



Comparison of Diagnostic Value of ESR, CRP and Leukocytosis with Pathological Findings among Patients with Acute Appendicitis

Sakineh Abedi¹, Mehdi Ebrahimi², Pounch Zolfaghari¹, Javad Nourian³, Mryam Yarmohammadi⁴, Elahe Yahyaei⁵, Mohammad Bagher Sohrabi^{1*}

¹ General Practitioner, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.

² Dept. of Surgery, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.

³ Dept. of Anesthesiology, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.

⁴ Dept. of Pathology, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.

⁵ Dept. of Management, Shahroud University of Medical Sciences, Shahroud, Iran.

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Abstract

Background: Acute appendicitis is a serious condition that is occasionally falsely diagnosed. The correct diagnosis of this condition helps reduce unnecessary surgeries or complications due to the lack of diagnosis. Laboratory tests are used to diagnose this condition. The present study was conducted to compare the diagnostic value of the ESR, the CRP level and leukocytosis with pathological findings in patients with acute appendicitis.

Methods: This descriptive study examined 125 cases with a primary diagnosis of appendicitis from August 2015 to October 2016 at Imam Hossein Hospital in Shahroud, Iran. The patients' blood samples were collected for ESR, CRP and leukocyte testing and were then sent to the laboratory. After the appendectomies, samples of their appendices were sent to the pathology laboratory for further examination. The blood test results were compared with the pathological findings and analyzed in terms of sensitivity, specificity and positive and negative predictive values.

Results: In this study, 59.2% of the cases were male and the rest were female. Acute appendicitis and other pathological appendices were confirmed in 91 patients (72.8%) based on their pathological evaluation and 34 cases (27.2%) were reported as normal. The sensitivity and specificity were obtained as 57.1% and 79.4% for ESR. These indices were 78.0% and 83.5% for CRP and 74.4% and 50% for leukocytosis.

Conclusions: The results of this study showed that, in addition to basic laboratory findings, ESR, CRP and leukocytosis testing can also be helpful in the correct diagnosis of acute appendicitis; however, the predictive value of CRP was the highest.

Keywords: Appendicitis, Sensitivity, Specificity, ESR, CRP, Leukocytosis.

*Corresponding to: MB Sohrabi, Email: mb.sohrabi@yahoo.com

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Introduction

The appendix is an immunological organ of the body that is capable of secreting immunoglobulin. Appendicitis occurs when the appendix is inflamed. The main cause of acute appendicitis is duct obstruction, which occurs either due to self-discharge or due to the feces blocked inside the duct and causing dilation and inflammation of the appendix.¹

Acute appendicitis is one of the most common surgical emergencies that is primarily diagnosed based on the patient's history and physical examination. The annual incidence of

appendicitis is reported as 11 per 10,000 people in the US. This problem is often more common in men (1.4 vs. 1.0) and over 40.0% of the cases occur in patients aged 10-29 years.¹⁻² In 55.0% of the cases, the diagnosis of this condition is made based on classic signs and symptoms such as abdominal pain, anorexia, nausea or vomiting, tenderness in the right iliac fossa, rebound tenderness and fever.³ Diet plays a critical role in the incidence of this disease.¹ Inflammatory parameters (i.e. CRP, leukocyte and lymphocytes) prevent half of the unnecessary cases of surgery and help reduce negative appendectomy to 15.2% and appendix rupture to 11.7%. Although laboratory tests and data are helpful in the diagnosis of acute appendicitis, no single test is conclusive.⁴⁻⁵ Leukocyte testing is the most useful tool that shows a slight increase in non-perforated appendicitis.⁶⁻⁷ The WBC count can sometimes be normal, but an elevated WBC count (over 15,000) helps confirm appendicitis.⁸ In most studies, CRP measurement has been effective in confirming appendicitis.⁹ Some studies have also reported an increase in the ESR.¹⁰ The present study measured the ESR and the CRP level to show their association with the pathology of appendicitis and thus opens the way for further research. These two criteria have been investigated in several studies in order to observe new cases of appendicitis.⁹⁻¹⁰ The most reliable diagnostic system (i.e. the Alvarado score) consists of clinical symptoms, signs and laboratory findings.¹⁻³ The Ohmann score and the Eskelinen score have also been proposed for specific groups, even though they have a small role in the diagnosis of this disease in today's world due to the advances in imaging techniques.¹¹ CT scan has also been a valuable differential diagnostic method, as it can rule out conditions such as intestinal malrotation.¹² In the western world, these methods are taken seriously in order to reduce negative appendectomies due to the decreased use of imaging tools.¹³ The value of MRI has been confirmed in the diagnosis of some diseases.¹²⁻¹³ Laparoscopy has also been effective in the diagnosis of lower abdominal pain in pregnant women.¹⁴ Nonetheless, the use of these methods is not available to all patients and physicians at all times and can also be very costly for the patients. Due to the lack of information on the sensitivity and specificity of each of these tests (ESR, CRP and leukocytosis) in detecting appendicitis, the present study was conducted to compare the diagnostic value of ESR, CRP and leukocytosis with pathological findings in patients with acute appendicitis.

Materials and Methods

This study was carried out with a descriptive analytical design to determine the value of C-reactive protein (CRP) levels, the Erythrocyte Sedimentation Rate (ESR) and leukocyte testing in the diagnosis and rejection of acute appendicitis. The study was conducted on a statistical population consisting of 125 patients presenting with acute abdominal symptoms such as abdominal pain in the lower right quadrant, nausea, anorexia and vomiting to the emergency department of Imam Hossein Hospital in Shahrud from August 2015 to October 2016 and suspected of appendicitis. The researchers observed the ethical requirements of research in this study and obtained oral consent from the patients. Those who met the inclusion criteria were approached by the authors and briefed on the study. The patients were then ensured of the confidentiality of the data and their right to withdraw from the study at any time and also of their facing no consequences in terms of the quality of care they received if they decided to withdraw after they had given their consent.

The final diagnosis was based on clinical symptoms and, if necessary, with the help of ultrasound evidence. Due to the large number of patients available, the sample was selected based on whether final pathological reports were available. The patients with a history of chronic diseases such as tuberculosis and rheumatoid arthritis or patients with a history of acute diseases such as the flu and common cold were excluded from the study. A sample of peripheral blood was collected from each patient at the time of admission and before discharge from the hospital. Blood samples were stored in citrate-treated and non-citrate tubes to count the WBC and measure the ESR and CRP level and were then transferred to the hospital laboratory. Appendectomy was normally performed in all the patients as an emergency procedure to remove the appendix. The positive and negative predictive values of all the laboratory findings/tests, including the WBC count and the ESR and CRP tests, were determined and analyzed. After the appendectomy, each patient's appendix was sent to the hospital laboratory for pathological examination.

Table 1 presents the normal values of WBC, ESR and CRP for different age groups. The patients' age is considered when determining the sensitivity and specificity of each of these tests.¹⁵ The pathology findings were then compared with the findings obtained from basic blood tests, such as the ESR and CRP tests and the WBC count. Pathology was considered the gold standard in the diagnosis of appendicitis.⁸ The patients' para-clinical findings (ESR, CRP level and WBC count) and pathological report and demographic data were also recorded. After completing the questionnaires, the data were analyzed in SPSS-16. The relationship between the data and the credit indices was calculated and evaluated using the Chi-square test and the t-test. The level of statistical significance was set at $P < 0.05$.

Table1. The normal ranges of WBC, ESR and CRP at different ages

Age	WBC Count	ESR	CRP Level
<3 years	5.5-15×10 ³	0-35 mm/h	1.2-1.5 mg/l
3-12 years	5-13.5×10 ³	0-30 mm/h	1-1.2 mg/l
13-60 years	4.5-11×10 ³	0-20 mm/h	0.8-1 mg/l
>60 years	4-10×10 ³	0-25 mm/h	0.8-1 mg/l

Results

A total of 125 patients with a primary diagnosis of appendicitis after appendectomy were investigated in this study. A total of 74 patients (59.2%) were male and 51 (40.8%) were female. Their average age was 24.85±13.52 years (range: 1-69 years). In the pathological study of the suspicious cases of appendicitis, 91 cases (72.8%) had pathological appendices and 34 cases (27.2%) had normal appendices. Table 2 presents the distribution of the pathological types of appendix.

Table 2. The distribution of the pathological types of appendicitis

Type of Appendicitis	Number	Percentage
Appendicitis	66	52.8
Perforated appendicitis	13	10.4
Phlegmon	3	2.4
Gangrene	9	7.2
Normal appendix	34	27.2
Total	125	100

In the laboratory study of the suspicious cases of appendicitis in terms of the ESR, 79 cases (63.2%) had positive (high) ESRs and 46 (36.8%) had normal ESRs. For the CRP level, 83 cases (66.4%) had positive CRPs and 41 (33.6%) had normal CRPs. As for the WBC count (leukocytosis), 66 cases (52.8%) had leukocytosis and 59 (47.2%) had normal WBC counts.

The sensitivity and specificity were 57.1% and 79.4% for the ESR. These indices were 78% and 83.5% for CRP and 74.4% and 50% for leukocytosis. Table 3 shows the distribution of sensitivity, specificity and positive and negative predictive values for the ESR, the CRP level and leukocytosis.

Table 3. The sensitivity, specificity and positive and negative predictive values of the ESR, the CRP level and leukocytosis in comparison with the pathological reports

Lab Test	Sensitivity ¹ (%)	Specificity ² (%)	PPV ³ (%)	NPV ⁴ (%)
ESR	57.1	79.4	88.1	40.9
CRP level	78.0	83.5	88.8	55.6
Leukocytosis	74.4	50	80.1	42.5

¹Sensitivity is the probability that a test (of ESR, CRP and leukocytosis) will come out as abnormal among cases with a diagnosis of appendicitis according to the pathological report.

²Specificity is the probability that a test (of ESR, CRP and leukocytosis) will come out as normal among cases with a diagnosis of normal appendix according to the pathological report.

³ Positive Predictive Value occurs in patients with abnormal test results who have pathological appendicitis / (patients with abnormal test results) × 100

⁴ Negative Predictive Value occurs in patients with normal test results who do not have pathological appendicitis / (patients with normal test results) × 100

Discussion

The results showed a sensitivity and specificity of 57.1% and 79.4% for the ESR, 78% and 83.5% for the CRP level and 74.4% and 50% for leukocytosis. Often, 7% of the population experiences acute appendicitis at one point in their life.¹⁶ Acute appendicitis is a condition requiring surgery that has a high prevalence in communities.¹ It is the most common cause of acute abdominal pain that requires appendectomy. There is, however, some controversy surrounding the management of acute appendicitis in critical cases.¹⁷⁻¹⁸

To increase the accuracy of appendicitis diagnoses, surgeons largely depend on the patients' medical history and detailed physical examination. The accuracy of these procedures increases if laboratory tests are also used. At times,

auxiliary diagnostic methods may be applied as well.¹⁹ To decrease the rate of negative appendectomy, surgeons require a rapid and highly-accurate detection of appendicitis.²⁰ Similar to in other studies, the percentage of negative appendectomy cases was 27.2% in the present study. These findings are inconsistent with the results of a study conducted on 266 patients, which showed 107 cases with acute appendicitis and 159 cases without any pathological findings.²¹ In the present study, the sensitivity and specificity were 57.1 and 79.4% for the ESR and 78.0% and 83.5% for the CRP level. These findings appear to be similar to the results of other studies in Iran.²²⁻²³ Researchers recommend using additional diagnostic tests to further reduce the false-negative appendectomy rate and false-positive errors in appendicitis evaluation, particularly in high-risk age groups (children, young women and older adults). These methods include taking the patient's medical history, physical examination, laboratory tests and diagnostic clinical and imaging procedures.²⁴ A combination of these procedures can certainly help surgeons make appropriate choices.²³ Some researchers have shown that, in patients with suspicious clinical examinations, a combination of two or more markers of inflammation help surgeons make better decisions.²⁵ The methods and procedures that complement diagnostic tools include CT scan, ultrasound, barium enema and laparoscopy.¹²⁻¹⁴ These methods may not all be available in every hospital and for every patient and may even have some side-effects or complications. Some of them are invasive, others are not economically feasible and some are too time-consuming.²⁶ Of the radiographic methods available, the most cost-effective one for pediatric purposes is abdominal ultrasound and CT scan following a normal ultrasound.¹²⁻¹³ In contrast, some researchers are questioning the value of clinical measures in the diagnosis of acute appendicitis. This group argues that the results of laboratory examinations are interpreted differently in different groups of patients.²⁷ Some studies have shown that, even with the best combination of standard diagnostic tests, the results obtained to reach an early diagnosis of appendicitis are different from the results of the pathological tests performed following surgery.²⁸

The diagnostic value of leukocytosis has been investigated in several studies to confirm suspected cases of acute appendicitis and this test has been proven useful for many surgeons.^{10, 29-30} The serial investigation of leukocytosis has also been proven valuable. Leukocytosis is an important component for measuring the Alvarado score and its worth has previously been demonstrated.¹⁶ Leukocytosis was found to have a high diagnostic value for acute appendicitis in this study. Many studies have shown that this criterion is helpful in the diagnosis of appendicitis, although it is not a dedicated criterion.¹⁰ Research shows that when leukocytosis and the percentage of blood neutrophils are estimated together, they can be beneficial in the diagnosis of acute appendicitis.²⁶

Other markers of inflammation have recently been investigated and the ESR and IL-6 levels have been proposed in addition to the CRP level. A study carried out in Germany on 211 children also confirmed the benefits of assessing CRP and IL-6 levels in the diagnosis of acute appendicitis.³¹

The present study investigated the value of these markers and the leukocytosis percentage in patients presenting with

signs of appendicitis, which is a step similar to that taken in previous studies.²⁵⁻²⁶

CRP synthesis in human hepatocytes is part of the total answer that leads to fever, largely because it is part of the immunologic activity.⁹ Many researchers have used CRP testing for detecting the intensity of the disease and the quality of the treatment. A meta-analysis showed that CRP testing has a moderate sensitivity in the diagnosis of appendicitis. An increased CRP level and WBC count in suspected cases of acute appendicitis offers valuable information for surgeons.³¹⁻³³ In patients with acute abdominal pain, positive CRP levels demonstrate the need for emergency surgery while negative CRP levels could be a sign of the absence of acute appendicitis in suspected cases.²²⁻²⁴ The evaluation of the ESR in the diagnosis of acute appendicitis is very time-consuming and does not have a high value.⁹⁻¹⁰ The sensitivity and specificity of the ESR have been reported differently in different studies, ranging from 59.4% to 76.0% and 25.0% to 73.6%.^{2,9,12}

Recent findings on the role of the CRP level and WBC count in acute appendicitis show that a normal range of CRP along with a normal WBC count decrease the possibility of acute appendicitis, and these patients can be discharged without further examinations for appendicitis.³⁴⁻³⁶ Some studies have even shown that the value of CRP testing is higher than the value of leukocytosis in the diagnosis of acute appendicitis. Due to its high sensitivity, CRP testing can help confirm clinical diagnoses of appendicitis and can help decrease unnecessary negative appendectomies.²⁹⁻³²

The diagnostic accuracy of CRP testing has been reported as 75.0% in one study, and the false-positive rate of CRP testing was calculated as 24.7% in another study.¹⁷⁻¹⁸ In the study conducted in Germany, CRP testing was not effective in the diagnosis of acute appendicitis despite its capacity to show signs of advanced appendicitis or appendix rupture.¹⁹

In the present study, the level of CRP increased in the patients confirmed to have acute appendicitis. CRP testing is recommended in suspected cases of acute appendicitis.³¹ Nowadays, time-consuming and costly diagnostic procedures are becoming less common for the diagnosis of appendicitis, and patients and health care providers both prefer to use technologies with lower costs and side-effects. Further research is needed to explore whether the results of this study make a strong contribution to the diagnosis of acute appendicitis.

The limitations of this study include the small sample size and the lack of time for lengthier follow-ups and the failure to repeat the tests in later days, which could have changed the results altogether.

Given the results obtained from the ESR, CRP testing and leukocytosis, the use of CRP testing and leukocytosis is more helpful in the diagnosis of appendicitis in suspected cases and can be used in conjunction with the clinical diagnosis made by the surgeon. The use of the CRP test for the accurate diagnosis of acute appendicitis can help resolve the problem of unnecessary surgeries, and if a diagnosis of appendicitis is suspected, a positive CRP test can make it more definitive and a negative test can decrease its likelihood significantly.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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