

Diagnostic Value of Leukocytosis, ESR and CRP in Patients with Suspected Acute Appendicitis

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Article information	Abstract
<p>Article history: Received: 28 Apr 2012 Accepted: 2 Mar 2013 Available online: 20 May 2013 ZJRMS 2013; 15(7): 59-63</p> <p>Keywords: Acute appendicitis Leukocytosis ESR CPR</p> <p>*Corresponding author at: Department of Surgery, Zahedan University of Medical Sciences, Zahedan, Iran. E-mail: drdahmardeezaums@yahoo.com</p>	<p>Background: This study aimed to determine the value of the ESR, CRP and Leukocyte count in the diagnosis of acute appendicitis.</p> <p>Materials and Methods: This is a retrospective (descriptive-analytic) study which was conducted from August 2007 until October 2008 in Zahedan. A sample of 426 available patients with suspected acute appendicitis –who had been admitted to Ali-ebne- Abitalib and Khatam-al-Anbia hospitals– were recruited to participate in this study. Patients' demographic data, their blood samples for ESR, CPR and Leukocyte count were collected and sent to the laboratory for analysis. SPSS-16 was used to analyze data.</p> <p>Results: A number of 426 patients were investigated. Nearly 59.9% were male and 81% of the patients had leukocytosis. 214 cases of inflamed papillae (50.4%), 102 cases of exudation (23.9%), 36 cases of gangrene (8.5%) and 25 cases of perforated appendicitis were observed during the operations. Seven cases had abscess or flegmon. Pathological reports of 84 patients (19.7) showed normal appendices. Sensitivity and specificity value of ESR and CRP tests were (71.9 & 39.0%) and (85.0% & 57.0%) respectively. Positive and negative predictive value (PPV and NPV) of both tests were 83, 25, 89, and 48% respectively. ESR and CRP and leukocytosis had significant statistical correlation with phonological results.</p> <p>Conclusion: The results of this study showed that in addition to physical examination, some basic laboratory findings such as ESR, CPR and leukocytosis can be helpful. Among these, the value of CPR in the diagnosis of acute appendicitis is higher.</p> <p>Copyright © 2013 Zahedan University of Medical Sciences. All rights reserved.</p>

Introduction

Acute appendicitis is one of the most common surgical emergencies which is primarily diagnosed based on the patient's history and physical exam. It is reported that the annual incidence rate of appendicitis is 11 cases in 10000 people in America. Often, this problem is more common in males (1.4 vs. 1.0) and that over 40.0% of cases occur in patients with 10-29 years old [1]. In 55.0% of cases, the diagnosis is based on the classic signs and symptoms [2]. Diet plays a critical role in the occurrence of the disease [3].

Inflammatory parameters (i.e. CPR, leukocyte, and lymphocyte) prevent half of the unnecessary surgeries; and would result in the reduction of 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]. Often if ESR, WBC are CRP are in a normal range before the operation, the diagnosis of appendicitis is unlikely and the surgeon should consider other diagnostic methods [6]. Leukocyte count is the most useful test and in non-perforated appendicitis has a slight increase [7]. Sometimes WBC count can be normal but an elevated WBC count (over 18000) helps confirm appendicitis [8].

The measurement of CRP in most studies has been effective in the approval of appendicitis [9]. Unusual cases such as increase in serotonin level have also been reported [10]. In the present study, ESR and CRP were measured to show their association with pathology of appendicitis which opens the way for a broad range of researches. These two criteria have been investigated in several studies in order to observe new cases of appendicitis [8] and in this study the same criteria were used and confirmed.

The most reliable diagnostic system (Alvarado) consists of signs, clinical symptoms and laboratory findings [5]. Ohmann and Eskelinen system scores have also been proposed for specific groups [11] even though nowadays they have a small role in the diagnosis of the disease due to the new advancements of imaging studies. CT scan has been a valuable diagnostic method in the refuse of some differential diagnoses such as intestinal malrotation [12]. In west, these methods are considered for the reduction of negative appendectomy because of decreasing the use of imaging tools [13]. The value of MRI in diagnosis of some diseases has been confirmed [14]. Laparoscopy has also been effective in the diagnosis of lower abdominal pain amongst pregnant ladies [15].

Materials and Methods

A descriptive-analytic design was used to determine the value of the reactive protein (ESR & CRP) and leukocyte count in the diagnosis and rejection of acute appendicitis. A total of 445 patients who were admitted to emergency departments of Ali-ebne-Abitalib and Khatam-al-Anbia hospitals in Zahedan were selected to participate in the study for a period of one year from August 2007 until October 2008. Due to the high number of available patients, the sample was selected based on the convenience sampling method. Patients with a history of chronic disease such as tuberculosis and rheumatoid arthritis or patients with a history of acute disease like flu and common cold were excluded from the study since these diseases would change the volume of blood cells. According 17 patients were excluded and a total of 426 patients with diagnosis of suspected acute appendicitis were chosen for investigation.

A sample of peripheral blood was collected from each patient at the time of admission and while discharging. Blood samples were stored within citrate-treated and non-citrate tubes to count WBC and to measure ESR and CRP and were then transferred to emergency department laboratory. Appendectomy was normally performed in all the patients as an emergency procedure to remove appendix when appendicitis was strongly suspected. The positive and negative predictive value of all laboratory findings/tests including WBC, ESR and CRP were determined and analyzed. After the surgery, all pathologic samples were sent to the pathology laboratory for more analysis. Pathology findings were then compared with the findings from basic blood tests of ESR, CRP and WBC count.

Patients' paraclinical findings (ESR, CRP and WBC count) and pathology and demographic data were lastly recorded. Collected data were imported into SPSS-16 data analysis tool to investigate the study objectives. χ^2 test was used to show the relationship between leukocytosis, increased CRP and ESR and acute appendicitis. All data were kept confidential and for privacy of patients, they were identified by codes/passwords.

Results

A number of 426 patients were investigated. Of whom, 255 patients (59.9%) were male and 171 (40.1%) were female. Over 76.0% of all patients were aged 30 years old or less. Nearly 81.0% of the patients had leukocytosis. Sixty three patients (14.8%) with suspected and confirmed cases of appendicitis had an Alvarado score of 10. It was observed that 42 patients (9.9%) have had

normal appendix during the appendectomy. It was also detected that 214 cases have inflamed papillae (50.4%), 102 cases have exudation (23.9%), 36 cases have gangrene (8.5%) and 25 cases have perforated appendicitis during the surgical operations. Seven cases had abscess and flegmon. Pathological reports of 84 patients (19.7%) had also showed normal appendices. To evaluate the sensitivity and specificity of ESR and CRP in appendicitis, computed error rate was measured according to the gold standard diagnostic test for suspected appendicitis (i.e. pathology report) (Table 1).

A significant correlation was found between ESR and patients' pathologic result ($p=0.02$). In addition, CRP results had a significant correlation with gold standard for the diagnosis of appendicitis ($p=0.0001$). 294 patients (86.0%) with appendicitis also had leukocytosis and there was a significant correlation between their pathology results and their leukocytosis. The CRP and ESR results were also investigated in different s groups; where the association was significant ($p=0.0001$). ESR was positive in all individuals under 10 years of age. It was positive in 90.6% cases aged 11-20 years old. The positive rate of ESR decreased gradually with the increase of age where our findings showed that only 33.3% of patients with 30-40 years old have had positive ESR ($p=0.0001$). CRP was also positive in half of the patients aged 10 years old or less. However, in contrast to ESR findings, the positive CRP had risen by increasing age. The relationship between these two variables was significant ($p=0.001$). The statistical relationship between patients' age and their leukocytosis was significant. Leukocytosis was seen in all patients within age group under 10 years old. Like ESR, the rate of leukocytosis decreased gradually with increasing age in different age groups. Leukocytosis in patients with age group between 11-20 years was about 80.5% while it was 90.0% among patients with 41-50 years old.

Statistical information of patients with different age groups and confirmed pathologic diagnosis were also compared. Patients under 10 years old were observed to have about 60.0% appendicitis, those with 11-20 years old accounted for 80.0% of appendicitis, and patients over 70 years old had totally appendicitis ($p=0.007$). Regarding the relationship between sex and positive ESR or CRP, it was found that ESR was positive in 71.8% of men and 66.7% of women. No significant statistical association was found between patients' ESR results and their gender ($p=0.262$). Similarly, the rate of CRP was positive in 71.4% of men and 80% women. No significant association was found between these groups. About 80.0% of men and 86.0% of women had leukocytosis.

Table 1. The diagnostic value of leukocytosis, ESR and CRP in patients with suspected acute appendicitis

Pathology	ESR		CRP		Leukocytosis	
	Low N (%)	High N (%)	Negative N (%)	Positive N (%)	Yes N (%)	No N (%)
Appendicitis	96(28.1)	246(71.9)	51(14.9)	291(85.1)	294(86.0)	48(14.0)
Normal	33(39.3)	61(60.7)	48(57.1)	36(42.9)	51(60.7)	61(39.3)

There was not any relationship between these two. Pathological diagnosis of appendicitis was positive in 84.7% of men and 73.7% of woman. From those appendices which were removed with normal pathological results, other associated pathologies were found (Fig. 1).

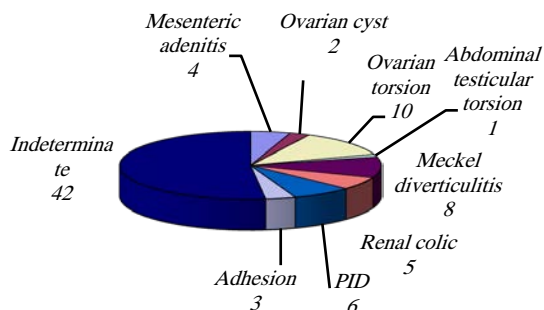


Figure 1. Distribution of pathologies in patients with suspected acute appendicitis

Discussion

This study was conducted to evaluate the designed to evaluate the association between leukocytosis, increased CRP and ESR and acute appendicitis. In this line, patients' demographic information was collected and was then compared with findings of similar studies. According to our investigation, the distribution of study samples does not have any significant difference with those of global or regional studies. The incidence of appendicitis in this study is similar to other findings have been reported globally, and that appendicitis is slightly more in males than females. The rate of negative appendectomy was about 20.0% even though there were some differential diagnoses in surgery which would reduce the rate of negative laparotomy in this study.

Usually 7% of the population experience acute appendicitis during their life. Of whom the ratio of male to female in the population with appendicitis is 1.6 to 1. This was confirmed in the current study [17]. The incidence rate of acute appendicitis in this study equals other reports reviewed. Acute appendicitis is a surgical disease that has a high prevalence in communities [1]. It is the most common cause of acute abdomen wherein its diagnosis makes it necessary to perform appendectomy. Nonetheless there is controversy over the management of acute appendicitis in critical situations [18]. Due to the similarity of signs and symptoms of appendicitis with other diseases, and because of differential diagnosis of appendicitis usually it is difficult to properly diagnose the disease [17].

To increase the accuracy of appendicitis surgeons highly depend on patients' history and detailed physical examinations. The accuracy of these procedures would more increase with laboratory tests. At times, auxiliary diagnostic methods may be applied [8]. To decrease the rate of negative appendectomy, surgeons need rapid, high accuracy detection of the appendicitis [19]. Like other

studies, the percentage of negative appendectomy was 19.7% (vs. 20.0%) in this study. These findings are against findings of a study of 266 patients which had found 107 cases with acute appendicitis and 159 cases without any pathologic results [18].

The value of leukocytosis was also examined in this study and it was found that it has a high value in diagnosing the appendicitis in all age groups. The relationship between leukocytosis and gold standard diagnostic test for suspected appendicitis (i.e. post-surgical pathology test) was significant. The rate of CRP was significantly higher in patients with confirmed appendicitis. In the present study the sensitivity and specificity values of ESR and CRP test were (71.9 & 39.0%) and (85.0% & 57.0%), respectively. It looks that these findings are similar to other studies in the same area.

It is recommended to use 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 Elderly). These include patient's medical history, physical examination, laboratory tests as well as clinical and imaging diagnostic investigations. A mix of these procedures would certainly help surgeons make appropriate choices. The combination of biochemical and clinical variables significantly decrease the perforation rate. Serial measurements of body temperature, Paraclinical tests and frequent clinical examination of suspicious cases of acute appendicitis are also recommended [8]. Some researchers have shown that in patients with suspicious clinical examinations, a combination of two or more markers of inflammation has helped surgeons make better decisions. Some of the additional methods and procedure which complement the above diagnostic tools are CT scan, ultrasound, barium enema and laparoscopy. It is noted that all of these methods may not be available for all and may have side-effects or disadvantages for some patients. Some of them are invasive, others are not economy and might be time-consuming. Among radio-photographic methods, the most cost-effective method for pediatrics is abdominal ultrasound and CT scan following a normal ultrasound diagnosis [12, 20].

In contrast, some researchers are questioning the value of clinical measures in the diagnosis of acute appendicitis. This group of people argues that the results of laboratory examinations in different groups of patients have its own interpretations [21]. Some studies show that even with best compound of the current standard diagnostic tests, the early diagnosed results of appendicitis is different from pathologic tests following the surgery [16]. Accordingly using a sensitive and accurate set of methods is necessary for diagnosis of the appendicitis in early stages [18, 21].

The diagnostic value of leukocytosis has been investigated in several studies to confirm suspected cases of acute appendicitis and it has been useful for many surgeons [22]. Serial investigation of leukocytosis has

also been valuable [4]. Leukocytosis is an important component to measure Alvarado and its value has been previously demonstrated. Nonetheless, it has been reported that leukocytosis has not been valuable in the diagnosis of appendicitis in children age 10 years old or less but it has been valuable in the diagnosis of the disease amongst older patients [23]. However, in the current study it was confirmed that leukocytosis plays an important role in the diagnosis of appendicitis in all age groups. Leukocytosis has a high diagnostic value in acute appendicitis in this study. The association of leukocytosis and the diagnosis of appendicitis based on gold standard (the pathology results after surgical operation) was meaningful. Many studies have shown that this criterion is helpful in the diagnosis of appendicitis but it can be very undedicated [9]. Available research shows that if leukocytosis and increased percentage of bloods neutrophils are applied together, they can be of benefit in the diagnosis of acute appendicitis [23].

For diagnosis of appendix rupture and peritonitis (or abdominal cocoon) physicians need a high clinical suspicion to manage the problem. Since many pediatric patients don't show symptoms associated with this condition it is recommended to use laboratory tests such as CRP and WBC count in order to diagnose the disease [18]. ESR and TNF tests have not been successful in the diagnosis of types of inflammation and as such it is recommended to examine serum amyloid A proteins and procalcitonine in order to differentiate appendicitis from non-specific abdominal pain or cramps [24]. Serotonin content of inflamed appendix of epithelium and lamina propria of inflamed tissue leads to an increase in the serum serotonin level in patients with acute appendicitis [10].

Recently, other markers of inflammation have been investigated and among these markers in addition to CRP, ESR and IL-6 has been proposed. In a study in Germany, the value of CRP and IL-6 has been approved for the evaluation of acute appendicitis in 211 children [4].

In this study we investigated the value of these markers and the percentage of leukocytosis in referred patient with suspicious signs of appendicitis. Movement of CRP synthesis in human hepatocytes is a part of total answer which leads to fever largely because it is a part of immunologic activity. Many researchers have used CRP in the diagnosis of intensity of disease and the quality of treatment. In a meta-analysis it was shown that CRP has a moderate sensitivity in the diagnosis of appendicitis. In another study it was found that the value of CRP was more in children with perforated appendicitis than in children with normal appendicitis [9]. Increasing level of CRP and white blood cell in suspicious cases of acute appendicitis can provided invaluable information for surgeons [24]. Positive CRP can show the need for emergency surgery while negative CRP in patients with acute abdomen shows the possibility of rejecting acute appendicitis in suspicious patients [18, 24].

Recent findings about the role of CRP and WBC count in acute appendicitis show that the normal range of CRP along with the normal count WBC would decrease the

possibility of acute appendicitis, and that the patient can be discharged without more reviews [25]. Even in some studies the value of CRP has been more than the value of leukocytosis in the diagnosis of acute appendicitis [11]. CRP with high sensitivity can be used in approving the clinical diagnosis of appendicitis, and would provide good reason to decrease unnecessary, negative appendectomy [17]. The possibility of acute appendicitis in patients that have had normal CRP level and white blood cell count is less than 5%, and the possibility of negative appendectomy in patients with both positive tests has been less than 10.0% [26]. According to many unspecific studies, the review of ESR in the diagnosis of acute appendicitis has been very time-consuming and does not have high value. Despite the correlation of leukocytosis with the severity of inflammation, sensitivity of ESR was 60.0-69.2% and its specificity was 8.3% [17]. In various studies the sensitivity of CRP has been 79.4-96.0% and its specificity has been 25.0-93.6% [12]. Results of another study showed that the sensitivity and specificity value of WBC test has been 98.1% and 37.1%, respectively [18].

In a study, the CRP sensitivity was 46.0-82.0% and in another study the declarative positive value of CRP has been 90.0% and negative declarative value of CRP has been 20.0% [17]. The diagnostic accuracy of CRP has been 75.0% in one study and the false-positive rate of CRP has been 24.7% elsewhere [15, 16]. In the conducted study in Germany CRP level has not been effective in the diagnosis of acute appendicitis whereas it has been a sign of advanced appendicitis or appendix rupture. The study showed that in children the CRP level is higher in perforated appendicitis compared with normal appendicitis where the CRP level is increasing at the beginning of the inflammation and would approximately increase 100 times [4].

In this study, the level of CRP has also increased in approved patients with acute appendicitis. The sensitivity and specificity of ESR were 71.9% and 39.0%, respectively. The sensitivity and specificity of CRP were 85.0% and 57.0%, respectively. The examination of CRP is recommended in patients suspicious to acute appendicitis [26]. Today, the use of time-consuming and costly diagnostic procedure in the diagnosis of appendicitis has been limited and patients and their health care providers 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.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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References

- Rosemart A, Kozar JI, Rosly N. Appendix. In: Schwartz SI. Principles of surgery. 8th ed. New York: McGraw-Hill; 2005; 2004-93.
- Souba WW, Fink MP, Jurkovich GJ, et al. ACS surgery: Principles and practice. 6th ed. New York: McGraw-Hill; 2007: 1720-1732.
- Rezaei E, Ghaemi M, Motamedolshareiati M and Rashed T. Diagnostic value of serum CRP and WBC count at diagnosis of patients with suspected acute appendicitis. J Gorgan Univ Med Sci 2004; 6(2): 83-86.
- Nordback L, Harju E. Inflammation parameters in the diagnosis of acute appendicitis. Acta Chir Scand 1988; 154(1): 43-8.
- Zinner MJ, Ashley SW. Maingot's abdominal operations. 11th ed. New York: McGraw-Hill; 2007: 589-611.
- Lawrence WW, Doherty G, Gerard M. Current Surgical diagnosis and treatment. 11th ed. New York: McGraw Hill; 2003: 668-674.
- Bainey KR, Bhatt DL. Acute pericarditis: appendicitis of the heart? Mayo Clin Proc 2009; 84(1): 5-6.
- Sack U, Biereder B, Elouahid T, et al. Diagnostic value of blood inflammatory markers for acute appendicitis in children. BMC Surg 2006; 6: 15.
- Baghi I. Association Rate of leukocytosis, increased CRP and ESR with acute appendicitis. J Guilan Univ Med Sci 2006; 15(57): 54-58.
- Vasei M, Zakeri Z, Azarpira N, et al. Serotonin content of normal and inflamed appendix: A possible role of serotonin in acute appendicitis. APMIS 2008; 116(2): 947-52.
- Kiyak G, Korukluoglu B, Ozgun Y, et al. [Evaluation of Ohmann and Eskelinen scores, leukocyte count and ultrasonography findings for diagnosis of appendicitis] Turkish [Abstract]. Ulus Travma Acil Cerrahi Derg 2009; 15(1): 77-81.
- Teyssedou C, Bigot P, Arnaud JP. Acute appendicitis in a patient with intestinal malrotation: The importance of CT imaging. J Chir (Paris) 2008; 145(6): 601-2.
- Cobben L, Bakker L, Puylaert J, et al. Imaging of patients with clinically suspected appendicitis in the Netherlands: conclusions of a survey. Br J Radiol 2009; 82(978): 482-5.
- Cobben L, Groot I, Kingma L, et al. A simple MRI protocol in patients with clinically suspected appendicitis: results in 138 patients and effect on outcome of appendectomy. Eur Radiol 2009; 19(5): 1175-83.
- Kirshtein B, Perry ZH, Avinoach E, et al. Safety of laparoscopic appendectomy during pregnancy. World J Surg 2009; 33(3): 475-80.
- Borhani M, Mohammad K, Holakoei-Naeini K. The accuracy of diagnostic tests in patients with suspected acute appendicitis, with ROC curve analysis. Payesh 2006; 5(4): 255-262.
- Hosseinpour M, Shahabedin M, Babaee F. Evaluation of the diagnostic value of high sensitive CRP for the diagnosis of 84 case of acute appendicitis in Shahid Beheshti Hospital (Kashan). Iran J Surg 2009; 17(2): 3-46.
- Khorshidi HR, Kashani K, Azimeian MH, et al. The value of CRP testing in the diagnosis of acute appendicitis. Sci J Hamadan Univ Med Sci 2006; 13(2): 60-63.
- Townsend Jr CM, Mattox KL, Mark B, editors. Sabiston textbook of Surgery. 18th ed. Philadelphia: W.B. Saunders; 2008: 1304-1345.
- Sarmast-Shoshtari M, Askarpour S, Alamshah M and Elahi A. Diagnostic value of quantitative CRP measurement in patient with acute appendicitis. Pak J Med 2005; 22(12): 300-303.
- Burkitt HG, Quick CR, Gatt D. Essential surgery. 2nd ed. Oxford: Churchill Livingstone; 1996: 285-298.
- Yeganeh R, Shadian-Loo M, Bashashati M. The accuracy of basic leukocytosis in diagnosis of acute appendicitis. J Army Univ Med Sci I. R. Iran 2005; 3(4): 705-708.
- Moosavinasab N, Moghimi MH. Diagnostic value of laboratory findings in patients with appendicitis. J Zanzan Univ Med Sci 2004; 12(48): 49-53.
- Mohebbi HA, Mehrvarz S, Khorrami MR. Evaluation of serum CRP, procalcitonin and WBC in the diagnosis of acute appendicitis. Iran J Surg 2011; 19(1): 41-46.
- 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(2): 113-5.
- Riazi A, Dashti S, Farzaneh MR. Diagnostic value of C-reactive protein (CRP) in acute appendicitis. Iran South Med J 2001; 4(2): 116-121.

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