

Evaluate Diagnostic Efficacy of Serum C-Reactive Protein Levels as a Marker for Predicting Acute Appendicitis.

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ABSTRACT

Background: Acute appendicitis is one of the most frequently encountered surgical emergencies, but the diagnosis can continue to be difficult due to variable clinical presentations and the inability to rely on any single laboratory test. The C-reactive protein (CRP) is an easily obtained and inexpensive inflammatory marker that could help identify patients with acute appendicitis. In the present study, the diagnostic performance of serum CRP was evaluated in comparison with histopathology as reference standard.

Objective: To determine the diagnostic accuracy of serum C-reactive protein levels for predicting acute appendicitis, taking histopathological examination as the gold standard.

Methods: This cross-sectional validation study was conducted in the Department of General Surgery, Rawalpindi Teaching Hospital, Rawalpindi, from 16 February 2026 to 16 June 2026. The patients of the study were 87, whose age range was 11-75 years and they were selected by the non-probability consecutive sampling technique with a presumed diagnosis of acute appendicitis. Pre-operative levels of serum CRP were analysed, and those levels >10 mg/L were taken as positive. All patients had an appendectomy performed and the appendix were examined histopathologically. The sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy and receiver operating characteristic analysis were calculated.

Results: Histopathology confirmed acute appendicitis in 70 (80.5%) patients. At the predefined CRP cutoff of >10 mg/L, serum CRP demonstrated a sensitivity of 80.0%, specificity of 82.4%, positive predictive value of 94.9%, negative predictive value of 50.0%, and overall diagnostic accuracy of 80.5%. The area under the receiver operating characteristic curve was 0.862, indicating good discriminatory performance. The ROC-derived optimal cutoff was approximately 12.4 mg/L, with a sensitivity of 78.6% and specificity of 88.2%.

Conclusion: Serum CRP demonstrated good diagnostic performance in patients with suspected acute appendicitis, particularly because of its high positive predictive value. However, its relatively low negative predictive value indicates that a normal CRP level cannot reliably exclude appendicitis. CRP should therefore be interpreted alongside clinical evaluation, scoring systems, and appropriate imaging rather than being used as a standalone diagnostic test.

Keywords: Acute appendicitis; C-reactive protein; CRP; diagnostic accuracy; histopathology; sensitivity; specificity.

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1. INTRODUCTION

Acute appendicitis is still one of the most common conditions for which a person has an acute abdominal complaint that does require an emergency surgical evaluation. Importance of early diagnosis and prompt treatment because delayed diagnosis can result in complications like perforation, abscess, peritonitis, long hospital stay and higher morbidity. Although there has been progress in the diagnosis of acute appendicitis, it remains challenging to diagnose because the clinical presentation often differs among patients and typical symptoms are not always present. Common presenting features are described as right lower abdominal pain, fever, nausea, and vomiting by the study protocol, and the diagnosis may not always be made by clinical findings (1-3).

The diagnosis of acute appendicitis is typically made based on history, physical examination, laboratory tests, clinical scoring systems and imaging. Laboratory tests typically include total leukocyte count, cell percentage of neutrophils and inflammatory markers including C-reactive protein. Diagnostic imaging modalities such as ultrasonography and computed tomography can increase the level of confidence in the diagnosis, but may not be widely available or affordable and are not without radiation exposure and operator dependence in some settings. Thus, the need for simple, low-cost, and readily accessible laboratory indicators that can aid clinical decision making, especially in low-resource settings, remains (4-6).

C-reactive protein is an acute phase reactant, which is produced mainly in the liver under the stimulation of inflammatory cytokines. It is a marker of systemic inflammation, and its levels rise during infection, tissue damage and inflammation. A measurable rise in serum CRP levels is found in acute appendicitis and higher concentrations have been shown to be correlated with the degree of inflammatory burden in acute appendicitis. The CRP, however, is not specific for any disease and may be raised in several other abdominal, infectious and inflammatory diseases. This restricts its role as a standalone marker, which emphasizes the need to assess its performance in relation to a proven reference standard. A serum CRP > 10 mg/L is used as a positive diagnosis for acute appendicitis in the study protocol (7-9).

A number of previous studies have found that CRP is sensitive, but less so than anticipated, and that it has variable specificity in patients with suspected appendicitis. These variations may be due to differences in patient population, symptom duration, inflammatory severity, assay methods, and selected cutoff values. Another possible reason is that CRP may not be sensitive enough early on in the process of appendiceal inflammation when time is too short for a large systemic inflammatory reaction to have occurred. Thus, measuring CRP in the local patient population is clinically relevant and important to determine if a commonly used cutoff can differentiate patients with histopathologically confirmed appendicitis from those who do not have the disease. One aspect of the protocol specifically highlights the continuing uncertainty of the standalone diagnostic value of CRP and the need to define an appropriate predictive cutoff in the local context (10, 11).

Accordingly, the present study was undertaken to evaluate the diagnostic efficacy of serum C-reactive protein in patients undergoing surgery for suspected acute appendicitis at Rawalpindi Teaching Hospital. Histopathological examination of the excised appendix was used as the gold standard, with acute appendicitis defined by the presence of transmural neutrophilic infiltration. The study aimed to determine the sensitivity, specificity, positive predictive value, negative predictive value, overall diagnostic accuracy, and receiver operating characteristic performance of serum CRP, thereby clarifying its potential role as a supportive marker in the diagnostic assessment of acute appendicitis.

2. METHODOLOGY

This cross-sectional validation study was conducted in the Department of General Surgery, Rawalpindi Teaching Hospital, Rawalpindi, from 16 February 2026 to 16 June 2026. The study was designed to determine the diagnostic accuracy of serum C-reactive protein (CRP) for predicting acute appendicitis, with histopathological examination of the resected appendix used as the reference standard. A total of 87 patients were enrolled through non-probability consecutive sampling. The sample size of 87 was based on a 95% confidence level, an anticipated frequency of acute appendicitis of 81%, expected CRP sensitivity of 76% and specificity of 87.5%, with a 10% margin of error. The research was approved by the College of Physicians and Surgeons Pakistan, Research Evaluation Unit, under Ref. No. CPSP/REU/SGR-2022-126-14499, dated 16 February 2026. Written informed consent was obtained from all participants, and confidentiality of patient information was maintained throughout the study.

Patients with clinical symptoms indicative of acute appendicitis, such as shifting right lower abdominal pain, fever, nausea or vomiting, Alvarado score >5, and scheduled for appendectomy were included. Written informed consent was obtained prior to participating. Patients who had other inflammatory or intra-abdominal disease that could affect the level of CRP, such as acute cholecystitis, pancreatitis, perforated peptic ulcer or diverticulitis, were excluded. Other exclusion criteria were recent major trauma, surgery or burns within the last 4 weeks, chronic inflammatory or autoimmune disorders, active malignancy, antibiotic use within the last 72 hrs, chronic renal or hepatic disease, pregnancy or lactation.

Demographic and clinic data were collected on a data collection form after enrolment. The variables studied were age, sex, BMI, living area, socioeconomic status, duration of symptoms, pain score, Alvarado score, ASA classification, smoking status, alcohol use, hypertension, diabetes mellitus, anemia and family history of appendicitis. Venous blood was drawn in

normal sterile condition and taken to the hospital laboratory for routine investigations and quantitative determination of the serum CRP. The serum CRP was measured in mg/L and values $>10\text{mg/L}$ were considered to be positive CRP and values $\leq 10\text{mg/L}$ were considered to be negative CRP.

All of the patients included later were then subjected to appropriate anesthesia for appendectomy. Appended excised and sent to histopathology department. Histopathology was believed to be the gold standard and the presence of transmural neutrophilic infiltration was thought to confirm acute appendicitis. The out-come of the CRP test was then correlated with histopathology and the results were considered as true negative, true positive, false positive or false negative. Sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy were calculated using the resulting 2×2 diagnostic table.

All data were entered and analyzed in IBM SPSS Statistics version 25.0. Quantitative variables were summarised as mean $\pm$ standard deviation or median (interquartile range) as appropriate and categorical variables were summarised as frequencies and percentages. The sensitivity, specificity, PPV, NPV and overall accuracy of serum CRP for the diagnosis was evaluated against histopathology. To measure the AUC and the discriminatory ability of CRP at various cut-off points, ROC analysis was carried out. The diagnostic performance was further evaluated in a stratification model that included pertinent clinical and demographic variables. A p-value <0.05 was considered statistically significant.

3. RESULTS

All 87 patients with clinical features suggestive of acute appendicitis were included in the analysis. The mean age of the participants was 31.84 ± 13.26 years, with ages ranging from 12 to 72 years. There were 56.3% males. The mean body mass index was $24.71 \pm 3.82 \text{ kg/m}^2$. The median symptom duration prior to presentation was 24 hours (IQR 14–36) and the mean Alvarado score was 7.16 ± 1.21 .

Table 1. Demographic and clinical characteristics of study participants (n=87)

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Variable	n (%) / Mean $\pm$ SD
Age, years	31.84 ± 13.26
11–20 years	19 (21.8)
21–30 years	27 (31.0)
31–40 years	20 (23.0)
>40 years	21 (24.1)
Gender	
Male	49 (56.3)
Female	38 (43.7)
BMI, kg/m^2	24.71 ± 3.82
Pain score	7.28 ± 1.31
Alvarado score	7.16 ± 1.21
Duration of symptoms, hours, median (IQR)	24 (14–36)
ASA classification	
ASA I	59 (67.8)
ASA II	24 (27.6)
ASA III	4 (4.6)
Residence	
Rural	30 (34.5)
Urban/semi-urban	57 (65.5)

The majority of patients were ASA I (67.8%) which meant that most did not have significant underlying systemic disease. Less were hypertensive, had diabetes or anemia, or had other pertinent risk factors. These features were then taken into account when stratified testing of the performance of CRP was conducted.

Table 2. Socioeconomic characteristics, risk factors, and comorbidities (n=87)

Variable	n (%)
Socioeconomic status	
Low	29 (33.3)
Middle	47 (54.0)
High	11 (12.6)
Smoking/tobacco use	17 (19.5)
Alcohol use	3 (3.4)
Hypertension	11 (12.6)
Diabetes mellitus	8 (9.2)
Anemia	13 (14.9)
Family history of appendicitis	15 (17.2)

Patients with histopathologically confirmed appendicitis had a significantly elevated CRP level in the serum. Patients with positive histopathology had a median CRP level of 28.60 mg/L (IQR: 17.40–52.30) whereas patients with negative histopathology had a median CRP level of 7.20 mg/L (IQR: 4.10–11.80). Overall, 59 patients (67.8%) had CRP levels above the predefined cutoff of 10 mg/L.

Histopathological examination confirmed acute appendicitis in 70 of 87 patients (80.5%), whereas 17 patients (19.5%) had negative histopathological findings.

Table 3. Serum CRP levels and histopathological findings

Variable	Result
Overall CRP, mg/L, median (IQR)	24.10 (12.30–44.70)
CRP in positive histopathology, mg/L	28.60 (17.40–52.30)
CRP in negative histopathology, mg/L	7.20 (4.10–11.80)
p-value	<0.001
CRP status (>10 mg/L)	
Positive	59 (67.8%)
Negative	28 (32.2%)
Histopathology	
Acute appendicitis present	70 (80.5%)
Acute appendicitis absent	17 (19.5%)

Among 17 patients who did not have histologically positive appendicitis, 14 had a negative CRP, and 3 had a false positive CRP. Out of 70 patients with histologically positive appendicitis, 56 were correctly identified with CRP, and 14 had CRP ≤10 mg/L.

Table 4. Diagnostic performance of serum CRP using histopathology as the gold standard

CRP result	Histopathology positive	Histopathology negative	Total
CRP positive (>10 mg/L)	56 (TP)	3 (FP)	59
CRP negative (≤10 mg/L)	14 (FN)	14 (TN)	28
Total	70	17	87
Diagnostic parameter	Value		
Sensitivity	80.0%		
Specificity	82.4%		
Positive predictive value	94.9%		
Negative predictive value	50.0%		
Diagnostic accuracy	80.5%		

Serum CRP showed a sensitivity of 80.0% and specificity of 82.4% with a pre-defined cutoff of >10 mg/L for the diagnosis of acute appendicitis. The positive predictive value was also relatively high at 94.9%, meaning that patients with elevated

CRP had a high risk of having histopathologically confirmed appendicitis. The negative predictive value was 50.0%, meaning that if a child's CRP was normal or only slightly elevated, it would not provide reassurance of the absence of the condition. The overall diagnostic accuracy was 80.5%. There was a reasonable consistency in the diagnostic performance of CRP following stratification based on major demographic and clinical variables. Accuracy was better with presentation more than 24 hours after onset of symptoms and was slightly lower with presentation within 24 hours.

Table 5. Stratified diagnostic accuracy of serum CRP for acute appendicitis

Variable	Sensitivity (%)	Specificity (%)	Accuracy (%)
Age			
≤30 years	78.8	83.3	79.5
>30 years	81.1	81.8	81.3
Gender			
Male	80.6	83.3	81.0
Female	79.4	81.8	78.9
BMI			
<25 kg/m ²	81.1	84.6	81.8
≥25 kg/m ²	78.8	75.0	78.6
Duration of symptoms			
≤24 hours	73.5	81.8	75.6
>24 hours	86.1	83.3	85.7
Diabetes mellitus			
Yes	75.0	100.0	75.0
No	80.6	81.3	80.8
Smoking			
Yes	76.9	75.0	76.5
No	80.7	84.6	81.4

The receiver operating characteristic curve (ROC) further showed that serum CRP had good discriminatory ability in the diagnosis of histopathologically confirmed acute appendicitis. The area under the ROC curve was 0.862 (95% CI: 0.772–0.952, $p < 0.001$). The analysis proposed a threshold value for the CRP of about 12.4mg/L with 78.6% sensitivity and 88.2% specificity.

Table 6. ROC analysis of serum CRP for prediction of acute appendicitis

ROC parameter	Result
Area under the curve (AUC)	0.862
Standard error	0.046
95% CI	0.772–0.952
p-value	<0.001
Protocol-defined cutoff	>10 mg/L
Optimal ROC-derived cutoff	12.4 mg/L
Sensitivity at optimal cutoff	78.6%
Specificity at optimal cutoff	88.2%

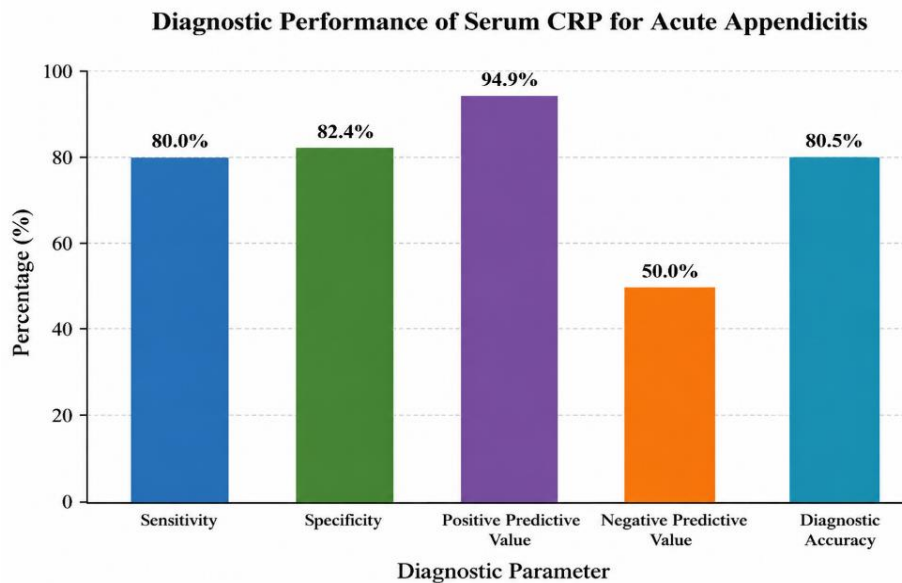


Figure 1. Diagnostic performance of serum C-reactive protein in predicting acute appendicitis.

Figure 1. Diagnostic performance of serum C-reactive protein in predicting acute appendicitis, showing sensitivity (80.0%), specificity (82.4%), positive predictive value (94.9%), negative predictive value (50.0%), and overall diagnostic accuracy (80.5%) using histopathology as the gold standard.

4. DISCUSSION

The present study evaluated the diagnostic performance of serum C-reactive protein for identifying acute appendicitis, using histopathological examination as the reference standard. Among 87 patients, histopathology confirmed acute appendicitis in 70 (80.5%), while 17 (19.5%) had negative histopathological findings. Serum CRP levels were substantially higher in patients with confirmed appendicitis, with a median value of 28.60 mg/L compared with 7.20 mg/L among patients without appendicitis. At the predefined cutoff of >10 mg/L, CRP showed a sensitivity of 80.0%, specificity of 82.4%, positive predictive value of 94.9%, negative predictive value of 50.0%, and overall diagnostic accuracy of 80.5%. These findings indicate that serum CRP is a useful supportive marker in patients with suspected acute appendicitis, particularly when interpreted alongside clinical assessment and histopathological findings (12, 13).

The high sensitivity detected in this study indicates that CRP may be useful to detect a significant number of patients with histologically confirmed appendicitis. The presence of 14 false-negative cases shows, however, that the absence of a positive test result for CRP should not exclude the disease, although a normal or only mildly elevated CRP concentration is associated with a low risk of the disease. This might be especially applicable in early presentation after symptoms begin, and before a significant elevation of CRP is achieved by the systemic inflammatory response. In the current study, the diagnostic performance was relatively better for the patients with symptoms duration >24 hours, which highlighted the biological correlation of the duration of inflammation with the acute-phase reactants elevation. For this reason, CRP should be interpreted along with history, physical examination, clinical scoring systems, and imaging and not as a standalone diagnostic test (14-16).

The specificity of 82.4% suggests that serum CRP also had a relatively good discriminatory power for patients with no histopathologically proven appendicitis. The 3 patients were considered as false positive giving a high positive predictive value of 94.9%. Clinically, this is significant because if the patient has clinical signs and symptoms that are compatible with acute appendicitis, and the CRP is very elevated, it can help support the diagnosis of acute appendicitis and make prompt decisions for surgery. However, CRP is not a specific marker of inflammation and can be elevated in a variety of infectious, inflammatory and tissue-injury states. For this reason, the exclusion criteria used in the present study were as significant as possible in minimizing the possibility of variability in serum CRP due to other diseases that could independently elevate the serum CRP level (17).

A receiver operating characteristic analysis confirmed the value of serum CRP in diagnosis. The area under the curve was 0.862 suggesting good ability to discriminate between histopathologically proven appendicitis and negative appendectomy. The ROC derived optimal cut-off level of 12.4 mg/L yielded a sensitivity of 78.6% and specificity of 88.2%, indicating that a slightly higher threshold for CRP could achieve a higher specificity, while sacrificing some sensitivity. The preset threshold of >10 mg/L, however, was still clinically realistic and gained a well-balanced overall diagnostic performance in the present study. Overall, it is important to note that the negative predictive value of 50.0% is lower than is regarded as

normal, which means that a negative CRP should not exclude the diagnosis of appendicitis despite a high clinical suspicion (18-20).

This study has several strengths: The sensitivity, specificity, predictive values, diagnostic accuracy and ROC characteristics were calculated directly, with histopathology serving as the reference standard. It should be noted however, that there are some restrictions. This study was carried out in one surgical centre and involved a relatively small number of patients (87), which may make the results of this study non-generalisable. Also, non-probability consecutive sampling can lead to selection bias. Additionally, the level of CRP may fluctuate depending on the length of inflammation, its severity, and repeated measurements were not assessed. Future multicenter studies with larger patient cohorts should evaluate the role of CRP in conjunction with the leukocyte count, neutrophil percentage, Alvarado score and imaging results for the creation of more precise algorithms to diagnose acute appendicitis..

5. CONCLUSION

Serum C-reactive protein demonstrated good diagnostic performance for predicting acute appendicitis, with a sensitivity of 80.0%, specificity of 82.4%, positive predictive value of 94.9%, and overall diagnostic accuracy of 80.5% at a cutoff of >10 mg/L. The ROC analysis also showed good discriminatory ability, with an AUC of 0.862. However, the relatively low negative predictive value indicates that a normal CRP level cannot reliably exclude acute appendicitis. Serum CRP should therefore be used as a supportive diagnostic marker in combination with clinical assessment, scoring systems and appropriate imaging, rather than as a standalone test.

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