



# DIAGNOSTIC VALUE OF CRP IN PATIENTS OF ACUTE APPENDICITIS

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## ABSTRACT:

**Objective:** To determine the diagnostic utility of elevated CRP for the diagnosis of acute appendicitis by taking histopathology as gold standard.

**Study design:** Descriptive study.

**Place and Duration of Study:** Department of Surgery, CMH, Rawalpindi from January 2020 to December 2020. 145 patients suspected of having acute appendicitis were included in the study.

**Material and Methods:** Patients suspected of acute appendicitis who met the inclusion and exclusion criteria were included. Brief clinical and demographic data was taken. Baseline blood samples were sent to the hospital laboratory for the measurement of C reactive protein level prior to surgery. Appendectomy was performed and histopathology was taken as gold standard for the diagnosis of acute appendicitis. Diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of were calculated for elevated CRP.

**Result:** Out of 145 patients, 80 (55.2%) were male and 65 (44.8%) were female. Mean age was 41.8±8.6 years. Diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of elevated CRP for the diagnosis of acute appendicitis were 88.2%, 89.8%, 81.4%, 95.4% and 64.7%.

**Conclusion:** Elevated C-reactive protein level is an accurate predictor for the diagnosis of acute appendicitis. It offers an affordable and reliable alternative diagnostic technique.

**Keywords:** Acute appendicitis, elevated C reactive protein and histopathology.

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## INTRODUCTION

Appendicitis remains one of the most common sources of community-acquired intra-abdominal infections in patients presenting with acute abdomen. Appendectomy is the most common abdominal surgical procedure done all over the world.<sup>1</sup> Despite the advancement in the diagnostic and laboratory methods accurate detection remains an enigmatic challenge for the surgeons involved in the care.<sup>2</sup> The diagnostic difficulties can lead to perforation, peritonitis and abscess formation. Whereas negative appendectomy account for about 15-30%.<sup>3</sup> Classically, acute appendicitis is diagnosed in patients presenting with abdominal pain radiating to the right iliac fossa, nausea and signs of local peritonitis.<sup>4</sup> However, at times the clinical presentations are atypical leading to a misdiagnosis. Timely recognition and treatment of the condition is necessary to prevent adverse outcomes and reduction of morbidity.<sup>5</sup>

Several diagnostic tests, scoring systems and imaging modalities have been introduced to diagnose acute appendicitis. However, the literature shows significant variation of diagnostic accuracy.<sup>6</sup> In this background, C-reactive protein (CRP) more recently has been proposed for laboratory evaluation in acute appendicitis. It is an acute phase reactant synthesized by liver and a marker of inflammation.<sup>7</sup> Normal serum concentration of CRP is less than 10 mg/l.<sup>8</sup> CRP can be measured in serum 6–12 h after the onset of symptoms in response to interleukin-6 and rapidly rises 10 to 1000 times. It is a non-specific inflammatory marker that can be added to the already existing laboratory tests to improve accuracy for early diagnosis of appendicitis hence reducing unnecessary operations.<sup>9</sup> Furthermore, it is easy and economical when health care system is driven by cost parameters. A study done by Asfar et al. eISSN1303-5150

included 78 patients who underwent appendectomy and found specificity and sensitivity of raised serum CRP to be 86.6% and 93.6% in diagnosing acute appendicitis.<sup>10</sup>

The current study is designed to assess diagnostic utility of CRP for the detection of acute appendicitis. Early diagnosis of appendicitis with CRP would reduce morbidity and mortality in developing countries like ours. Finally, this study would potentially offer new information to clinician that can influence clinical practice and help in replacing expensive diagnostic modalities.

## MATERIALS AND METHODS

A cross sectional study from 01-01-2020 to 31-12-2020 at Department of Surgery, CMH Rawalpindi. 145 cases between 20-60 of either gender who presented with suspected acute appendicitis were included. Consent was obtained from the patients after full disclosure. All data obtained for the study was kept confidential throughout the study period. Provisional diagnosis of acute appendicitis was made by history and clinical examination by consultant surgeons based on the presence of direct tenderness in the right lower quadrant (VAS>4), percussion and rebound tenderness, pyrexia, anorexia, nausea and vomiting for more than 6 hours. Patients admitted for interval appendectomy following recurrent appendicitis or appendicular mass previously treated conservatively, comorbidities (diabetes mellitus type II, hypothyroidism, chronic obstructive pulmonary disease, chronic kidney disease), concomitant conditions where CRP is elevated (rheumatoid arthritis, SLE, glomerulonephritis, gout, inflammatory bowel disease, malignant neoplasm, myocardial infarction), gynecological causes like ovarian cyst, ectopic pregnancy, ovarian torsion, pelvic inflammatory disease, tubo-



ovarian abscess and urological causes like urinary calculi, urinary tract infections were excluded.

Suspected patients with acute appendicitis underwent appendectomy performed by general surgery faculty and residents. Blood sample was collected after aseptic measures with the help of paramedical staff and sent to the hospital laboratory for serum C-reactive protein levels. All patients having CRP  $\geq 6$  mg/l will be labeled as elevated CRP. The open approach used a traditional oblique or transverse incision over McBurney's point. All patients received a preoperative dose of antibiotics as per hospital protocol. Postoperative antibiotics administration varied and was determined by the surgeon according to the surgical findings. The patients were given non-narcotic analgesia as first medication for postoperative pain control, but narcotic analgesics were liberally used if pain was not optimally controlled. They were given oral liquids a few hours after surgery. Gradually, once they were fully awake and showed no signs of nausea or abdominal pain, the diet was progressed as tolerated. Patients were discharged home once they were afebrile, had good pain control and tolerated soft diet. The histopathology report was considered as the final diagnosis.

Data was analyzed by using SPSS Version 22. Mean and standard deviation were calculated for quantitative data. Mean  $\pm$  SD will be reported for the normally distributed while median (IQR) will be reported for the non-normality distributed quantitative variables. Frequency and percentages were calculated for qualitative variables. Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the CRP was calculated taking histopathology as gold standard for diagnostic confirmation.

**True positive (TP)**- CRP values  $\geq 6$  mg/l and histopathology report of excised appendix specimen shows acute appendicitis.

**False positive (FP)**- CRP values  $\geq 6$  mg/l and histopathology report of excised appendix specimen did not show acute appendicitis.

**True negative (TN)**- CRP values  $< 6$  mg/l and histopathology report of excised appendix specimen did not show acute appendicitis.

**False negative (FN)**- CRP values  $< 6$  mg/l and histopathology report of excised appendix specimen shows acute appendicitis.

Sensitivity  $SN = (TP / (TP + FN)) \times 100$

Specificity  $SP = (TN / (TN + FP)) \times 100$

Positive predictive value

$PPV = (TP / (TP + FP)) \times 100$

Negative predictive value

$NPV = (TN / (TN + FN)) \times 100$

Diagnostic accuracy

$= (TP + TN / (TP + FN + TN + FP)) \times 100$ .

## RESULTS

There were 145 cases of suspected appendicitis that were included in our study. The mean age of the patients was  $41.8 \pm 8.6$  years (range 24–54 years). There were 80 males (55.2%) and 65 females (44.8%). Majority of patients, 50 (34.5%) were aged between 41-50 years, 41 (28.3%), 34 (23.4%) and 20 (13.8%) belonged to age group 20-30 years, 34-40 years and 51-60 years respectively. (Table-1)

Pathologic review demonstrated that the 81.4% and 18.6% were positive and negative for acute appendicitis. Furthermore, 111 (76.6%) patients who had elevated CRP were found to have acute appendicitis. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of elevated CRP came out to be 89.8%, 81.4%, 95.4%, 64.7% and 88.2% respectively. (Table-2-3)

## DISCUSSION

Appendectomy is a common surgical intervention for acute appendicitis and removal of the appendix is the gold standard

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of treatment.<sup>11-12</sup> Acute appendicitis requires timely and accurate diagnosis to prevent irreversible progression of disease eventually leading to perforation. The symptoms range from mild symptoms to signs of generalized peritonitis.<sup>13-14</sup> In pursuit of these goals, RIPASA and Modified ALVARADO scores were designed which make use of clinical history, physical examination and laboratory findings for the diagnosis of acute appendicitis. Moreover, since the clinical variables have low likelihood to aid in the diagnosis of acute appendicitis emphasizing the need of biochemical testing. Literature review showed that elevated C-reactive protein has a potential role.<sup>15-17</sup>

In this study, the CRP has a sensitivity and specificity of 89.8% and 81.4%. This is comparable to the study done by Asfar et al<sup>10</sup> and Jaiswal et al<sup>18</sup> where sensitivity was (91.6% and 86.6%) and specificity was (93.6% and 81.8%). Sengupta et al. study concluded sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for C-reactive protein (CRP) alone was higher in comparison both WBC and CRP when combined.<sup>19</sup> Sher et al study showed that 104(77.04%) were true positive, 5 (3.70%) were false positive, 8 (5.93%) were true negative and 18 (13.33%) were false negative with a sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate of 92.86%, 78.26%, 94.39%, 69.23% and 90.37%.<sup>20</sup> In another study<sup>21</sup> these values were 93.42%, 79.17%, 93.42%, 79.17% and 59%, the only difference with our results was lower diagnostic accuracy. Different authors believe that elevated CRP improved the detection of acute appendicitis as seen in diagnostic accuracy.<sup>22-25</sup> The results were contrary with one study<sup>6</sup> showing these findings as 75%, 72%, 90%, 46% and 75.5%, however it cannot be used to replace the

clinical judgement of a surgeon. Majority of the studies concluded that normal CRP value probably indicates a normal non-inflamed appendix.

Patients presenting with typical clinical findings suggestive of acute appendicitis along with elevated CRP can aid and support the surgeon's diagnosis and hence avoid chances of misdiagnosis especially due to atypical presentations. Therefore, we believe that the normal CRP levels of the patients closely correspond to normal appendix on histopathological examination. C-reactive protein, an acute phase protein, can be measured in the serum 6–12 h after the onset of inflammation and can be used as a diagnostic screening tool, as a marker of disease activity. Physiologically, CRP has a potential role in boosting the cell-mediated immunity and is always associated with pathological condition. Quantitative assessment of CRP levels yields more information than qualitative assessment as it is more economical in a surgical setup. Clinical diagnosis is crucial in ruling out alternative diagnoses and other conditions which might give a false positive value on CRP estimation. Hence, it is the earliest to measure inflammatory marker with universal availability, cost-effectiveness and is rapidly emerging as a diagnostic tool with proven use for preoperative diagnosis of acute appendicitis.

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## CONCLUSION

CRP can be a good diagnostic aid and should be measured routinely in patients with suspected diagnosis of acute appendicitis. Elevated serum CRP levels support the surgeon's clinical diagnosis.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

**TABLE 1: CHARACTERISTICS OF PATIENTS WITH ACUTE APPENDICITIS**

DEMOGRAPHY		NUMBER	PERCENTAGE
AGE	20-30 YEARS	41	28.3%
	31-40 YEARS	34	23.4%
	41-50 YEARS	50	34.5%
	51-60 YEARS	20	13.8%
GENDER	MALE	80	55.2%
	FEMALE	65	44.8%
DURATION OF SYMPTOMS	<48 HOURS	101	69.7%
	>48 HOURS	44	30.3%
TEMPERATURE	<38° C	78	53.8%
	>38° C	67	46.2%
ACUTE APPENDICITIS ON CRP (≥6 MG/L)	POSITIVE	111	76.6%
	NEGATIVE	34	23.4%
ACUTE APPENDICITIS ON HISTOPATHOLOGY	POSITIVE	118	81.4%
	NEGATIVE	27	18.6%

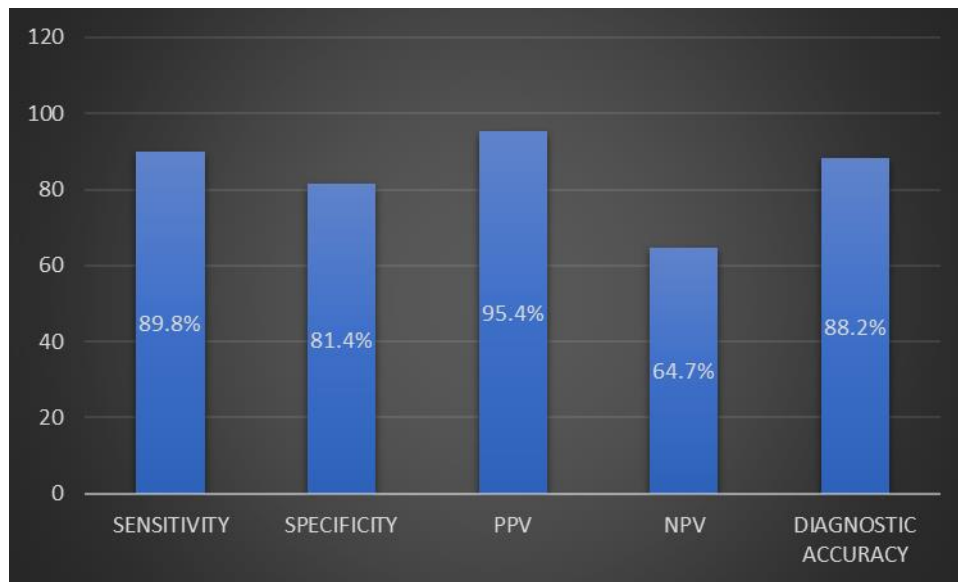
**TABLE 2: RESULTS OF ELEVATED CRP TAKING HISTOPATHOLOGY AS GOLD STANDARD**

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VARIABLE		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
ELEVATED CRP	POSITIVE	106(TP)	05(FP)	111
	NEGATIVE	12(FN)	22(TN)	34
TOTAL		118	27	145



**TABLE 3: SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES AND DIAGNOSTIC ACCURACY OF THE ELEVATED CRP TAKING HISTOPATHOLOGY AS GOLD STANDARD**



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