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:
Appendicectomy 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 100 patients were included in this study that presented to our hospital with acute right iliac fossa pain and later on operated and had appendicectomy. Blood for the measurement of serum C-reactive protein (CRP) was collected preoperatively from all the patients. The patients divided into two groups, those who had 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 overall negative appendicectomy 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. 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.

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. Acute appendicitis is a disease of young adults. It is more common in males as compared to females. 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
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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 (9).

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 surgeon on call.

In all of these 100 patientsassigned in four groups:

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

Group 2: Those with catarrally 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)
In the other 16 (16%) patients the appendices were found to be normal on histopathological examination (negative exploration). The rate of normal appendicectomy 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

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

Serum CRP measurement in patients with acute appendicititis 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

<table>
<thead>
<tr>
<th>Statistical parameters</th>
<th>CRP-study results %</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive (TP)</td>
<td>72</td>
</tr>
<tr>
<td>False positive (FP)</td>
<td>3</td>
</tr>
<tr>
<td>True negative (TN)</td>
<td>13</td>
</tr>
<tr>
<td>False negative (FN)</td>
<td>12</td>
</tr>
</tbody>
</table>

Specificity=81.25
Sensitivity=85.7%
Positive Predictive value =96%
Negative Predictive value =52%
P <0.05
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WBC count was done for all patients only. 28 (28%) patients had leukocytosis (the WBC count was more than 11×10^9/dl) all of them were with inflamed appendices. In all patients with perforated appendix (4 patients) the WBC count was highly elevated (>18×10^9/dl). While the others (24 patients) had obstructive type of appendicitis. As shown in table (4).

<table>
<thead>
<tr>
<th>TYPE</th>
<th>NO.</th>
<th>No. of patients with elevated wbc count</th>
<th>WBC×10^9/L</th>
<th>No. of +ve CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforated</td>
<td>4</td>
<td>4</td>
<td>18-24</td>
<td>4</td>
</tr>
<tr>
<td>Obstructive</td>
<td>64</td>
<td>24</td>
<td>&gt;11-18</td>
<td>24</td>
</tr>
<tr>
<td>Catarhal</td>
<td>16</td>
<td>-</td>
<td>4-11</td>
<td>13</td>
</tr>
<tr>
<td>Negative exploration</td>
<td>16</td>
<td>-</td>
<td>4-10</td>
<td>3</td>
</tr>
</tbody>
</table>

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 (15) who showed that serial CRP measurement can improve the accuracy of diagnosis acute appendicitis a result which was not proved by Thompson (16). 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 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 pre-operative 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 appendicitis is not recommended when the WBC and CRP were normal preoperatively (18).

In this study we found, the increased level of preoperative 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 (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 appendicectomy in this group of patients would probably reduced the rate of unnecessary appendicectomies.

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.

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