

# Accuracy of C-Reactive Protein Level in the Diagnosis of Acute Appendicitis on Histopathology

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## ABSTRACT

**Background:** Acute appendicitis (AA) is one among most common condition requiring emergency surgery throughout the world. Acute appendicitis most common diagnosis in patients seeking medical help in emergency room due to acute abdomen causing 72,000 deaths among 16 million cases reported globally. This study will help the surgeons in making timely decisions, thus reducing the morbidity and mortality associated with complicated appendicitis. The aim of this study was to accuracy of C-reactive protein (CRP) levels in acute appendicitis.

**Material and Methods:** Six-month descriptive cross-sectional research from 16 February to 16 August 2019 was completed. The Khyber Teaching Hospital in Peshawar served as the study's location. A total of 216 patients were monitored throughout this investigation. The history, clinical examination, and regular laboratory tests, such as the total leucocyte count (TLC) and differential leucocyte count (DLC) on admission, were used to make the diagnosis of acute appendicitis. All of these patients were given Nil by Mouth to prepare them for emergency surgery, and baseline testing included HBs Ag and Anti-HCV serology as well as pre-operative serum CRP levels (Liver function tests, renal function tests and serum electrolytes). Following preparation, every patient on the emergency list had surgery. Intra-operative results were recorded, and a biopsy was collected from the excised appendices and forward to histopathology for further processing.

**Results:** The mean age in this research was 48 years, with an SD of 12.311. Male patients made up 55% of the total population, while female patients made up 45%. The diagnostic accuracy of C-reactive protein levels was determined to be 84.2% in this study. The specificity was found to be 33.3%, while the sensitivity was observed to be 85.7%. By using histopathology, it was discovered that the positive predictive value was 97.2% and the negative predictive value was 84.2%.

**Conclusion:** According to our study, using histopathology, the diagnostic accuracy of C-reactive protein levels was 84.25% with sensitivity of 85.71%, specificity of 33.33%, and positive predictive values of 97.25% and 184.25%. The findings will also open the door for any further research in this area. The higher CRP levels will therefore predict the complexity of acute appendicitis and help the general practitioners to do early referrals therefore avoiding life threatening complications

**Keywords:** Acute Appendicitis, C-Reactive Protein, Histopathology, CRP, Gold Standard

## INTRODUCTION

Acute Appendicitis is one among the frequent cause of acute abdominal pain necessitating

emergency surgery both worldwide and in our country<sup>1,2</sup>. Most common surgical condition requiring emergency surgery worldwide<sup>1</sup>. According to Global burden of disease 2013, Acute Appendicitis is the most common diagnosis in patients seeking medical help in emergency room due to acute abdomen causing 72,000 deaths among 16 million cases reported globally<sup>2,3</sup>. The life time risk of AA is 16.33% for males and 16.34% for females in South Korea<sup>4</sup>. In Pakistan, about 400,000 appendectomies are routinely carried out in surgical departments each year.<sup>5</sup>

Despite significant improvements in diagnostic techniques, nearly 30–40% of patients still require the surgeon's clinical judgment<sup>3</sup>. This increases the percentage of unsuccessful appendectomies to about 20%, which entails both mortality and morbidity risks<sup>4, 6</sup>. One of the key contributing elements in diagnostic mistakes is atypical clinical presentations, which are rather common since many inflammatory and non-inflammatory conditions resemble the clinical picture of the disease. Women in the reproductive age range and patients at the age extremes commonly make these diagnostic errors. The most difficult clinical scenario is caused by the variability in organ anatomical placements<sup>5, 7</sup>.

The patient's medical history, physical examination, and a few supplementary tests, notably the Total Leukocyte Count, play a significant role in the diagnosis of acute appendicitis (TLC). In order to improve diagnostic accuracy, scoring systems like the Alvarado, Ohmann, and Eskelinen scores have been developed<sup>7</sup>. In addition, abdominal computerised tomography (CT scan) and ultrasonography (USG) are employed to aid in disease diagnosis; nevertheless, each has its own inherent drawbacks. The TLC test

is frequently used to identify acute appendicitis. Though it is difficult to find a sensitivity and specificity of TLC greater than 83% and 62.1%, respectively, when searching the literature<sup>8</sup>. Other inflammatory indicators that may be useful in the diagnosis of acute appendicitis have recently attracted more attention. Hepatocytes produce the acute phase protein C-reactive protein (CRP), which is a marker for acute inflammation<sup>9</sup>. Within 4 to 6 hours of stimulation, its blood levels begin to rise, peaking 36 to 48 hours later. Many writers have emphasised the CRP's accuracy in the diagnosis of acute appendicitis, despite the fact that it is a non-specific test<sup>9</sup>. Their research has shown that in persons with symptoms of the condition for more than 24 hours, a normal level of CRP has a negative predictive value for acute appendicitis of about 100%<sup>10,11</sup>. CRP testing is a fairly easy and non-invasive laboratory procedure. There are no health risks to the patient from it. It is independent of the operator. The clinician has access to the test findings in one hour. The whole price is one hundred Pakistani rupees. For patients in our setting, it is quite advantageous and cheap due to all these features taken together. Most patients appear in complicated states as a result of challenging diagnoses, inadequate healthcare infrastructure, and low knowledge in our nation. CRP is a low-cost and practical test that is routinely applied to patients in emergency rooms who are feverish or infected. It has been widely employed as a prognostic or severity indication in many acute and chronic disorders, as well as several cancers. It has also been used as a biomarker for therapy monitoring<sup>10, 11, 12</sup>. According to Kim et al., the serum CRP level was one of the important variables that could reliably differentiate between difficult and non-complicated appendicitis<sup>11</sup>. CRP has a good predictive accuracy for difficult appendicitis diagnosis,<sup>12</sup>

In a retrospective study various blood indicators was looked at, including CRP, and concluded that CRP may have a role in

complex appendicitis<sup>13</sup>. With diagnostic accuracy of 83.2%, sensitivity 85.1%, specificity 72%, and positive predictive value of 94.7%, Xharra et al. shown in a study of 173 patients surgically treated for AA that the intensity of inflammation is closely associated to elevated levels of CRP<sup>14</sup>.

Acute appendicitis is the leading cause of acute abdominal pain necessitating emergency surgery both locally and worldwide. The diagnosis becomes more difficult when dealing with patients at extreme of ages and women. A long-standing goal of researchers has been to develop tests that would facilitate earlier diagnosis and treatment of acute appendicitis and thereby decrease morbidity and mortality from this disease. For a poor patient of country like Pakistan there is a need to adopt a cheaper, safer and accurate procedure. CRP is a diagnostic test that is non-invasive, easily performed, cost effective and less hazardous. Measurement of CRP levels along with other standard tests will undoubtedly increase surgeons' confidence in the diagnosis of acute appendicitis and lower the negative appendectomy rate, which is a burden not only on our overburdened hospitals but also on the patient and society at large because surgery has socio-economic effects in the form of missed workdays and decreased productivity. Negative appendectomy should be avoided to prevent postoperative consequences such as intestinal blockage from adhesions and issues with female fertility. This study's objective was to assess the precision of C-reactive protein measurements in the diagnosis of acute appendicitis using histology as the reference method.

## MATERIAL AND METHODS

The department of surgical at Khyber Teaching Hospital (KTH) in Peshawar undertook this descriptive cross-sectional study. Six months, from February to August 2019, were spent doing the study. Taking into account the prevalence of acute appendicitis (22.71%), the sample size was 216. error margin of 10%, and confidence interval of 95%.

The method of sample gathering utilized was non-probability sequential sampling. We included in the research any patient with acute appendicitis lasting 1-2 days who was between the ages of 18 and 45, regardless of gender. While individuals with illnesses that affect CRP levels, such as autoimmune disorders, acute coronary syndrome, aortic aneurysm/dissection, acute cholecystitis, acute pancreatitis, pelvic inflammatory disease, chronic liver disease, pneumonia, burn damage, malignancies, and urinary tract infection, etc.

Following receipt of informed written consent, all patients satisfying the inclusion criteria were contacted after receiving approval from the hospital's ethical committee and the CPSP research committee. Through the Out Patient Department (OPD) or Emergency Room (ER) of Khyber Teaching Hospital, Peshawar, all 216 patients with acute appendicitis (as per operational criteria) were included in the research. The history, clinical examination, and regular laboratory tests, such as the total leucocyte count (TLC) and differential leucocyte count (DLC) on admission, were used to make the diagnosis of acute appendicitis. All of these patients were given Nil by Mouth to prepare them for emergency surgery, and baseline testing included HBsAg and AntiHCV viral serology as well as pre-operative blood CRP levels (Liver function tests, renal function tests and serum electrolytes). Following preparation, every patient on the emergency list had surgery. A sample of the excised appendix was collected and sent for histology as part of the intraoperative results. An experienced pathologist with at least five years of experience completed all the histopathology reports. Third-year students under the supervision of a CPSP fellow supervisor with at least five years of experience carried out all appendectomies.

SPSS 20 was used to analyse all the data. Age, the length of the symptoms, and CRP are examples of continuous variables for which mean and standard deviation were determined. For categorical variables such as gender, CRP, and histopathological

results, frequencies and percentages were calculated. Tables and graphs were used to display all of the findings.

## RESULTS

In this study, the age distribution of the 216 patients was examined, and it was found that 146 (68%) of the patients were between the ages of 18 and 30 and 69 (32%), between the ages of 31 and 45. With an SD of 12.311 years, the mean age was 48 (Table 1).

Table 1: Patients were distribution age-wise

Age	Frequency	Percentage
18-30 Years	146	68%
31-45 Years	69	32%
Total	216	100%

Analysis of the gender distribution among 216 patients revealed that 119 (55%) of the patients were male and 97 (45%) were female (Table 2).

Table 2: Patients were distribution gender-wise

Gender	Frequency	Percentage
Male	119	55%
Female	97	45%
Total	216	100%

When 216 individuals with acute appendicitis had their histology examined, it was discovered that 210 (97% of the patients) had the condition whereas just six (3% of the patients) did not. While 32 (15%) individuals had a negative CRP test for acute appendicitis, 184 (85%) patients had a positive test for it (Table 3 & 4).

Table 3: Acute Appendicitis on Histopathology

Histopathology	Frequency	Percentage
Positive	210	97%
Negative	6	3%
Total	216	100%

Table 4: Acute Appendicitis on C Reactive Proteins

CRP Findings	Frequency	Percentage
Positive	184	85%
Negative	32	15%
Total	216	100%

Histopathology was used as the gold standard for the analysis of the diagnostic accuracy of acute appendicitis, and CRP showed sensitivity of 85.71%, specificity of 33.33%, positive predictive value of 97.25%, negative predictive value of 84.25%, and total diagnostic accuracy of 84.25%. (Table 5).

Table 5: CRP Vs Histopathology

Parameters		Histopathology		Total
		Positive (+)	Negative (-)	
CRP	Positive (+)	A 180(94%) TP	B 4 (6%) FN	184(85%)
	Negative (-)	C 30(88%) FP	D 2(12%) TN	32(15%)
	Total	210(97%)	6(3%)	216

$$\text{Sensitivity} = 180/180 + 30 * 100 = 180/210 * 100 = 85.71\%$$

$$\text{Specificity} = 2/2 + 4 * 100 = 2/6 * 100 = 33.33\%$$

$$\text{Positive predictive value} = 180/180 + 4 * 100 = 180/184 * 100 = 97.82\%$$

$$\text{Negative predictive value} = 2/2 + 30 * 100 = 2/40 * 100 = 6.25\%$$

$$\text{Diagnostic Accuracy} = 180 + 2/216 * 100 = 182/216 * 100 = 84.25\%$$

## DISCUSSION

According to our analysis, the mean age was 48 years, with an SD of 12.311. Male patients made up 55% of the total population, while female patients made up 45%. Histopathology was used as

the gold standard in the analysis of the diagnostic accuracy of acute appendicitis CRP; the results showed that the test's sensitivity was 85.71%, specificity was 33.33%, positive predictive value was 97.25%, negative predictive value was 184.25%, and overall diagnostic accuracy was 84.25%.

Similar findings were found in a different study which involved 173 patients who underwent surgical treatment for AA. The study's findings revealed that the degree of inflammation is directly correlated with elevated CRP levels, with diagnostic accuracy ratings of 83.2%, sensitivity of 85.1%, specificity of 72%, and positive predictive value of 94.7%<sup>14</sup>. Both the pre-operative leukocyte count and serum CRP were considerably elevated in this study's population of patients with histologically verified acute appendicitis ( $P=0.025$  and  $P0.001$ , respectively). 19.2% of appendicitis examinations turned up nothing ( $n=15$ ), which is consistent with earlier results. Within eight hours of tissue damage, CRP concentration rises, peaks in the next 24 to 48 hours, and then stays high as long as infection or tissue loss is present<sup>15, 16</sup>. As the initial inflammatory process subsides, the serum CRP levels rapidly decreases because of its short half-life (4–7 hours)<sup>17</sup>. Bhopal FG et al<sup>21</sup> found that TLC was a good indicator of acute appendicitis but CRP proved to be far superior in predicting complicated cases like perforation/gangrene or abscess of the appendix. The sensitivity and specificity of serum CRP was 98% and 87.5% respectively with a predictive value (PV) of positive test almost 98% and that negative test in the range of 87.5%. They advocated that if C-reactive protein can be added to the already existing laboratory tests then the diagnosis of acute appendicitis with clinically suggestive signs can be made with a fair degree of accuracy and unnecessary appendectomies can be avoided. Conflicting findings have been found in the several publications that have examined the effectiveness of CRP in raising acute appendicitis diagnosis accuracy. Serial CRP measurements can increase the precision of the acute appendicitis diagnosis, according to a multivariate analysis by Oosterhuis et al. Other reports refuted this assertion<sup>18, 19</sup>. Furthermore, a 1997 meta-analysis of 22 publications found that CRP is a test with medium accuracy for identifying acute appendicitis<sup>20</sup>.

## CONCLUSION

Our study concludes that the diagnostic accuracy C-reactive protein levels was 84.25% with sensitivity 85.71%, specificity 33.33%, Positive predictive value 97.25%, Negative predictive value 184.25% by taking histopathology.

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