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The role of total leucocyte count and C reactive protein in assisting with the diagnosis of acute appendicitis

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Abstract
Introduction: Once patients present with pain in the right lower quadrant, one of the most common surgical conditions that they have to treat is acute appendicitis. Our aim is to study the value of preoperative C - reactive protein and total leucocyte count in diagnosing acute appendicitis and to correlate its value in grading of acute appendicitis as compared to Histopathological reports.
Material and Methods: This is hospital based retrospective comparative study conducted in the Department of General Surgery at Yenepoya Medical College and Hospitals, Mangalore, a period of 5 years from, 2014-2019, to evaluate the accuracy of total leukocyte count and C - Reactive Protein (CRP) in the diagnosis of acute appendicitis. All patients above the age of 15 years diagnosed clinically to have acute appendicitis and subjected to appendicectomy were included. Patients with history of recurrent pain in right iliac fossa, patients with appendicular mass or peritonitis and concomitant conditions where C-reactive protein or Leukocyte Count is elevated were excluded.
Results: There are about 80.6% cases of acute appendicitis, 2.3% appendicular mass, 8.4% complicated acute appendicitis, 8.0% malignancy and 0.8% others. CRP level had a sensitivity of 86.27% and specificity of 66.67% in predicting acute appendicitis. Total leucocyte count had a sensitivity of 87.65% and specificity of 100% in predicting acute appendicitis.
Conclusion: Inflammation is known to cause an increase in CRP, but after complications have occurred, this increase is much more pronounced. The measurement of CRP or the counting of leucocytes on their own could be sufficient to prevent negative appendectomies.

Keywords: CRP, TLC, Acute appendicitis, appendicectomy, inflammation

Introduction

Once patients present with pain in the right lower quadrant, one of the most common surgical conditions that they have to treat is acute appendicitis. When it comes to community-acquired abdominal infections, this particular pathogen is by far the most common source of infection [1, 2, 3]. The incidence ranges from 42 to 175 cases per 100,000 people. Clinical signs and symptoms, such as fever, pain in the right lower quadrant, muscle guarding, and tenderness, are typically used to arrive at a conclusion regarding the diagnosis [4]. The rate of perforation is quite high, and it has been reported that the accuracy of clinically based diagnoses can range anywhere from 71% to 97% of the time, depending on the clinician's level of experience [6]. Therefore, it is still challenging to make an accurate diagnosis of acute appendicitis [7-9]. In general surgical procedures, perforated appendicitis is the leading cause of death around the world [10]. Patients who are thought to have acute appendicitis have blood tests that measure inflammatory markers such as white blood cell (WBC) counts and Creactive protein (CRP) levels. It has been emphasised how important it is to look at these blood inflammatory markers before making a decision about whether or not to discharge a patient or admit them for further investigation [11-16]. Surgery has traditionally been the primary method of treatment for appendicitis. However, initial treatment by non-surgical management has been shown to be both safe and effective for patients who present with catarrhalis appendicitis or phlegmnous appendicitis. This type of appendicitis is characterised by inflammation that occurs within the mucous membrane [17, 18]. However, more severe forms of appendicitis, such as gangrenous appendicitis, require immediate surgical intervention to be treated. The C - reactive protein is a non-specific inflammatory marker that is routinely used in some centres as an aid in the diagnostic process for patients who present with an acute abdomen [19]. It is a protein that is produced in the liver during the acute phase of the disease [20, 21].

After an infection or trauma, the normal serum concentration is less than 10 mg/l for eight to twelve hours. The production of CRP is under the control of interleukin-6, which causes a 1,000-fold increase in a matter of minutes. Infections, autoimmune disorders, inflammatory arthritis, neoplasia, and the natural ageing process all lead to an increase in CRP levels [20-25]. According to a number of studies, the diagnostic accuracy of these inflammatory markers is poor in cases of acute appendicitis [26-28]. However, the findings of some articles come to the conclusion that WBC counts and C - reactive protein levels are accurate indicators of the severity of the disease and that there is a significant correlation between the two and the pathological findings [29].

When both the white blood cell count and the C-reactive protein value are normal, appendicitis is not likely to be present, according to the findings of a number of studies [30]. Only about eighty-four percent of patients who have their appendix removed have a pathological finding that confirms they had appendicitis. This is because the symptoms of appendicitis are not typical and it can be difficult to make an accurate diagnosis. There are a significant number of appendectomy procedures that end in failure. Since appendectomy results in socio-economic impacts such as decreased productivity and loss of working days, negative appendicectomies are one of the burdens that are borne not only by the general surgeon but also by the patient and by society as a whole. In cases of perforated or gangrenous appendicitis, postponing surgery leads to a significant increase in the likelihood of early and later complications, as well as an increase in the length of time patients spend in the hospital. Therefore, it is necessary to detect appendicitis early and treat it appropriately in order to reduce the risk of complications following surgery [31]. Investigations for the early detection of complicated appendicitis are still at a relatively early stage. The diagnosis of complicated appendicitis is currently dependent on the onset of symptoms as well as a physical examination; as a result, there is a high likelihood of inaccuracy as a result of subjective interpretation. Because of this, there is a growing demand for a test that can assist in the diagnosis of acute appendicitis and accurately predict how severe the condition will become. Our aim is to study the value of preoperative C - reactive protein and total leucocyte count in diagnosing acute appendicitis and to correlate its value in grading of Acute Appendicitis as compared to Histopathological reports.

Material and Methods

This is hospital based retrospective comparative study conducted in the Department of General Surgery at Yenepoya Medical College and Hospitals, Mangalore, a period of 5 years from, 2014-2019, to evaluate the accuracy of total leukocyte count and C - reactive protein (CRP) in the diagnosis of acute appendicitis. In this study, all patients who came to the General surgery Outpatient Department and to the Emergency Department who presented with right iliac fossa pain and were diagnosed as acute appendicitis were considered for the study. They underwent routine blood investigations which included total leucocyte count and CRP. Histopathological reports of the resected appendix specimen of the patients who underwent emergency appendicectomy were considered in the study. Finally, an analysis was done to correlate the sensitivity and specificity of total leukocyte count and CRP in diagnosing acute appendicitis. The histopathological report was used to confirm the diagnosis of acute appendicitis. Patients admitted in Yenepoya Medical College Hospital in the past 5 years who underwent appendicectomy. All cases that fit the inclusion criteria in the stipulated 5-year period were included. Total leucocyte count, C-reactive protein and Histopathology reports were collected. All patients above the age of 15 years diagnosed clinically to have acute appendicitis and subjected to appendicectomy were included. Patients with history of recurrent pain in right iliac fossa, patients with appendicular mass or peritonitis and concomitant conditions where C-reactive protein or Leukocyte Count is elevated were excluded.

Descriptive statistics were reported as mean (SD) for continuous variables, frequencies (percentage) for categorical variables. Receiver operator characteristic curve was illustrated for the diagnostic accuracy. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 26.0., IBM Corp. and Chicago, IL.

Results

There are about 80.6% cases of acute appendicitis, 2.3% appendicular mass, 8.4% complicated acute appendicitis, 8.0% malignancy and 0.8% others (Table 1). CRP level had a sensitivity of 86.27% and specificity of 66.67% in predicting acute appendicitis (Table 2, Figure 1). Total leucocyte count had a sensitivity of 87.65% and specificity of 100% in predicting acute appendicitis (Table 3, Figure 2).

Table 1: Distribution of primary code among the study participants (N = 263)

SL. No	Variable	Frequency	Percentage
1	Acute appendicitis	212	80.6
2	Appendicular mass	6	2.3
3	Complicated Acute appendicitis	22	8.4
4	Malignancy	21	8.0
5	Others	2	0.8

Table 2: Diagnostic accuracy of CRP with primary diagnosis of appendicitis among the study participants (N=263)

SL. No	Diagnosis	CRP >10	CRP < 10
1	Appendicitis	201	10
2	Others	32	20

Statistic	Value	95% CI
Sensitivity	86.27%	81.17% to 90.41%
Specificity	66.67%	47.19% to 82.71%
Disease prevalence (*)	88.59%	84.12% to 92.17%
Positive Predictive Value (*)	95.26%	92.36% to 97.10%
Negative Predictive Value (*)	38.46%	29.33% to 48.48%
Accuracy (*)	84.03%	79.03% to 88.24%

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.548	0.058	0.392	0.434	0.662

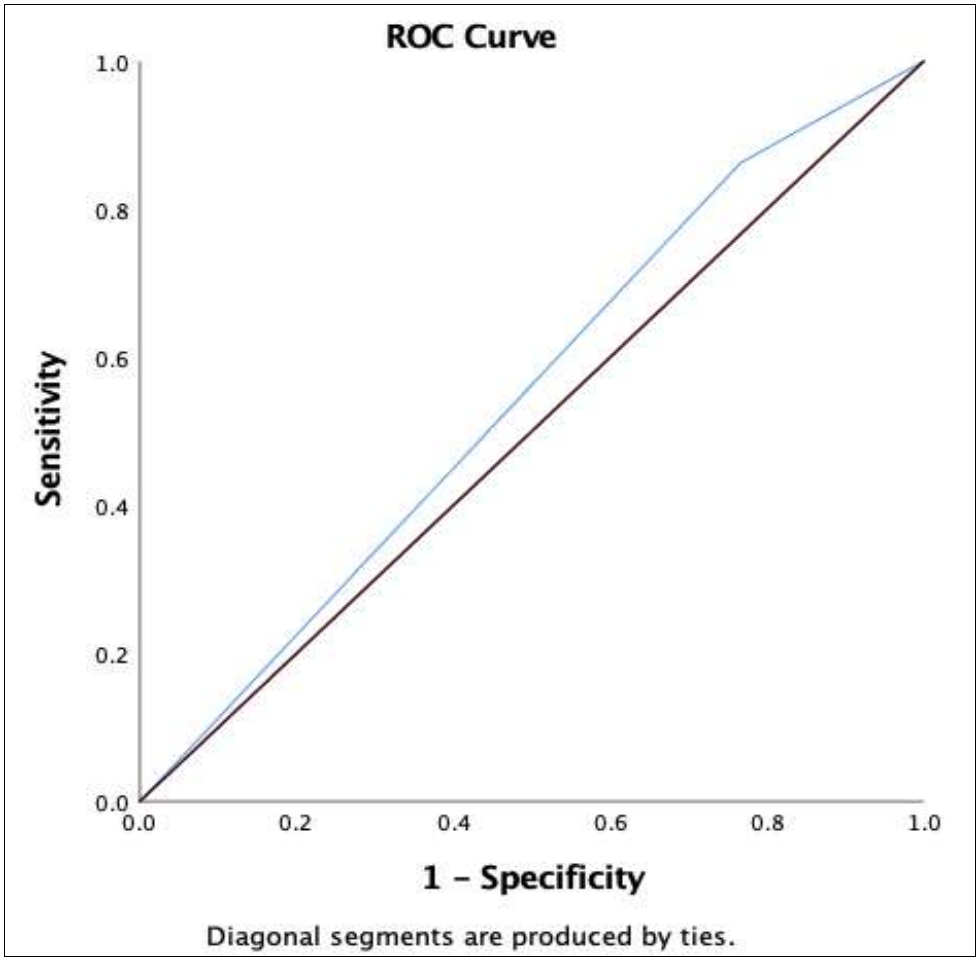

Fig 1: Diagnostic accuracy of CRP with primary diagnosis of appendicitis among the study participants (N = 263)

Table 3: Diagnostic accuracy of total leucocyte count with primary diagnosis of appendicitis among the study participants (N=263)

Sl. no	Diagnosis	TLC>10	TLC < 10
1	Appendicitis	213	0
2	Others	30	20

Statistic	Value	95% CI
Sensitivity	87.65%	82.85% to 91.51%
Specificity	100.00%	83.16% to 100.00%
Disease prevalence (*)	92.40%	88.50% to 95.29%
Positive Predictive Value (*)	100.00%	99% to 100%
Negative Predictive Value (*)	40.00%	32.29% to 48.24%
Accuracy (*)	88.59%	84.12% to 92.17

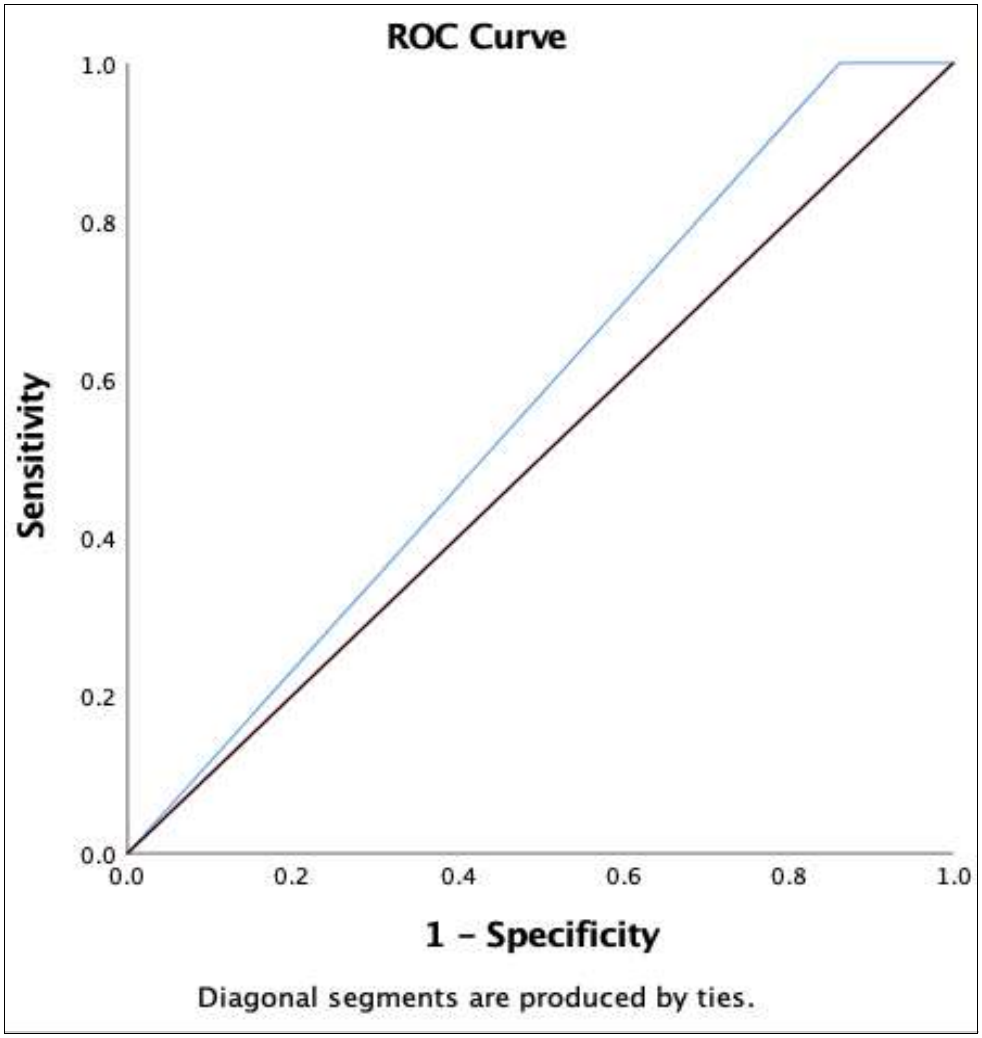

Fig 2: Diagnostic accuracy of total leucocyte count with primary diagnosis of appendicitis among the study participants (N = 263)

Area	Std. Error [a]	Asymptotic Sig. [b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.569	0.050	0.221	0.470	0.667

Discussion

The most common medical emergency requiring emergency abdominal surgery is acute appendicitis.[5] Appendectomy after a false-positive diagnosis of appendicitis, also known as a negative appendectomy, is performed in up to 15 to 25 percent of cases. This is because the clinical diagnosis of acute appendicitis is difficult [6]. In women of reproductive age, some authors have even reported negative appendectomy rates as high as fifty percent of the time [7]. It has been generally accepted that such negative explorations are an unavoidable consequence of the principle of early exploration to prevent perforation of the appendix; however, this practise is being questioned more and more these days. The majority of patients who have acute appendicitis present with lower abdominal pain on the right side, nausea, and vomiting; however, these symptoms are not particularly specific to the condition. In point of fact, any acute abdominal condition can present symptoms similar to those of appendicitis. Because of this, the list of differential diagnoses is lengthy, which is why it is not uncommon to remove an appendix that is otherwise healthy. The diagnosis is likely to be correct if there is localised tenderness as well as evidence of peritoneal inflammation (tenderness to guarding and percussion). In most cases, the results of laboratory investigations contribute very little and can even be misleading [8]. Even though appendicectomy is generally regarded as a risk-free procedure, it can still result in a number of complications. The complications that are most likely to arise are wound infection, intraabdominal abscess, adhesions and bowel obstruction, as well as pulmonary complications resulting from the use of general anaesthesia. In addition, some patients continue to experience symptoms even after the surgery has been performed. Patients who are like this put a strain on the facility's resources and, on the whole, are dissatisfied with the care they receive from the medical professionals.

The first studies on the use of C-reactive protein in the diagnosis of acute appendicitis were carried out in 1967 by Russian surgeons. These studies evaluated the diagnostic and prognostic role of C - reactive protein [32]. Only the triple combination of C – Reactive Protein, total white blood cell count, and total neutrophil count has been suggested to be of diagnostic value in acute appendicitis by Dueholm, *et al.* in 1989. This suggests that acute appendicitis is unlikely when all three of these tests come back negative at the same time [33]. In 1997, Hallan and Asberg conducted a review of 22 eligible articles on the accuracy of C - reactive protein in patients with suspected appendicitis. The patients included a total of 3436 individuals. Both sensitivity and specificity showed a wide range of variation, ranging from 40 to 99 percent and 27 to 90 percent, respectively. They came to the conclusion that the C - reactive protein test had a moderate degree of accuracy and that it was not possible to reach a definitive decision regarding the usefulness of the test [33].

Between May 1, 1999 and September 31, 2007, Yokoyama *et al.* reviewed 150 patients who had appendectomies and had pathologically confirmed appendicitis in an effort to clarify the role of C-reactive protein as a surgical indication marker for appendicitis. These patients had undergone appendectomies between the dates of May 1, 1999 and September 31, 2007. This study showed that white blood cell counts and neutrophil percentage are not useful for surgical indication. On the other hand, univariate analysis indicated that only C - reactive protein was significantly different between the surgery necessary group and the unnecessary group, and multivariate analysis showed that only C - reactive protein was an independent marker for necrotic appendicitis. In conclusion, this study demonstrated that the white blood cell counts and neutrophil percentage are not useful for surgical indication [34]. A prospective study was conducted by Salem *et al.* in 2003 on patients who were admitted to the surgical department of a large referral hospital reporting nontraumatic, acute abdominal pain. The study lasted for one year. Nonspecific abdominal pain (nSAP), surgical non-operative group, and surgical operative group were the three categories into which patients were categorised. Despite the fact that there were statistically significant differences between the groups, the authors were unable to determine a useful level of C-Reactive Protein that could differentiate between patients who had nSAP and those who needed either operative or non-operative management.

According to Khan, *et al.* (2004) [36], the sensitivity and specificity of C - Reactive Protein in the diagnosis of acute appendicitis were estimated to be 75.6 percent and 83.7 percent respectively [35]. In 2004, Andersson examined 28 distinct diagnostic variables in the evaluation of patients suffering from acute appendicitis in 24 primary research articles that were eligible for the study. According to the findings of the author, each component of the history, examination, and laboratory markers of inflammation has a low capacity for discrimination and prediction. On the other hand, the likelihood of the diagnosis being correct increases when more than one factor is taken into consideration [36].

Shafi *et al.* conducted a study in 2007 on 110 patients who had surgery for acute appendicitis to determine the role of total leucocyte count (TLC), C-reactive protein, and percentage of neutrophil count in the diagnosis of acute appendicitis. The study was carried out on patients who had undergone surgery for the condition. According to the findings, the sensitivity of the C - reactive protein test was 95.6 percent, while its specificity was 77.77 percent, and its positive predictive value was also 95.6 percent. When measured together, TLC, CrP, and neutrophil count, the authors came to the conclusion that these inflammatory markers can be helpful in the diagnosis. This is because measuring them together increases both their specificity and their positive predictive value [37].

Even if clinical symptoms and signs indicate acute appendicitis, the majority of authors agree that acute appendicitis is unlikely in adult patients with a normal leukocyte count and C - reactive protein value [38]. This is the consensus among the vast majority of authors. As a consequence, these patients should not go through with the operation. In addition, a number of studies have demonstrated that the accuracy of both tests can be improved by combining the results of the total leukocyte count and the C-reactive protein value. These two sets of findings are consistent with the findings of our research. In children, an appendicitis diagnosis cannot be conclusively ruled out even if the leukocyte count and C-reactive protein value are both normal [39-40].

Conclusion

Inflammation is known to cause an increase in CRP, but after complications have occurred, this increase is much more pronounced. An early indicator of appendix inflammation is an increase in the total number of leucocytes in the blood. The measurement of CRP or the counting of leucocytes on their own could be sufficient to prevent negative appendectomies. Numerous studies on the subject determining the role of TLC and CRP preoperatively and postoperatively in the diagnosis of acute appendicitis need to be carried out.

Conflict of Interest

Not available

Financial Support

Not available

References

1. Kozar RA, Roslyn JJ. In: Principles of Surgery. 7. Schwartz SI, Shires GT, Spencer FC, editor. New York-London: The McGraw-Hill Companies Inc; the Appendix; c1999. p. 1383-1393.
2. Pal K, Khan A. Appendicitis: A continuing challenge. J Pak Med Assoc. 1998;48(7):189-92.
3. Sartelli M. *et al.* Complicated intra-abdominal infections in Europe: preliminary data from the first three months of the CIAO Study. World Journal of Emergency Surgery. 2012;7(1):15.
4. Birnbaum BA, Wilson SR. Appendicitis at the millennium. Radiology. 2000;215:337-48.
5. Gurleyik E, Gurleyik G, Unalmişer S. Accuracy of serum C-reactive protein measurements in diagnosis of acute appendicitis compared with surgeon's clinical impression. Dis Colon Rectum. 1995;38(12):1270-1274.
6. John H, Neff U, Kelemen M. Appendicitis diagnosis today: clinical and ultrasonic deductions. World J Surg. 1993;17:243-9.
7. Shakhatreh HS. The accuracy of C-reactive protein in the diagnosis of acute appendicitis compared with that of clinical diagnosis. Med Arh. 2000;54(2):109-110.
8. Kim-Choy N, Shin-Wei L. Clinical Analysis of the related factors in Acute Appendicitis. Yale J Biol Med. 2002;75:41-45.
9. Pieper R, Kager L, Nasman P. Acute appendicitis: A clinical study of 1018 cases of emergency appendectomy. Acta Chir Scand. 1982;148:51-62.
10. Beauchamp RD, Evers BM, Mattox KL. Sabiston Textbook Of Surgery: The Biological Basis of Modern Surgical practice,19th edition. 2012;2(51):1279-1291.
11. Ortega-Deballon P, Ruiz deAdana-Belbel JC, Hernández-Matías A, García-Septiem J, Moreno-Azcoita M. Usefulness of laboratory data in the management of right iliac fossa pain in adults. Dis Colon Rectum. 2008;51:1093-9.
12. Khan MN, Davie E, Irshad K. The role of white cell count and C-reactive protein in the diagnosis of acute appendicitis. J Ayub Med Coll Abbottabad. 2004;16:17-19.
13. Grönroos JM, Grönroos P. Leucocyte count and C-reactive protein in the diagnosis of acute appendicitis. Br J Surg. 1999;86(501-4):92.
14. Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Tröbs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. BMC Surg. 2006;6:15.

15. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Laboratory tests in patients with acute appendicitis. ANZ J Surg. 2006;76:71-4.
16. Nordback I, Harju E. Inflammation parameters in the diagnosis of acute appendicitis. Acta Chir Scand. 1988;154:43-8.
17. Eriksson S, Granstrom L. Randomized controlled trial of appendicectomy versus antibiotic therapy for acute appendicitis. Br J Surg. 1995;82:166-169.
18. Oliak D, Yamini D, Udani VM, Lewis RJ, Arnell T, Vargas H, Stamos MJ. Initial nonoperative management for periappendiceal abscess. Dis Colon Rectum. 2001;44:936–41.
19. Mason RJ. Surgery for appendicitis: is it necessary? Surg Infect (Lancet) 2008;9:481-88.
20. Mohammed AA, Daghman NA, Aboud SM, Oshibi HO. The diagnostic value of Creactive protein, white blood cell count and neutrophil percentage in childhood appendicitis. Saudi Med J. 2004;25(9):1212-1215.
21. Asfar S, Safar H, Khoursheed M, Dashti H, Al-bader A. Would measurement of Creactive protein reduce the rate of negative exploration for acute appendicitis? J R Coll Surg Edinb. 2000;45:21-24.
22. Albu E, Miller BM, Choi Y, Lakhanpal S, Murthy RN, Gerst PH. Diagnostic value of C-reactive protein in acute appendicitis. Dis Colon Rectum. 1994;37:49-51.
23. Davies AH, Bernau F, Salisbury A, Souter RG. C-reactive protein in right iliac fossa pain. J R Coll Surg Edinb. 1991;36:242-244.
24. Andersson RE, Hugander A, Ravn H, Offenbartl K, Ghazi SH, Nyström PO, *et al.* Repeated clinical and laboratory examinations in patients with an equivocal diagnosis of appendicitis. World J Surg. 2000;24:479-485.
25. Shoshtari MHS, Askarpour S, Alamshah M, Elahi A. Diagnostic value of Quantitative CRP measurement in patients with acute appendicitis. Pak J Med Sci July - September. 2006;22(3):300-303.
26. Amalesh T, Shankar M, Shankar R. CRP in acute appendicitis is it a necessary investigation? Int J Surg. 2004;2:88-9.
27. Johansson EP, Rydh A, Riklund KA. Ultrasound, computed tomography, and laboratory findings in the diagnosis of appendicitis. Acta Radiol. 2007;48:267-73.
28. Kessler N, Cyteval C, Gallix B, Lesnik A, Blayac PM, Pujol J, *et al.* Appendicitis: evaluation of sensitivity, specificity, and predictive values of US, Doppler US, and laboratory findings. Radiology. 2004;230(472-8):93.
29. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Laboratory tests in patients with acute appendicitis. ANZ J Surg. 2006;76:71-4.
30. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Role of leukocyte count, neutrophil percentage, and C-reactive protein in the diagnosis of acute appendicitis in the elderly. Am Surg. 2005;71:344-347.
31. Kim JI, Seong MK, Lee KY. Preoperative prediction of acute perforative and gangrenous appendicitis by clinical features of patients. J Korean Surg Soc. 1993;44:1048-10.
32. Dueholm S, Bagi P, Bud M. laboratory aid in the diagnosis of acute appendicitis. A blinded, prospective trial concerning diagnostic value of leukocyte count, neutrophil differential count and C-reactive protein. Dis Colon rectum. 1989;32:855-859
33. Hallan S, Asberg A. The accuracy of C-reactive protein in diagnosing acute appendicitis: A meta-analysis. Scand J Clin lab Invest. 1997;57:373-380.
34. Yokoyama S, Takifuji K, Hotta T, *et al.* C-reactive protein is an independent surgical indication marker for appendicitis: A retrospective study. World J Emerg Surg; c2009. p. 36.
35. Salem TA, Molloy rG, O'dwyer PJ. Prospective study on the role of C - reactive protein in patients with an acute abdomen. Ann r Coll Surg Engl. 2007;89:233-237.
36. Khan Mn, davie E, Irshad K. The role of white cell count and C-reactive protein in the diagnosis of acute appendicitis. J Ayub Med Coll Abbottabad. 2004;16:17-19.
37. Andersson rE, Hugander A, ravn H, *et al.* repeated clinical and laboratory examinations in patients with an equivocal diagnosis of appendicitis. World J Surg. 2000;24:479-485.
38. Shafi SM, Afsheen M, reshi FA. Total leucocyte count, C-reactive protein and neutrophil count: diagnostic Aid in acute appendicitis. Saudi J Gastroenterol. 2009;15:117-120.
39. Gronroos JM. Do normal leukocyte count and C-reactive protein value exclude acute appendicitis in children? Acta Paediatr. 2001;90:649-651.
40. Gronroos JM. Too many unnecessary appendectomies. leukocyte count and CrP value for safer diagnosis. Lakartidningen. 2002;99:891-893.

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