

Diagnostic Value of C Reactive Protein Measurement in Patients with Acute Appendicitis

Maitham H. Kenber

ABSTRACT:

OBJECTIVES :

To evaluate the role of crude measurement of C-reactive protein in the diagnosis of acute appendicitis.

BACKGROUND:

Appendectomy for suspected acute appendicitis is a common procedure. The rate of normal appendices unnecessarily removed remain high(15%-30%) ; despite several techniques and investigations used to improve the diagnostic accuracy . Many studies investigated the role of raised C-reactive protein (CRP) in improving the diagnosis of acute appendicitis, but with conflicting results.

PATIENTS AND METHODS :

This is a randomized prospective study from February to July 2006 . A total of 100patients were included in this study that presented to our hospital with acute right iliac fossa pain and later on operated and had appendectomy .Blood for the measurement of serum C-reactive protein(CRP) was collected preoperatively from all the patients. The patients divided in to two groups ,those who are positive appendicitis proved by operative finding and histopathological examination and those with negative appendicitis proved by histopathological examination.

RESULT:

A total of 100 patients were included in this study, and out of these 16 (16%) had normal appendix giving an over all negative appendectomy rate of 16% out of these 5 were males and 11 were females ,the age range was (6-47 years) with a median age of (25.92) years . Among the 84 who had appendicitis, 64 patients had obstructive type of appendicitis which were noticed during the operation ,and CRP was positive in all patients, but only 9 of them were with CRP negative . 4 perforated appendicitis were found in which all of them were CRP positive, and 16 patients with catarrhal appendicitis were diagnosed by histopathological examination and only 3 patients out of those had negative CRP while the remainder were positive.

CONCLUSION:

The positivity of CRP was related to the severity of inflammation; but it is more reliable to depend on negative results to postpone the operation and observe the patient .Thus unnecessary removal of normal appendices may be reduced.

KEY WORDS : acute appendicitis , C- reactive protein .

INTRODUCTION:

Acute appendicitis is still one of the commonest surgical emergencies⁽¹⁾.The diagnosis usually depends on clinical history, physical examination and leukocytosis . Atypical presentations are not uncommon as many inflammatory and non-inflammatory conditions may mimic the presentation of acute appendicitis.The picture is more confused by the variable positions of the appendix. These and other factors resulted in the relatively high rate (15-30%) of negative explorations for acute appendicitis⁽²⁻⁴⁾.

The reported postoperative morbidity associated with these negative explorations is (5-15%) despite advances in diagnostic modalities the diagnosis is still doubtful in (30-40 %) of cases⁽⁵⁾. Acute appendicitis is a disease of young adults . It is more common in males as compared to females⁽⁶⁾. Additional tests that would improve the diagnostic accuracy and reduce the number of unnecessary operations are needed. This is particularly important in these days where health planning is driven by cost containment.

C-reactive protein (CRP) (which is an acute phase reactant protein synthesized by the liver in response to bacterial infection)was first found in the serum of

Department of Surgery , College of Medicine , University of Kufa.

patients suffering from pneumonia caused by *Streptococcus pneumoniae* ⁽⁷⁾. Together with other acute phase-proteins, the serum level of CRP rises in response to any tissue injury. It also increases in response to infections (bacterial and viral) and in non-infectious conditions like myocardial infarction, malignancies and rheumatic disorders ⁽⁸⁾.

CRP concentration increases within 8 hours of the onset of tissue injury, peaks in 24-48 hours and remains high as long as there is continuing infection or tissue destruction ^(9,10). Due to its short half-life (4-7 hours) serum CRP concentration rapidly declines as the acute inflammatory process subsides. The normal level of CRP is variable from one laboratory to other but in general it is about (0-0.8mg/dl) ⁽¹¹⁾.

Many reports have investigated the value of CRP in improving the diagnostic accuracy of acute appendicitis with conflicting results ^(12, 13).

In this study we correlated the positivity of CRP with the inflammation of the removed appendix.

PATIENTS AND METHODS:

This prospective study was carried out at AL-Sader teaching hospital which is a general hospital in AL-Najaf city in Iraq. This study included a randomized collection of 100 patients during the period from February to July 2006, who had been admitted with the clinical diagnosis of acute appendicitis. The final diagnosis and the decision to operate was already made by the surgeon on call.

Samples for quantitative serum CRP measurement and WBC count were collected from all these patients before going to the operating room. The decision to operate was made independent of the CRP level as the result was not available to the surgical team during the hospital stay of these patients.

The laboratory staff were not aware of the clinical findings, decisions and outcomes (double blind study).

Provisional diagnosis of acute appendicitis was made on the basis of :-

-History of abdominal pain localized to the right iliac fossa or lower abdomen.

-Clinical findings of tenderness, guarding and/or rigidity in the right iliac fossa or lower abdomen.

Although the leukocytes count was performed for all patients and its results were available preoperatively but the surgeon on call did not take it as a significant factor in the diagnosis. All patients presented with in (1-120) hours of the onset of pain. During operation

the degree of inflammation of the appendix was noted.

For statistical purposes these 100 patients assigned in to four groups:-

Group 1-Those who have normal appendices which was proved by histopathological examination (16 patients).

Group 2-Those with catarrhally inflamed appendices which was proved by histopathological examination (16 patients).

Group 3-Those with obstructive appendicitis which was diagnosed macroscopically during operation and observation of fecolith (64 patients) ; and

Group 4- Those with frankly perforated appendicitis. The white blood count (WBC) ,CRP level and histopathological findings were compared to assess the impact of serum CRP measurements on the diagnosis of acute appendicitis. The positive serum CRP was assigned into those with strong positive and those with weak positive depending on the degree of agglutination between the serum of the patient and the adding of the reagent substance because the titration method used for accurate measurement in milligrams was not available in our laboratory and in this method the test would only be positive if the CRP is raised above normal levels .

RESULTS:

A total of 100 patients with a diagnosis of acute appendicitis were collected over the period of the study and they were 56 males (56%) and 44 females (44%). The mean age of the patients was 25.92 (6-47)years . Appendicectomies were performed for all the 100 patients , of these 84(84%) patients were appendicitis positive and grouped as follow:-

- In 64(76.19%) patients the diagnosis of acute appendicitis was of obstructive type , depending on gross appearance .CRP was positive in all but 9 (14.06%) patients ; of which 39 (60.93%) were with strongly positive CRP and 16 (25%) were with weakly positive CRP.

- In 16 (19.04%) patients acute appendicitis diagnosed as catarrhal type which was proved by histopathological examination , out of these 3(18.75%) patients have negative serum CRP . Those with CRP positive serum were assigned as 9 (56.25%) with strongly positive CRP and 4(25%) with weakly positive CRP.

- The appendix was grossly perforated in 4 (4.76%) patients , all of them were with strongly positive serum CRP. As shown in table (1)

ACUTE APPENDICITIS

Table (1):Positive acute appendicitis in relation to CRP level

TYPE	NO.	+VE CRP	STRONG +VE	WEAK +VE	-VE CRP
obstructive	64(76%)	55	39(61%)	16(25%)	9(14%)
Catarrhal	16(19%)	13	9(56%)	4(25%)	3(19%)
Perforated	4(5%)	4	4(100%)	-	-
total	84	72	52	20	12

In the other 16 (16%) patients the appendices were found to be normal on histopathological examination (negative exploration). The rate of normal appendectomy was (16%) in this report and the finding of these patients were illustrated in table (2)

Table(2):Finding of negative exploration in relation to CRP level and WBC count

Case	sex	Age years	Wbc× 10 ⁹ /dl	CRP	Final diagnosis
1	F	20	6	negative	Ruptured ovarian cyst
2	F	28	4	negative	Non specific abdominal pain
3	F	23	4	negative	Non specific abdominal pain
4	F	18	7	positive	Non specific abdominal pain
5	F	30	4	negative	Non specific abdominal pain
6	F	28	5	positive	Ruptured ovarian cyst
7	F	25	6	negative	Ectopic pregnancy
8	F	15	10	negative	Non specific abdominal pain
9	F	18	5	negative	Non specific abdominal pain
10	F	20	4	negative	Non specific abdominal pain
11	M	27	10	negative	ovarian cyst
12	M	30	3	negative	Non specific abdominal pain
13	M	35	8	positive	Non specific abdominal pain
14	M	25	4	negative	Non specific abdominal pain
15	M	23	7	negative	Non specific abdominal pain
16	M	20	4	negative	Non specific abdominal pain

Serum CRP measurement in patients with acute appendicitis was with a sensitivity of (85.7%)and a specificity of (81.25%) as shown in table (3).

Table (3) : Statistical results of CRP study

Statistical parameters	CRP-study results %
True positive (TP)	72
False positive (FP)	3
True negative (TN)	13
False negative (FN)	12

Specificity=81.25
Sensitivity=85.7%
Positive Predictive value =96%
Negative Predictive value =52%
P <0.05

ACUTE APPENDICITIS

WBC count was done for all patients only, 28 (28%) patients had leukocytosis (the WBC count was more than $11 \times 10^9/\text{dl}$) all of them were with inflamed appendices.

In all patients with perforated appendix (4 patients) the WBC count was highly elevated ($>18 \times 10^9/\text{dl}$). While the others (24 patients) had obstructive type of appendicitis. As shown in table (4).

Table (4): Relation of WBC count with acute appendicitis

TYPE	NO.	No. of patients with elevated wbc count	WBC $\times 10^9/\text{L}$	No. of +ve CRP
Perforated	4	4	18-24	4
Obstructive	64	24	$>11-18$	24
Catarrhal	16	-	4-11	13
Negative exploration	16	-	4-10	3

DISCUSSION:

In this study our work based on the crude measurement of positivity of C-reactive protein. The results showed that cases with acute appendicitis proved by operative finding and histopathological examination were associated with a significant rise in CRP preoperatively ($p < 0.05$) this result is in accord with Oostrhuis et al⁽¹⁴⁾ who showed that serial CRP measurement can improve the accuracy of diagnosis acute appendicitis; a result which was not proved by Thompson⁽¹⁵⁾. But a recent Hallans meta-analysis of 22 published articles concluded that CRP is a test of medium accuracy in diagnosing acute appendicitis⁽¹⁶⁾.

The subgrouping of patients in to strong positive and weak positive rising in serum CRP carried no statistical importance ($p \text{ value} > 0.5$).

The rate of negative explorations for appendicitis was (16%) which is in accord with other reports⁽¹⁻³⁾. The majority of the cases were women 62.5% (10 cases out of 16) as was expected owing to gynecological disorders which mimic acute appendicitis⁽¹⁷⁾. In this group of patients, the pre-operative CRP levels were found to be negative in all but 3 patients (81.25%). These results would suggest that negative preoperative serum CRP level is not associated with acute appendicitis.

This study also showed the significance of raised preoperative WBC count with cases of acutely inflamed appendices in combination with positive CRP ($p < 0.05$). These findings are in accord with Gronroos who showed no rise in the preoperative WBC count or CRP level in all patients in whom the removed appendix was normal. The authors concluded that appendectomy is not recommended when the WBC and CRP were normal preoperatively⁽¹⁸⁾.

In this study we found, the increased level of pre-operative serum CRP together with WBC count,

were high sensitivity and specificity in relation to the serum CRP (85.7% and 81.25% respectively) and highly specific in relation to the WBC (100%) in the diagnosis of acute appendicitis which is in accordance with other studies.

A study also held by Gronroos found that WBC count was a better laboratory test than CRP value in diagnosing uncommon appendicitis⁽¹⁷⁾.

CONCLUSION:

The data presented in this study would suggest that a negative pre-operative CRP level is not likely to be associated with acute appendicitis.

Deferring emergency appendectomy in this group of patients would probably reduced the rate of unnecessary appendectomies.

According to our results in this study we strongly support the use of pre-operative rising in serum CRP and WBC count as a guidance in the diagnosis of acute appendicitis.

Further prospective studies are required to verify the validity of this proposition.

REFERENCES:

1. Pal K, Khan A. Appendicitis: a continuing challenge. J Pak Med Assoc 1998;48,189-92.
2. Jess P, Bjerregaard B, Brynitz S et al. Acute appendicitis: prospective trial concerning diagnostic accuracy and complications. Am J Surg 1981;141, 232-4
3. Pieper R, Kager L, Nasman P. Acute appendicitis: a clinical study of 1018 cases of emergency appendectomies. Acta ChirScand 1982;148,51-62
4. Hoffmann J., Rasmussen O. Aids in the diagnosis of acute appendicitis. BrJSurg 1989; 76: 774-9
5. Peltokallio P, Tykka H. Evaluation of the age distribution and mortality of acute appendicitis. Arch Surg 1981;116, 153-6.

ACUTE APPENDICITIS

6. Tillet WS, Francis T. Serological reactions in pneumonia with a non- protein somatic fraction of pneumococcus. *JExpMed*1930; 52: 561-71
7. Pepys MB, C-reactive protein fifty years on. *Lancet* 1981; 1,653-6
8. Young B, Gleeson M, Cripps A. C-reactive protein: a critical review. *Pathology* 1991; 23, 118-24
9. Kragbjerg P, Holmberg H, Vikerfors T. Serum concentrations of interleukin-6, tumour necrosis factor and C-reactive protein in patients undergoing major operations. *EurJSurg* 1995; 161,17-22
10. Pepys MB, Baltz ML. Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *Adv Immunol* 1983; 34, 141-2 11
11. Eriksson S, Granstrom L, Carlstrom A. The diagnostic value of repetitive pre-operative analyses of C-reactive protein and total leucocyte count in patients with suspected acute appendicitis. *Scand Gastro Enterol* 1994; 29,1145-9
12. Albu E, Miller B.M. Choi Y. Lakhanpal S, Murthy RN, Gerst PH. Diagnostic value of C-reactive protein in acute appendicitis. *Dis Colon Rectum* 1994; 37, 49-5 1
13. Oosterhuys WP, Zwinderrnan AH, Teeuwen M, van An del G, Oldenziel H, KerkhoffJF, Siebbeles HW, van der Helm HJ. C-reactive protein in the diagnosis of acute appendicitis. *Fur JSurg* 1993; 159, 115-9
14. Thompson MM, Underwood MJ, Dookeran KA, Lloyd DM, Bell PR. Role of sequential leucocyte counts and C-reactive protein measurements in acute appendicitis. *Br JSurg* 1992;79, 822-4
15. Hallan S, Asberg A. The accuracy of C-reactive protein in diagnosing acute appendicitis - a meta-analysis. *ScandfClin Labin vest* 1997; 57, 373-80.
16. Gronroos JM, Gronroos P. A fertile-aged woman with right lower abdominal pain but unelevated leucocyte count and C-reactive protein. Acute appendicitis is very unlikely. *Langenbecks Arch Surg* 1999 ;384,437-40
17. Gronroos JM and Gronroos P. Leucocyte count and C- reactive protein in the diagnosis of acute appendicitis. *BrlSurg* 1999; 86, 501-4.