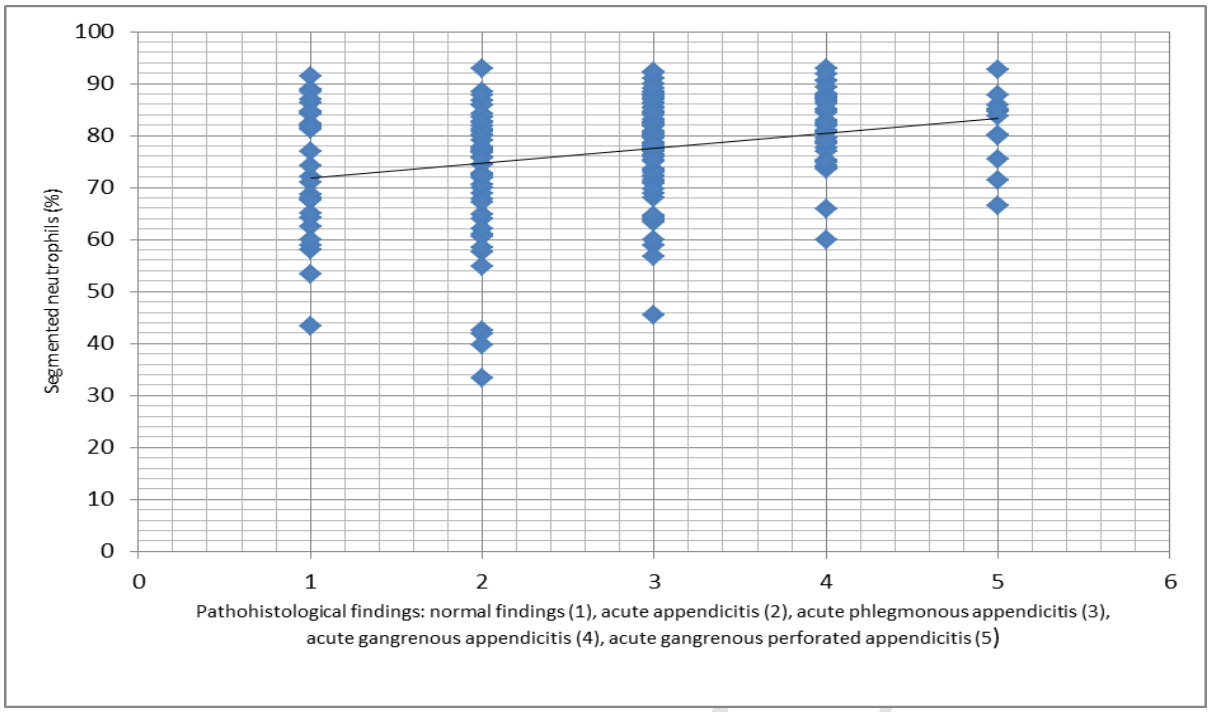


**Fig.2**: Scatter plot: relationship between pathohistological finding and the percentage of segmented neutrophils.

**Table-1**: Contingency table: The relationship between pathohistological finding and leukocyte count.

| Leukocyte count | Positive pathohistological findings | Negative pathohistological findings | Total |
|---|---|---|---|
| Leukocytes $\geq 10*10^9$ /L | 169 | 21 | 190 |
| Leukocytes $\leq 10*10^9$ /L | 12 | 9 | 21 |
| Total | 181 | 30 | 211 |

**Table-2**: Contingency table: The relationship between pathohistological finding and the percentage of segmented neutrophils.

| Percentage of segmented neutrophils | Positive pathohistological findings | Negative pathohistological findings | Total |
|---|---|---|---|
| Segmented neutrophils ≥75% | 129 | 15 | 144 |
| Segmented neutrophils ≤75% | 52 | 15 | 67 |
| Total | 181 | 30 | 211 |

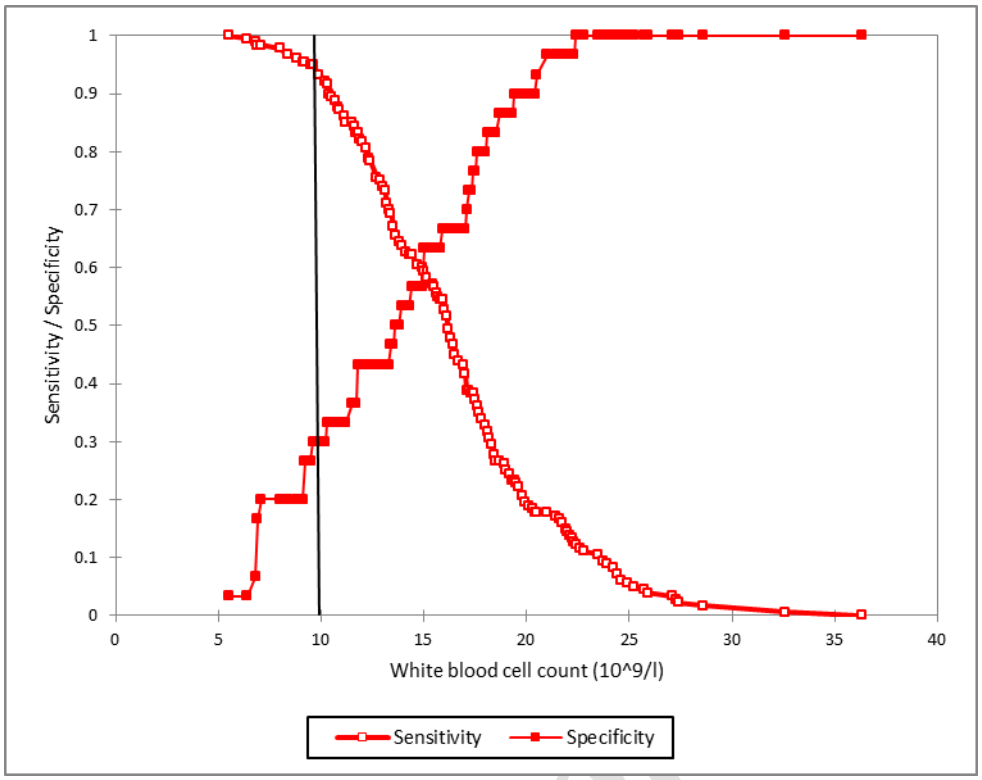


**Fig.3**: Sensitivity / Specificity for leukocytes.

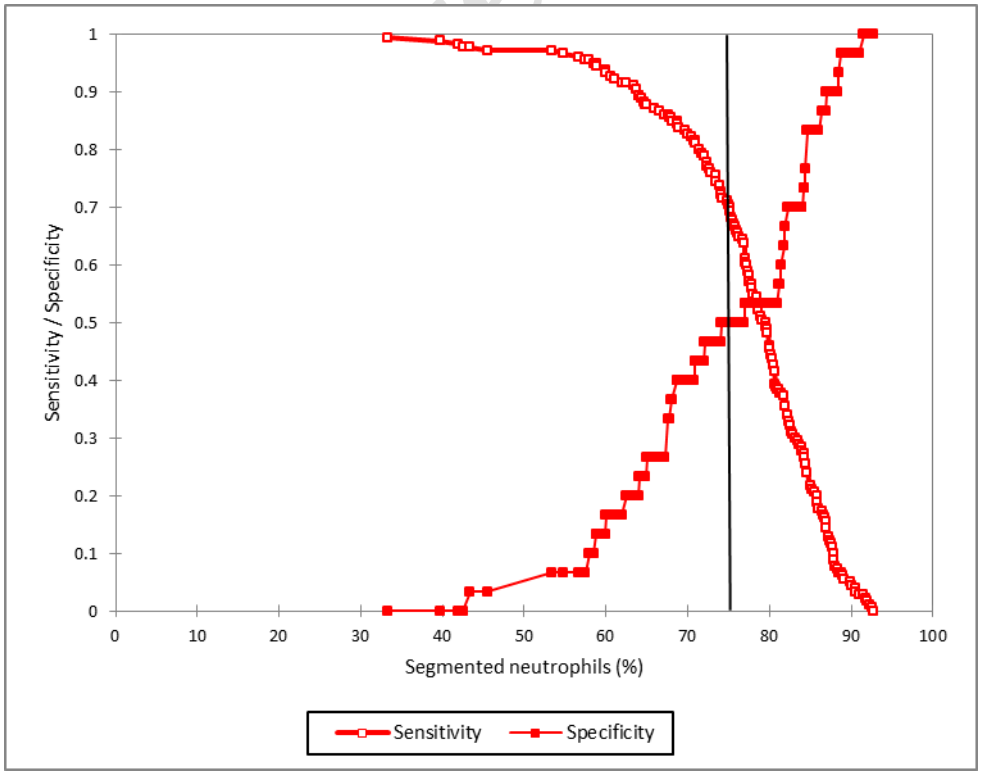


**Fig.4**: Sensitivity / Specificity for segmented neutrophils.

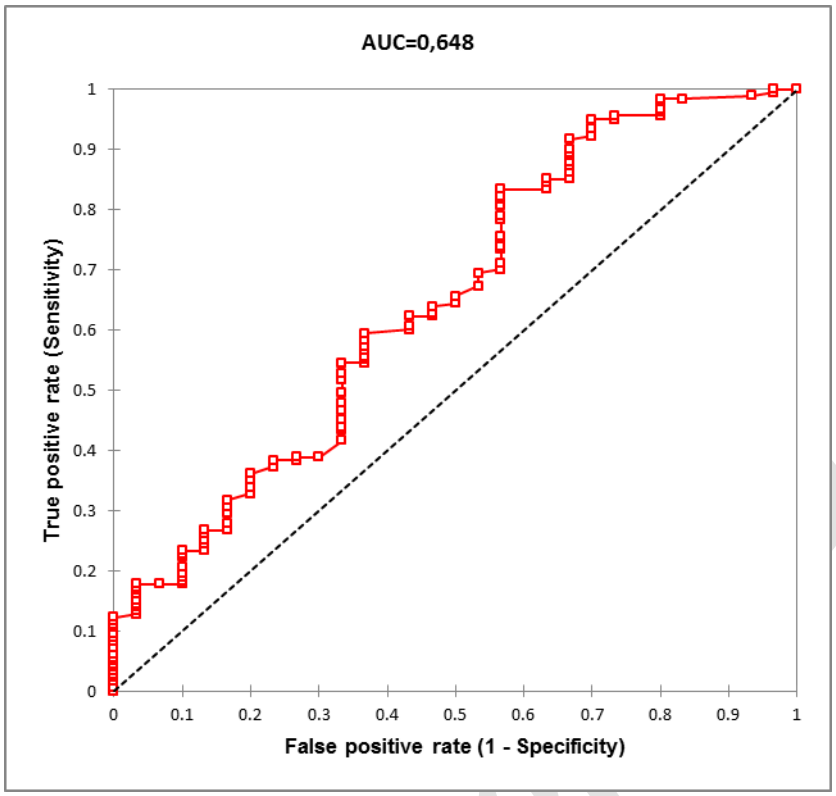


**Fig.5**: ROC curve for leukocytes.

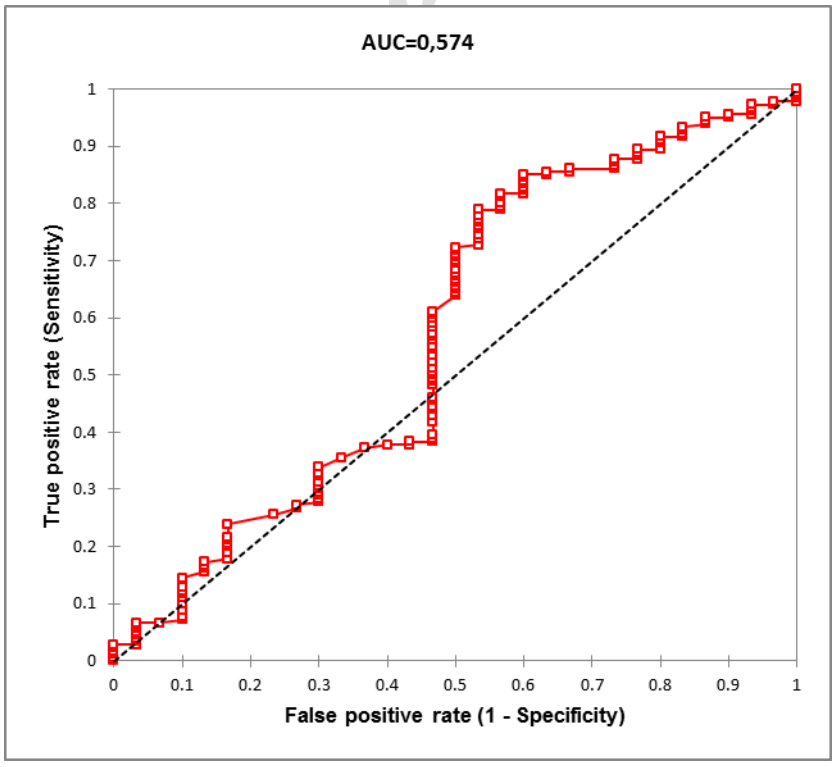


**Fig.6**: ROC curve for segmented neutrophils.

## 4- DISCUSSION

In our study we had a negative rate of appendectomy of 14.2% which is in accordance with the rates of negative appendectomy (NA) of 5% to 15% (4). The most recent reports quote NA rates below 5% (5, 6), which we should strive in the future. Bates et al. analyzed all NAs, to detect common characteristics that, in the future, might further decrease false-positive rate (7). Absence of an elevated white blood cell count (WBC) count is a risk factor for NA. Withholding appendectomy for WBC counts, 9,000 and 8,000 per mL reduces the NA rate to 0.6% and 1.2%. In our study, out of a total of 30 negative appendectomy, 9 patients (30%) had an orderly leukocyte count (≤10*109 /L), while 15 patients (50%) had a percentage of segmented neutrophils < 75%. Stefanutti et al. concluded that WBC count at admission has no proven additional value in the diagnosis of acute appendicitis and can be omitted without modifying diagnostic pathway and without affecting diagnostic accuracy (8).

The purpose of Mathews et al. study was to determine if Immature Granulocytes (IG)% would add additional discriminatory ability, in conjunction with traditionally utilized laboratory values, in differentiation of acute and perforated appendicitis in a pediatric population. In that study, they found that elevated C-reactive protein (CRP) and presence of a left shift were reliable predictors of perforated appendicitis. However, IG% did not add any additional benefit in making the diagnosis (9). In the Kulik et al. study, the pediatric Appendicitis Score (PAS) and Alvarado scores were the best validated but neither met the current performance benchmarks. A high quality well validated and consistently high-performing clinical prediction rules (CPR) was not identified. They concluded that further research is needed before a CPR for children with suspected appendicitis can be used in routine practice (10). According to Wang et al. study (11), elevated WBC counts had a sensitivity of 67% and a specificity of 80%. Using left shift alone as an indicator for appendicitis was associated with a sensitivity of 59% and a specificity of 90%. However, when a high WBC count and left shift were combined, the sensitivity climbed to 80%, and specificity remained at 79%. The sensitivity fell to 47% when both a high WBC count and left shift were analyzed, and specificity climbed to 94%. The positive likelihood ratio for a high WBC count and left shift was 9.8. Sensitivity of leukocytosis (93%) and shift to left (71%) in Gwynn study (12) was analogous to ours, while the specificity of leukocytosis was 38% and shift to left 68%. In the study Ko et al. (13) leukocytosis and shift-to-the-left were better predictors than CRP (the sensitivity and specificity are: leukocytosis (> 10,000/mm3): 85. 2%, 65%; leukocytosis with a shift-to-the-left (neutrophil > 75%): 81.5%, 70%; elevated CRP (> 0.9 mg/dl): 70.4%, 65%). In our study, we did not calculate sensitivity and specificity for CRP because it is only available in only 34 patients.

We did not find an article that would show whether there was a statistically significant correlation between the leukocyte count and the percentage of segmented neutrophils compared to the pathohistological finding in children. Tatar et al. (14) calculated the correlation between appendiceal diameter - WBC count and appendiceal diameter - Alvarado score. The correlation between appendiceal diameter and WBC count was 80% ($p = 0.01 < 0.05$). The correlation between appendiceal diameter and Alvarado score was 78.7% ($p = 0.01 < 0.05$). Sousa-Rodrigues et al. (15) evaluated the possible correlation between the scale of Alvarado (EA) and macroscopic appearance (MA) of the appendix in patients with acute

appendicitis. The Spearman correlation test used for EA and MA was + 0.77 (95% CI 0.65-0.85, p < 0.0001). Bhatti Hafeez et al. (16) wanted to determine the correlation of WBC counts, age and duration of symptoms with severity of acute appendicitis. They determined that WBC counts and duration of symptoms are not good predictors of severity of disease in appendicitis. In conclusion of the study Grönroos et al. (17) WBC remained the best laboratory method for diagnosing uncomplicated acute appendicitis and seemed to be a very early marker of appendiceal inflammation. They calculated Spearman rank-order correlation between WBC, CRP, and lipoprotein-associated phospholipase A2 (Lp-PLA2).

Grönroos in his study (18) concluded that, contrary to adult patients, normal leucocyte count and CRP value do not effectively exclude acute appendicitis in children. Gulzar et al. (19) said that clinical assessment is the best criteria to reach a confident diagnosis. Total leucocyte count and other investigations should be used as diagnostic aid in doubtful cases but they don't replace the clinical skills of surgeons. In their study total leucocyte count was less than 10,000/mm3 in 38.8% cases and more than 10,000/ mm3 in 61.2% cases. The sensitivity and specificity of raised TLC for acute appendicitis were 80% and 67%, respectively.

## 5- CONCLUSION

Although daily attempts to find better (more sensitive and more specific) tests in the diagnosis of acute appendicitis in children, leukocyte count and the percentage of segmented neutrophils within the Alvorado score continue to be the leading position with the highest sensitivity and specificity of all tests. Given the correlation results obtained, the clinical experience of physicians will still have one of the leading roles in diagnosing acute appendicitis in children.

## 6- CONFLICT OF INTEREST: None.

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