Significance of WBC Count and CRP Quantitation to Reduce the Chance of Negative Exploration In Acute Appendicitis

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ABSTRACT

INTRODUCTION: Acute appendicitis is one of the commonest causes of acute abdomen in ER. Despite the advances in diagnostic modalities, clinical decision plays a key role in its diagnosis. However, some easily available laboratory tests like WBC count and CRP value may augment to prevent negative explorations.

METHOD: After being investigated for WBC and CRP quantitatively preoperatively, 100 consecutive subjects with clinical features of acute appendicitis were operated at Bir Hospital, from January 2007 to July 2007. The HPE report, along with the WBC and CRP values, which were made available only after surgical exploration, were analyzed and conclusions were drawn accordingly, considering p< 0.05 as statistically significant.

RESULT: Ninety-one percent of the subjects had acutely inflamed appendix intraoperatively and rest showed normal looking appendix. Histopathology confirmed acute appendicitis in 86% and rest with normal appendix. Among the histopathologically proven cases, 74% of the patients with acute appendicitis and 9% with normal appendix had simultaneously (concurrently) raised WBC count. Contrary, despite of normal WBC count, 12 patients had histologically proven acute appendicitis. However, 5% patient with normal appendix also had normal WBC count. Similarly, CRP values of 78% patients with acute appendicitis along with 9% patient with normal appendix were raised than normal. Eight percent of the patients with acute appendicitis along with 5% of the subjects with normal appendix had CRP value within normal level.

CONCLUSION: Clinical diagnosis of acute appendicitis can be augmented by WBC and CRP reducing the chance of negative exploration.

KEY WORDS: Acute Appendicitis, CRP, Negative Exploration, WBC

INTRODUCTION

Acute appendicitis is one of the commonest causes of acute abdomen with surgical emergencies in emergency department. Despite advances in medical technologies, its diagnosis is still doubtful in 30-40% of cases and necessitates dependence on a clinical decision, augmented by appropriate tests and imaging. Clinical diagnosis alone can lead to removal of normal appendix in 15 – 30% of cases, causing unacceptable (5-15%) post-operative morbidity and mortality. Experienced surgeons can diagnose acute appendicitis accurately in more than 90% of cases on clinical ground, but there is a general trend to rely on laboratory tests for the patient with equivocal signs or sometimes even with convincing signs. Apart from a careful history and clinical examination, additional laboratory tests like total WBC count and CRP values that would improve the diagnostic accuracy and reduce the chance of negative explorations are therefore preferred.

Total white blood cell count has remained an important factor in the diagnosis of appendicitis, but studies have shown that this can be very non-specific
at times, especially above 30000/cu mm. Recently interest has also grown in other inflammatory markers like C-reactive protein, which could be helpful in diagnosing appendicitis. These laboratory tools though not very specific, are reliable and many reports have investigated the value of raised serum CRP measurement along with WBC count in improving the diagnosis of acute appendicitis.

Therefore the current study was conducted to correlate the level of WBC count and CRP value with the clinical decision to explore for the emergency appendectomy. After exploration, the operative finding were also correlated accordingly with the histopathological report to determine the specificity and sensitivity of the WBC and CRP level in preventing negative appendectomies.

**METHOD**

The entire patients presenting to the emergency department, NAMS from January – July 2007, consulting for acute abdomen and admitted to surgical department with provisional diagnosis of acute appendicitis were included in the study. A good clinical history and proper physical examination was performed. Some subjects requiring additional period of observation were reevaluated frequently and findings were recorded accordingly. No any additional diagnostic tests were done unless indicated for other medical purposes other than diagnosing for acute appendicitis.

The subjects who were finally diagnosed with acute appendicitis were planned for emergency open appendectomy and counseled accordingly, specially mentioning the least possibility of misdiagnosis leading to negative exploration. After drawing blood samples for total WBC and CRP value determination, the result of which were made available to the surgical team after surgery only, emergency appendectomy was done on one hundred consecutive consented subjects. Intra operative findings were noted in all subjects and the specimens, including the normal looking appendix, were sent for HPE. HPE report, which was considered as final diagnosis, was correlated and analyzed with intra operative findings and also with the WBC value and CRP level. The data were analyzed individually as well as in combination of each other using the “or” rule using Pearson’s Chi Square ($\chi^2$) test.

**RESULT**

Among the 100 subjects studied with age ranges from 16-62 years, 68% were male of mean age 27±10.2 and 32% were female of mean age 30.2±11. Since this hospital has no pediatric surgery department, no pediatric subjects were included in this study.

Intra operatively, 91% was diagnosed to have acute appendicitis at their various stages of inflammation viz. acutely inflamed (70%), gangrenous (19%) and perforated (2%); and 9% showed normal looking appendix. However, considering HPE as final diagnosis, 86% were having acute appendicitis and the rest underwent to negative exploration.

![Intra operative diagnosis of the patients with clinical features of acute appendicitis](image)

**Table No. 1: Comparison between intra operative diagnosis versus HPE report**

<table>
<thead>
<tr>
<th></th>
<th>HPE Diagnosis</th>
<th>Normal Appendix</th>
<th>Acute Appendicitis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra Operative Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal looking appendix</td>
<td></td>
<td>(7 M-2, F-5)</td>
<td>2 (M-2, F-0)</td>
<td>9</td>
</tr>
<tr>
<td>Appendicitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Acutely inflamed)</td>
<td></td>
<td>(7 M-2, F-5)</td>
<td>84 (M-62, F-22)</td>
<td>91</td>
</tr>
<tr>
<td>(Gangrenous)</td>
<td></td>
<td>(0)</td>
<td>(63)</td>
<td>(70)</td>
</tr>
<tr>
<td>(Perforated)</td>
<td></td>
<td>(0)</td>
<td>(19)</td>
<td>(19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2)</td>
<td>(2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

OR = 42.0, 95% CI (5.97, 447.67), p<0.0001, sn= 97.7, 91.1, 99.6, sp= 50.0, 24.0, 76.0 ppv= 92.3, 84.3, 96.6, npv=77.8, 40.2, 96.1 False positive rate = 50.0%, False negative rate = 2.3% Accuracy rate = 91.0%
Though only 9% of the patients were diagnosed intra-operatively as normal appendix, 14% turned to be normal appendix by HPE. Out of 9 patients who were diagnosed intra-operatively as normal looking appendix, only 7 were compatible with HPE report and other 2 were appendicitis. Similarly, out of 91% of subjects diagnosed intra-operatively as appendicitis, 7 had normal appendix and rest were compatible with the HPE report. Therefore, there seems a good correlation between the intra-operative and histopathological diagnosis (p=0.0002).

Statistically, gender has no significant predilection towards the acute appendicitis. However, the possibility of negative exploration in female subjects (31%, 10/32) seems significantly higher (p=0.001) in compare to that of male (6%, 4/68).

LABORATORY TESTS:

**White Blood Cell (WBC) count:** The total WBC count of >10000/cu mm was taken as cutoff level for the study. Among the 83% of the subjects with raised WBC, only 74% of the subjects had acute appendicitis and rest being normal appendix. Contrary to that, among 17% subjects with WBC count within normal limit, 12% were diagnosed as the case of acute appendicitis and the rest came to be normal appendix. Therefore, though the chance of diagnosing acute appendicitis in raised WBC count is increased by more than 3 folds [OR 3.43, 95% CI (1.24-8.81)], the statistical correlation between them seems poor (p=0.059).

**C-Reactive Protein:** The CRP level of > 5 mg% was considered as significantly higher. Among the 86% of the subjects diagnosed pathologically as acute appendicitis, 78% had simultaneously raised CRP level and rest (8%) with normal values. Likewise, out of 14% of negative exploration, only 5% had concomitantly normal CRP level and 9% had raised CRP despite the finding of normal appendix. Statistically, therefore, the chance of having acutely inflamed appendix in the subjects with raised CRP level is increased by more than 5 folds and its correlation with acute appendicitis seems, though not an absolute, is stronger in comparison to that of WBC count. (p=0.017 vs p=0.059).

### Table No. 2: WBC count in patient diagnosed with acute appendicitis

<table>
<thead>
<tr>
<th>WBC count (cu mm)</th>
<th>Normal Appendix</th>
<th>Acute Appendicitis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10000</td>
<td>5</td>
<td>12</td>
<td>0.059</td>
</tr>
<tr>
<td>&gt;10000</td>
<td>9</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio=3.43, 95% CI (1.24-8.81)  
Positive predictive value = 89.2%, 95% CI (79.9, 94.6)

### Table No. 3: CRP level in patient diagnosed with acute appendicitis

<table>
<thead>
<tr>
<th>CRP value</th>
<th>Normal Appendix</th>
<th>Acute Appendicitis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 mg/l</td>
<td>5</td>
<td>8</td>
<td>0.017</td>
</tr>
<tr>
<td>&gt;5 mg/l</td>
<td>9</td>
<td>78</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio=5.42, 95% CI (1.12-23.62)  
Positive predictive value = 89.7%, 95% CI (80.8, 94.9)  
Negative predictive value = 38.5%, 95% CI (15.1, 67.7)  
Sensitivity = 90.7%, 95% CI (82.0, 95.6)  
Specificity = 35.7%, 95% CI (14.0, 64.4)  
False positive rate = 64.3%  
False negative rate = 9.3%  
Accuracy rate = 83.0%

### Table No. 4: WBC Vs CRP

<table>
<thead>
<tr>
<th>WBC count (cu mm)</th>
<th>Normal Appendix</th>
<th>Acute Appendicitis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10000</td>
<td>5</td>
<td>12</td>
<td>0.059</td>
</tr>
<tr>
<td>&gt;10000</td>
<td>9</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio=3.43, 95% CI (1.24-8.81)  
Positive predictive value = 89.2%, 95% CI (79.9, 94.6)  
Negative predictive value = 29.4%, 95% CI (11.4, 56.0)  
Sensitivity = 86.0%, 95% CI (76.5, 92.3)  
Specificity = 35.7%, 95% CI (14.0, 64.4)  
False positive rate = 64.3%  
False negative rate = 14.0%  
Accuracy rate = 79.0%
were not able to show abnormal laboratory values. On the other hand, though 29% (4/14) subjects with negative exploration had both the laboratory values within normal limit, more than half, 57% (8/14), of negative exploration showed both the laboratory values raised.

Table No. 4: Comparison of WBC count and CRP level in patient diagnosed with acute appendicitis

<table>
<thead>
<tr>
<th>WBC/CRP values</th>
<th>Normal Appendix</th>
<th>Acute Appendicitis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal WBC</td>
<td>4</td>
<td>2</td>
<td>0.003</td>
</tr>
<tr>
<td>Normal CRP</td>
<td>1</td>
<td>10</td>
<td>0.028</td>
</tr>
<tr>
<td>Raised WBC</td>
<td>1</td>
<td>6</td>
<td>0.103</td>
</tr>
<tr>
<td>Raised CRP</td>
<td>8</td>
<td>68</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Figure 3: Comparison of WBC count and CRP value in the patient diagnosed as acute appendicitis.

DISCUSSION

Diagnosis of acute appendicitis remains difficult since earlier. To improve its diagnostic accuracy, surgeons have not only relied on a good history and sound clinical examination but also seek help from diagnostic tools, ranging from simple laboratory investigations to modern sophisticated tools. Among all, looking at the WBC count has been very favorite test for the surgeons in deciding for exploration. However, studies have shown that these tests have a low accuracy and the question of specificity and sensitivity of these tests therefore still remains open. ⁵,⁶

To improve the sensitivity and specificity of the laboratory tests, surgeons have tried sequential leukocyte counts and neutrophil: lymphocytic ratio. ⁷,⁸,⁹ Recently attention has also been focused on other inflammatory markers like CRP, which can also be raised in acute appendicitis. Therefore, the current study was carried out to evaluate the role of WBC count and CRP value in diagnosing acute appendicitis, ultimately preventing the negative exploration among the patients consulting to ER with acute abdomen secondary to acute appendicitis.

Post-operative morbidity and mortality following negative exploration for appendicitis though is small, but cannot be neglected. Intestinal obstruction, for example, alone comprises up to 0.9 – 5.0% of morbidity following negative exploration. ¹⁰ Therefore, intra operative diagnosis made by operating surgeon is also equally important to rule out the etiology of acute abdomen, if not primarily due to the acute appendicitis.

In the present study, the accuracy of intra operative diagnosis was correlated with HPE report, which was found to be statistically highly significant (p=0.0002). The accuracy (91%), sensitivity (97.7%) and specificity (50%) of the operative diagnosis seems superior in comparison to the similar international studies. ¹¹,¹²

The prevalence ratio of acute appendicitis in male to female was found to be 2.9:1. Though the exact cause of male preponderance is not clear; it is in accordance with other previous studies. ³,⁸,¹³,¹⁴ The diagnostic accuracy in male compared to female (91%, 64/68 vs 30%, 22/32) subjects is significantly high (p=0.001) and comparable with the figure of 59-97% reported in the literatures. ¹⁵-¹⁷ The low diagnostic accuracy in female subjects could be due to various possible pathological states mimicking the acute appendicitis. In this study, the negative exploration rate of 14% is also within the acceptable international figures of 5 – 30%. ¹³,¹⁴,¹⁸,¹⁹

LABORATORY TESTS:

Controversy exists regarding the relative usefulness of laboratory tests in the diagnosis of acute appendicitis. The WBC count is most often used by surgeons to augment the diagnostic accuracy. Several reports suggest that an elevated leukocyte count is usually the earliest laboratory test to indicate possibility of appendiceal inflammation, and most of the patients with acute appendicitis present with leukocytosis. ⁸,⁹,¹⁰,¹¹,²² The sensitivity of leukocyte count noted in the study (86.0%), is in accordance with other
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Studies of 82–96% but the CRP has relatively higher sensitivity of 90.7% in this regard. The results of the study clearly demonstrates that, though either of these laboratory values were elevated in the vast majority of patients with acute appendicitis, subject with normal values in all subsequent tests could possibly go for negative exploration at most and should be analyzed with extra caution before exploration.

With the combination of leukocyte count and CRP level, their common sensitivity approaches to 97.1% with extremely low specificity of 33.3%. Normally, the ideal diagnostic tests are those with a high sensitivity and specificity. From this point of view, the high sensitivity and low specificity of the WBC-CRP combination for acute appendicitis does not fulfill the criteria for an optimal diagnostic test. Nevertheless, the high sensitivity of their combination implied that at least one of the two measurements was above the normal limit in nearly all patients with acute appendicitis. Therefore, acute appendicitis seems very unlikely in a patient with both the values simultaneously within the normal limits, and such patients should be treated with careful reevaluation before surgery even if clinical symptoms and signs indicate acute appendicitis.

Our study indicates that the total WBC count and CRP value, either alone or in combination, cannot be relied upon to make a diagnosis of acute appendicitis, but can carry contributory diagnostic information that may aid in the clinical judgment of surgeons. Since these laboratory tests are more effective in supporting a clinical diagnosis of acute appendicitis than to exclude the diagnosis, a good clinical assessment by an experienced surgeon remains reliable and superior to either of these laboratory investigations.

CONCLUSION

None of the laboratory tests used can replace the clinical skills of experienced surgeons in diagnosing the case of acute appendicitis, but their use in combination of clinical skill can be recommended to prevent negative exploration, if not to augment the accuracy in diagnosing a positive case.

REFERENCES


