

# DIAGNOSTIC VALUE OF QUANTITATIVE CRP MEASUREMENT IN PATIENTS WITH ACUTE APPENDICITIS

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## ABSTRACT

**Background:** Acute appendicitis is one of the most common surgical emergencies. Main stay of diagnosis of acute appendicitis is accurate history, clinical evaluation and physical examination. It is further reinforced by laboratory investigation like raised leukocytes count. To avoid unnecessary removal of normal appendices more laboratory tests like C-Reactive Proteins (CRP) have been evolved.

**Methods:** This is a prospective and cognitive study from January to June 2004 of all those patients who had appendectomies at the Golestan and Imam Khomeini Hospital of Medical University, Jundi-Shapour, Ahwaz.

**Results:** Out of a total of 98 patients, on histological examination 88 (89.7%) had acute appendicitis whereas 15 (10.3%) were normal with no sign of inflammation. Range of CRP varied between 3.8 to 19.5 mg/1 (mean 6.34 mg/1), in patients with normal appendix and between 3.8 to 468.5 mg/1 (mean 49 mg/1), in patients with simple appendicitis and 30.1-408 mg/1 mean (113/2) in patients with complicated appendicitis. Normal CRP range of CRP was noted in 9 patients with acute appendicitis, and in 8 cases with normal appendectomy.

**Conclusions:** Positive predictive value of CRP was 97.5%, specificity 89.7% sensitivity 80% and accuracy 88.7% Raised value of CRP was directly related to the severity of inflammation (p-value<0.05). Taken in conjunction with leukocyte count the diagnostic accuracy became more reliable. CRP monitoring enhances the diagnostic accuracy of acute appendicitis thus unnecessary removal of normal appendices may be reduced to about half.

**KEY WORD:** CRP, Diagnostic value, Appendicitis.

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## INTRODUCTION

Appendicitis remains one of the most common acute surgical diseases.<sup>1,2</sup> The average rate of normal appendectomy is 16 percent, with female comprising 68 percent of those patients found to have inflamed appendix at exploration.<sup>1</sup> Diagnosis of acute appendicitis in young children and elderly is more difficult than in adults and also perforation rate is higher.<sup>1</sup> In elderly the causes of abdominal emergency are greater and differential diagnosis is more problematic.<sup>3</sup> Acute appendicitis is a clinical diagnosis and no laboratory or radiological tests are 100% accurate.<sup>4</sup> Mild leukocytosis, ranging from 10,000 to 18,000 is usually present in patients with acute, uncomplicated appendicitis and is often accompanied by a moderate polymorphonuclear predominance.<sup>1,5</sup> Sensitivity of leukocytosis is

from 52% to 96% and sensitivity of shift to left is from 39% to 96% and sensitivity and specificity for the use of neutrophil to lymphocyte ratio greater than 3.5 has been reported.<sup>6</sup> In WBC above 30,000, other diagnosis must be considered.<sup>7</sup>

To reduce the incidence of normal appendectomies, many studies have been published on quantitative analysis of CPR. C-reactive protein is an acute phase protein that is produced in the liver. Normal serum concentration is less than 10 mg/l.<sup>8</sup> 8-12 hours after infection or trauma, the increase of acute phase protein in liver the CRP is more important in clinical practice.<sup>9</sup> Production of CRP is controlled By Interleukin-6<sup>10</sup> and in few minutes increases from 10 to 1000 times.<sup>9,10</sup> CRP is increased in infections, inflammatory arthritis, autoimmune disorders, neoplasia, pregnancy and aging.<sup>11</sup> Automatic methods of quantity measurement of CRP are limited in level less than 3.8mg/l. Immuno-turbidimetric, and immuno-nephelometric methods with high sensitivity are available. In older methods qualitative and semi quantitative measurement of CRP with agglutination are possible.<sup>12</sup>

## PATIENTS AND METHODS

This is a prospective, double blind study of 98 appendectomised patients in Golestan and Imam Khomeini Hospital in Jundi-Shapour Medical University of Ahwaz from January to June 2004. A preoperative sampling of blood was obtained and CRP measurement with method of immunoassay nephelometry were performed. CRP up to 10mg/l, WBC up to 10,000/mm<sup>3</sup> and leukocytosis up to 70% was considered as upper limit of normal. Intraoperative findings and histopathological reports were recorded. Patients with other infections were excluded from study.

## RESULTS

Males were 70% (N=69), females 29.5% (N=29), and children were 23.5% (N=23). Based on histopathological report, patients were categorized in three groups. In Group-A

with normal appendix were 10.2% patients (N=0), In Group-B with acute simple appendicitis 67.3% (N=67) and in Group-C with complicated appendicitis the patients were 22.5% (N=22).

In group-A the CRP values ranged from 3.8 to 19.5 with a mean of 6.3. In group-B these were from 3.8 to 468.5 with a mean value of 49, and in group-C these were 38.1 to 408 with a mean of 113.2. In 9 patients with acute appendicitis CRP range was within normal limits. False positive results were seen in 20% and false negative in 10.2%, with sensitivity 89.7% and specificity 80%, positive predictive value 97.5% and calculated negative predictive value of 47%.

Similarly when WBC count was assessed in Group-A it varied from 3800 to 17000 (mean 11210), in Group-B: from 5100 to 22500 (mean 13390) and in Group-C: from 6200 to 22000 (mean 14836). Mean of WBC in Group-C was greater than Group-B (p-value=0.09) and greater than Group-A (p-value<0.05) False positive were 60% and false negative were 14.7% with a sensitivity of 85.2% and specificity 40%, positive predictive value was 92.5% and negative predictive value was calculated to be 23.5%.

Whereas Neutrophil percentage in Group-A varied from 43 to 85 with a mean of 71.7. In Group-A it was 49 to 97 with a mean of 79.8. In Group-C it varied from 50 to 96 with a mean of 80.8%.

When CRP and WBC were considered together in 67 patients both were positive (in Group-B 69 Patients and In Group-C 28) and five patients were negative in Group-A and Group-B). There was no false positive and false negatives were 2.8%. The sensitivity was 1% and specificity was 100%. Positive predictive value was calculated 100% and negative value 60%.

Finally CRP, WBC and Neutrophil taken together 63 patient were positive and 2 patients were negative, with no false positive and only 1.5% were negative. Sensitivity was 98.4%, specificity were 100%, positive predictive value 100% and the negative predictive value was 50%.

## DISCUSSION

Positive CRP is more accurate than WBC and Neutrophil counts and combined together it further improves diagnostic accuracy. In double blind study Asfar and Coworkers reported sensitivity and Specificity of CRP as 86.6% and 93.6% respectively. They concluded that normal CRP value probably indicates a normal non inflamed appendix.<sup>13</sup> It is a more sensitive test than WBC and Neutrophil combined significantly increase sensitivity and specificity. Arkrasp in a positive study on 102 patients reported that sensitivity and specificity of CRP were 96% and 78% respectively<sup>14</sup> positive predictive value was 100%. In a retrospective study of Wu & Co workers concluded that combined usage of WBC neutrophil count & CRP monitoring increased the positive predictive value to combined usage of CRP WBC & neutrophil count which significantly increases the negative predictive value in diagnosis of acute appendicitis.<sup>15</sup> Gronroos in one study conclude that when both WBC and CRP are normal, acute appendicitis is very unlikely.<sup>16</sup> In our study from 88 patients with acute appendicitis 2 patients had CRP and WBC in normal range (2.2%). Shakhathreh in a prospective study concluded that CRP measurement is very useful in diagnosis of acute appendicitis but it doesn't replace the clinical judgment of surgeon.<sup>17</sup> Accuracy of CRP (89%) is greater than WBC (81%) and neutrophil count (80%). Combination of these increase the accuracy to 98.5%. Anderson in a prospective study on 420 patients with borderline diagnosis of appendicitis concluded that WBC and neutrophil count are the better criteria for the subsequent examinations.<sup>18</sup> Mean of CRP in simple acute appendicitis (Group-B) is significantly greater than normal appendix (Group-A) ( $p < 0.05$ ), and also in complicated acute appendicitis (Group-C) CRP is significantly greater than normal appendix and acute appendicitis ( $p < 0.05$ ). WBC and neutrophil count are also increased based on severity of inflammation but the increase count is not significant ( $p > 0.05$ ). None of these tests are 100% diagnostic.

Eryilmaz concluded that CRP measurement or leukocyte count by itself are not completely preventive from negative appendectomy.<sup>19</sup> Gronroos in one study on 200 children concluded that unlike the adult normal leukocyte and CRP dose not rule out acute appendicitis in pediatric.<sup>20</sup>

## CONCLUSIONS

Combination of CRP WBC and neutrophil count have greater diagnostic accuracy and significantly decrease false positive and false negative diagnosis but none of these are 100% diagnostic of acute appendicitis.

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