Received: 22 February 2021 | Revised: 17 May 2021 | Accepted: 28 May 2021

DOI: 10.1002/hsr2.326

Health Science Reports Open Access WILEY

RESEARCH ARTICLE

# A cross-sectional study on evaluation of complete blood count-associated parameters for the diagnosis of acute appendicitis

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## Abstract

**Background and aims:** Acute appendicitis is one of the common causes of abdominal surgeries, however, the rate of negative appendectomy is as high as 20% as the diagnosis of appendicitis is challenging. The study aimed to evaluate complete blood count (CBC)-associated parameters among positive and negative appendectomy patients and determine their diagnostic importance.

**Methods:** In this cross-sectional study, patients who suspected of acute appendicitis were included. Preoperative blood samples taken from these patients for a complete blood count. Following parameters evaluated from their CBC: white blood cell (WBC), platelet (PLT), mean platelet volume (MPV), neutrophils-to-lymphocytes ratio, platelets-to-lymphocytes ratio, red cell distribution width (RDW), and platelet distribution width (PDW). These parameters analyzed for the positive and negative appendectomy patients using statistical analysis.

**Results:** Of 200 patients included in the study, 30 patients (15%) underwent negative appendectomy. The mean neutrophils, WBC, red blood cells, neutrophils-to-lymphocytes, and platelets-to-lymphocytes ratio was significantly high among positive appendectomy patients, ($P < .05$), whereas MPV to platelet ratio was significantly less in this group. The highest diagnostic power for the diagnosis of appendicitis was of neutrophils-to-lymphocytes ratio with the sensitivity of 83.5% and the specificity of 90%.

**Conclusion:** The findings of our study indicate that neutrophils-to-lymphocytes ratio alone is not sufficient for preoperative diagnosis of acute appendicitis and other CBC-related parameters did not have good sensitivity and specificity. Further studies are therefore required in this area.

KEYWORDS
acute appendicitis, appendectomy, CBC, lymphocytes, neutrophils, parameters

## 1 | INTRODUCTION

Appendicitis is the most reported cause of abdominal surgery.[1] The lifetime known risk of appendicitis in the United States is 8.6% in men and 7.6% in women, with an annual rate of 38.9%.[2,3] In the United States, an estimated 326 000 appendectomies were performed in 2007.[4] In the UK, approximately 42 000 and 47 000 appendectomies were performed between 2007 and 2012.[5] Studies in the United Kingdom and the United States have shown that complicated appendicitis is reported in about 16.5% to 24.4% of appendectomies.[6]

Acute appendicitis is characterized by severe acute abdominal pain, globally.[7,8] Proximal occlusion of the lumen of the appendix leads to closed loop obstruction,[9] which is the continuation of natural secretion by the mucosa and leads acute appendicitis).[10] Although classic pain is common, patients may be presented with non-classical pain.[11] In general, the prevalence of perforated appendicitis is 8.25%.[12] Children under 5 y of age and patients over 65 y of age have the highest incidence of perforated appendicitis (45% and 51%, respectively).[13-15] In most cases, walling-off occurs.[4] If the body is unable to contain the infection, generalized peritonitis can also occur.[16] In the cases of perforated appendicitis, numerous possibly serious adverse events or complications may occur,[17] such as bacterial peritonitis, sepsis, small bowel obstruction, and abdominal abscess.[18] Advanced bacterial peritonitis, if untreated has a mortality rate of 80% to 100%.

Extensive and detailed researches are required to discover reliable diagnostic tools to rule out acute appendicitis.[19] A complete blood count (CBC), is a very common blood test performed in laboratories,[20] and is performed in emergency room surgeons as part of a preoperative evaluation to determine inflammatory lesions.[21] Increased white blood cell count (WBC) and neutrophil count are the first signs of inflammation in acute appendicitis[22]; nevertheless, the sensitivity and diagnostic value vary broadly, depending on the study population, the duration of symptoms, and laboratory results.[23] A number of other parameters are studied, to increase preoperative diagnostic precision of appendicitis such as neutrophils-to-lymphocytes ratio (NLR), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and red cell distribution width (RDW).[24] The set of laboratory tests recommended by some physicians for the early diagnosis of acute appendicitis in suspected patients is the measurement of platelet count, MPV, PDW, and RDW.[25,26] A set of platelet-related parameters is obtained as part of a complete blood count.[13] Interleukin-6, which is increased in inflammatory diseases, activates megakaryocytes in the bone marrow and promotes the release of young platelets in the blood, leading to increased MPV.[14] New evidence suggests that PLT in certain diseases can be used as diagnostic and prognostic markers.[27]

This study was designed to investigate the complete blood count-related parameters among positive and negative appendectomy patients and their diagnostic importance for the diagnosis of acute appendicitis.

## 2 | METHODS

This cross-sectional study included all patients with abdominal pain and RLQ tenderness suspected of appendicitis who referred to the emergency department of the Madani Hospital and underwent appendectomy during our study period June 2019 to December 2019. The exclusion criteria was: lack of access to tests and interpretation of sample pathology, disagreement to participate in the study, previous history of hematological diseases, history of the previous appendectomy and abdominal surgery, intestinal disease and infectious disease, pregnant women, cancer patients, inflammatory disease, abdominal trauma, surgery or invasive abdominal procedure in the last 7 d, use of corticosteroids in the last 14 d, receiving chemotherapy or immunosuppressive drugs in the last 29 d, patients with urinary tract infection or urinary tract pathology (WBC > 20 and RBC > 30 in urine analysis).

After entering the study, patients were examined for the diagnosis of acute appendicitis and complete blood cell count (CBC differential) was performed where mean platelet volume, platelet count, mean platelet volume to platelet count, neutrophils-to-lymphocytes ratio, red blood cell distribution width, platelet distribution width, and platelets-to-lymphocytes ratio was calculated. Patients with a high probability of appendicitis underwent appendectomy. The removed appendix was then sent for histopathological analysis. After fixing the samples in formalin buffer 10%, the tissue was cut lengthwise from the distal part and transversely from the middle and proximal parts as per the usual method. Tissue preparation steps were performed according to the routine method and the incisions were molded in paraffin. Then, three-micron sections were made on the samples by microtome device and hematoxylin-eosin staining was performed and diagnosis was established. The gold standard for the diagnosis of appendicitis was pathology results and the diagnostic value of the desired indicators (sensitivity, specificity, and predictive value) were evaluated in comparison with the pathology results. Negative appendectomy was defined as patients who underwent appendectomy where no appendicitis was seen.

The research data included information regarding age, sex, symptoms (RLQ tenderness), clinical examination, patient history, CBC, and pathology results that were filled in the questionnaire. All study participants signed a written consent for the participation in the study.

The sample size was estimated according to similar studies and considering the 95% confidence limit and error coefficient of 0.05 using the sample size determination formula of 200 people.

$\alpha = 5\%$, $S_n = 85\%$, $N = 196$, $d = 5\%$

$$n = \frac{\left(z_{1-\alpha_2}\right)^2 s_n(1-s_n)}{d^2}.$$

The data was evaluated by SPSSv17 software. Student T-test and ANOVA, Chi-square, Fisher and Mann-Whitney tests were used, when required and $P$ value less than 5% was considered significant. Results were presented as a mean and standard range. The ROC (receiver operator characteristic) curve was used to determine the diagnostic value, sensitivity, specificity, predictive

value, and area under the curve (accuracy) within the 95% confidence interval.

This research was accepted by the Research Ethics Board of Alborz University of Medical Sciences (IR.ABZUMS.REC.1399.082).

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## 3 | RESULTS

In this study, 200 patients underwent appendectomy, of which 30 (15%) had negative appendectomy. The mean age of the subjects was 27.59 ± 13.26 y. Of those included in the study, 142 (71%) were male and 58 (29%) were female. The mean age and the gender distribution of the patients with positive ($P = .411$) and negative appendectomy ($P = .436$) was not statistically different.

The mean WBC among patients with and without appendicitis was 13 554.1 ± 3396.74 and 7343.33 ± 1735.36 $10 \times 6/mm^3$. The difference was statistically significant among the two groups ($P < .001$). The mean neutrophils levels among the two groups were 11 038.6 ± 3432.05 and 4634.0 ± 1596.74 $10 \times 6/mm^3$, which was also significantly different ($P < .001$). The mean lymphocytes among the patients with positive and negative appendectomy was 1937.27 ± 1362.19 and 2332.9 ± 1079.97 $10 \times 6/mm^3$, which was also statistically significant, $P = .005$. Similarly, mean RBC, MPV to platelet ratio, neutrophils-to-lymphocytes ratio, and platelets-to-lymphocytes ratio was significantly different between the two groups ($P < .05$), Table 1. As the distribution of these variables was not normal, Mann-Whitney test was used for statistical analysis.

The area under the ROC curve of the mean platelet volume for the diagnosis of acute appendicitis was 0.391 and the best cut-off point for the mean platelet volume in the diagnosis of acute appendicitis is 8.75.

The area under the ROC curve for the diagnosis of acute appendicitis using platelet count was 0.597 and the best cut-off point for the platelet count in the diagnosis of acute appendicitis equal to 190 500 $10 \times 6/mm^3$.

The area below the ROC curve of the ratio of mean platelet volume to platelet count for the diagnosis of acute appendicitis was 0.372 and the best cut-off point of the ratio of mean platelet volume-to-platelet count for the diagnosis of acute appendicitis is 0.0417.

Similarly, the area under ROC curve of the neutrophils-to-lymphocytes was 0.902 with the cut-off 3.669. The area under the ROC curve of the RDW was 0.58, with the cut-off of 55.12 and that of PDW was 0.588 with the cut-off of 55.13. The area under the ROC for platelets-to-lymphocytes ratio was 0.717 with the cut-off of 128.43. The highest diagnostic power for the diagnosis of appendicitis was of neutrophils-to-lymphocytes ratio with the sensitivity of 83.5% and the specificity of 90% Other CBC-related findings did not have high diagnostic accuracy (Table 2).

**TABLE 1** Mean and SD of the variables in the studied patients based on the appendectomy

| Variables | Negative appendectomy | Acute appendicitis | *P*-value |
|---|---|---|---|
| WBC ($10^6/mm^3$) | 7343/33 (±1735/36) | 13 554/1 (±3396/74) | <.001 |
| Neutrophil ($10^6/mm^3$) | 4634 (±1596/74) | 11 038/6 (±3432/05) | <.001 |
| Lymphocyte ($10^6/mm^3$) | 2332/9 (±1079/97) | 1937/27 (±1362/19) | .005 |
| RBC ($10^6$/micl) | 4/75 (±0/47) | 5/04 (±0/972) | .035 |
| Platelets ($10^6/mm^3$) | 218 300 (±49 362/2) | 241 341/17 (±61 936/79) | .091 |
| MPV | 9/93 (±0/844) | 9/62 (±0/950) | .056 |
| PDW | 12/11 (±1/414) | 11/78 (±1/946) | .1 |
| RDW(fl) | 12/56 (±0/904) | 12/80 (±0/953) | .123 |
| Platelets/MPV | 0/05 (±0/053) | 0/04 (±0/018) | .025 |
| Neutrophil/lymphocyte | 2/61 (±2/133) | 7/9 (±4/811) | <.001 |
| Platelets/lymphocyte | 119/32 (±108/740) | 157/29 (±77/081) | <.001 |

**TABLE 2** Sensitivity and specificity, positive and negative predictive value of the studied variables in the diagnosis of acute appendicitis

| Variables | TP | FP | TN | FN | Sensitivity | Specificity | PPV | PNV | PP | PN | Accuracy | Contingence | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MPV | 137 | 26 | 4 | 33 | 80.5 | 13 | 84 | 10.8 | 0.925 | 1.8 | 70.5 | κ | *P* |
| Platelets | 134 | 18 | 12 | 36 | 78.8 | 40 | 86.4 | 25 | 1.31 | 0.53 | 73 | 0.05 | .429 |
| MPV/platelets | 92 | 18 | 12 | 78 | 54.11 | 40 | 83.6 | 13 | 0.901 | 1.14 | 52 | 0.151 | .026 |
| Neutrophil/lymphocyte | 142 | 3 | 27 | 28 | 83.5 | 90 | 97.9 | 49 | 8.35 | 0.183 | 84.5 | 0.032 | .55 |
| RDW | 95 | 11 | 19 | 75 | 55.8 | 63 | 89.6 | 20.2 | 1.5 | 0.7 | 57 | 0.102 | >.001 |
| PDW | 33 | 5 | 25 | 137 | 19.4 | 83 | 86.8 | 15.4 | 1.14 | 0.971 | 29 | 0.01 | .052 |
| Platelets/lymphocyte | 99 | 5 | 25 | 71 | 58.2 | 83 | 95.1 | 26 | 3.42 | 0.5 | 62 | 0.218 | .724 |

Abbreviations: FN, false negative; FP, false positive; PN, probability negative; PNV, predictive value negative; PP, probability positive; PPV, predictive value positive; TN, true negative; TP, true positive.

## 4 | DISCUSSION

This study was performed on 206 healthy individuals and 226 patients with an initial diagnosis acute appendicitis. In patients with acute appendicitis, a significant decrease in MPV was observed compared to healthy controls. The MPV cut-off point for appendicitis was reported to be 7.6 fl, which had 73%, 84%, 84%, and 74% with sensitivity, specificity, positive predictive value, and negative predictive value, respectively. As MPV is evaluated from CBC, it increases the sensitivity and negative predictive value of WBCs for diagnosing appendicitis. The study concluded that MPV could be time and cost-effective parameter to predict initial diagnosis of appendicitis. However, in our study, it was found that the diagnostic power of MPV is low with the cut-off point of 8.75 fl, and its specificity and predictive value is very low, 13% and 10.8%, respectively.

In 2010, Yavuz et al examined the mean platelet volume as a new factor in the diagnosis of acute appendicitis.[28] In 2017, Gu et al investigated the diagnostic value of platelet markers for diagnosing acute appendicitis and compared it with histopathological findings among 165 patients.[29] Based on histopathology, patients were divided in the groups of perforated appendicitis, acute appendicitis without perforation, and negative appendectomy. Characterization, sensitivity, positive predictive value, and negative predictive value of laboratory parameters were evaluated. The findings showed that the rate of negative appendectomy in 165 patients was 15.1%. The number of leukocytes in acute appendicitis ($14.9 \times 10^3/\mu L$) was higher than the negative appendectomy group ($6.9 \times 10^3/\mu L$). The two groups were significantly different in terms of platelet count. The sensitivity, specificity, PPV, and NPV of leukocyte count were 95.9%, 24%, 99.1%, and 92.7%, respectively. WBC and platelet count were reported to be positively correlated. As a result of increased leukocyte count and platelets, the diagnosis of acute appendicitis was seen to be associated with histopathological results. Thus, inflammatory markers, positive clinical findings, and imaging together improve the diagnostic accuracy in acute appendicitis.

In our study, it was also found that leukocytes levels had significantly higher diagnostic accuracy than other laboratory findings, although the agreement reached was moderate, which requires the study of leukocytes along with other clinical findings and imaging.

In 2018, Bosh et al evaluated white blood cells, neutrophil count, lymphocyte count, NLR, platelets, MPV, PDW, RDW, and C-reactive protein (CRP) among appendicitis patients.[30] The results showed that 125 (62.5%) patients had acute uncomplicated acute appendicitis, 20 (10%) had acute complicated appendicitis, while 55 (27.5%) had normal appendicitis. The difference in MPV levels between the groups was negligible. RDW levels were higher in other groups as compared to acute uncomplicated appendicitis ($P = .006$). However, there was no significant difference between positive and negative appendectomy groups. The study concluded that increased PDW combined with elevated WBC and neutrophil count may can be useful for the diagnosis of acute appendicitis, whereas MPV and RDW levels alone are not useful diagnostic markers. The findings of our study also do not support MPV and RDW alone as diagnostic markers; concluding that leukocytes could increase diagnostic accuracy.

In a study conducted by Kahramanca et al, the diagnostic value of platelet to lymphocyte ratio for acute appendicitis in 569 patients who underwent appendectomy was studied.[31] During this study, 475 had a positive appendectomy and 94 had negative appendectomy. The cut-off value of platelets-to-lymphocytes ratio in this study was 136.5. This ratio was higher among positive appendectomy patients and the study concluded that platelets-to-lymphocytes ratio is a reliable parameter for the diagnosis of acute appendicitis.[19] In our study, it was found that the ratio of platelets-to-lymphocytes is high in patients with acute appendicitis, but its diagnostic power is not high. A study by Yildirin et al determined platelets-to-lymphocytes and leukocytosis to differentiate between complicated and uncomplicated appendicitis.[32] Platelets-to-lymphocytes cut-off was reported to be 169.7. There was a significant difference between leukocytosis and PLR between the two groups. Platelets-to-lymphocytes had a sensitivity of 74% and specificity of 73.5% and it was concluded that it can be a prognostic marker for the severity of appendicitis with higher sensitivity and specificity. In our study, PLR did not have high diagnostic power in identifying acute appendicitis, however, comparison was based on positive and negative appendectomy patients in our study.

In a study by Alexander et al. in Nigeria, NLR, platelets-to-lymphocytes ratio, and mean platelet volume (MPV) were used as diagnostic markers.[33] The cut-off value was 0.2 for neutrophils-to-lymphocytes ratio, 137 for platelets-to-lymphocytes ratio, and 10.6 for MPV. The following results were obtained during the studies: NLR and platelets-to-lymphocytes ratio of elderly people (51-85 y) were lower than younger people (18-50 y), also PLR was higher in men than women, while MPV and NLR were not affected by gender. The study found that the diagnostic power of platelets-to-lymphocytes and MPV is not high for the diagnosis of acute appendicitis.[21] Despite that MPV and platelets-to-lymphocytes are inflammatory markers, studies have not confirmed its role in the diagnosis of appendicitis.[34] The findings of this study are completely consistent with our results. In our study, it was found that the diagnostic power of platelets-to-lymphocytes and MPV in the diagnosis of acute appendicitis is not high, although our study did not encompass gender and age-based analysis. Furthermore, a comparison of these parameters with baseline values can help us understand the low diagnostic power of MPV. Prescreening patients for underlying inflammatory conditions can also provide better understanding.

A study by RoozRokh et al evaluated the value of CRP, ESR, leukocytosis, and the ratio of neutrophils to peripheral blood lymphocytes for the diagnosis of acute appendicitis in children under 14 y of age. They reported that white blood cell count was more sensitive and in the ROC curve analysis, the highest area under the curve was that of WBC count.[35] In the combination of two diagnostic tests, CRP and WBC count, the sensitivity was 96.1%, and sensitivity for all four diagnostic parameters was 99.1%. In this study, paraclinical tests such as CRP, ESR, WBC count, and NLR did not have reliable efficacy in diagnosing acute appendicitis, although the combined use of these

tests and the normality of the results can increase the suspicion of acute appendicitis. The findings of this study are quite similar to our study. In our study, it was found that NLR in patients with acute appendicitis is high and has high sensitivity and specificity, but the agreement with the pathology results is moderate, which is due to the reduction of negative predictive value, therefore, NLR alone does not have sufficient diagnostic power.

## 5 | CONCLUSION

Findings of our study showed that 15% of patients undergoing appendectomy had a negative pathology. Therefore, it can be concluded that none of the CBC findings alone should be diagnostic criteria for acute appendicitis. However, future studies regarding combinational accuracy of these parameters along with other clinical, paraclinical, and imaging studies are recommended to reduce the burden of negative appendectomy.

### CONFLICT OF INTEREST

The authors deny any conflict of interests.

### FUNDING

This research did not receive any kind of funding.

### TRANSPARENCY STATEMENT

Leila Haji Maghsoudi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

### AUTHORS' CONTRIBUTION

Conceptualization: Mojtaba Ahmadinejad.
Data Curation: Mojtaba Ahmadinejad.
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Methodology: Arghavan Khas Ahmadi
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Supervision: Leila Haji Maghsoudi
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Writing – Review and Editing: Haleh Pak.

All authors have read and approved the final version of the manuscript.

Mojtaba Ahmadinejad had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

### ETHICAL STATEMENT

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### CONSENT TO PARTICIPATE

Written consent was signed for all the patients of aged 18 y or above. For patients under 18, a legal guardian or parent signed the consent form.

### CONSENT FOR PUBLICATION

Not applicable.

### DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

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**How to cite this article:** Maghsoudi LH, Kabir K, Soltanian A, Pak H, Ahmadinejad M, Ahmadi AK. A cross-sectional study on evaluation of complete blood count-associated parameters for the diagnosis of acute appendicitis. *Health Sci Rep*. 2021;4:e326. https://doi.org/10.1002/hsr2.326