

Diagnostic Accuracy of C-Reactive Protein in Acute Appendicitis

Waqas Ranjha, Hassan Tariq*, Shahum Khan, Shafqat Hussain, Ahmed Bilal**, Muhammad Sajid Hussain***

Department of Surgery, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan,

*Department of Surgery, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

**Department of Medicine, Armed Forces Institute of Cardiology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

***Department of Medicine, Combined Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To determine diagnostic accuracy of C-reactive protein in acute appendicitis.

Study Design: Cross-sectional study.

Place and Duration of Study: Surgical unit Combined Military Hospital Gujranwala Pakistan, from Apr 2019 to Jan 2021.

Methodology: One hundred and twenty patients were included in the study following the inclusion criteria after their written permission and willingness. C-reactive protein levels were sent pre-operatively to the Pathology department of Combined Military Hospital Gujranwala. Patients were operated on by two classified surgeons. After open and laparoscopic appendectomies, specimens were sent to Histopathologists at Armed Forces Institute of Pathology Rawalpindi. Results were compared to determine the diagnostic accuracy of C-reactive protein.

Results: Out of 120 patients, 72(60%) were males and 48(40%) were females. The diagnostic accuracy of C-reactive protein in acute appendicitis was calculated by keeping tissue diagnosis histopathology as the gold standard, where 82(68.33%) were true positive, 7(5.84%) were false positive, 13(10.83%) were true negative, and 18(15%) were false negative. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were 89.13%, 67.86%, 90.11%, 65.52% and 84.17% respectively.

Conclusion: The of C-reactive protein level test for the diagnosis of acute appendicitis was very sensitive but not very specific. C-reactive protein levels should be measured routinely in suspected cases of acute appendicitis, along with Total Leucocyte Count and ultrasound abdomen, as a useful marker for early diagnosis, thus reducing negative appendectomy rates.

Keywords: Acute appendicitis, Appendectomy, C-reactive protein (CRP), Diagnosis.

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INTRODUCTION

Acute appendicitis is a very common clinical condition routinely encountered in trauma and emergency bays.¹ Males and females are almost equally affected.² The prevalence of this disease is 28.6%.³ Acute appendicitis is mainly diagnosed based on history, clinical evaluation and examination.⁴ Many laboratory investigations aid in diagnosing, but none can confirm the diagnosis.⁵ Various abdominal causes, both medical and surgical, present, like acute appendicitis.⁶ If not appropriately diagnosed, it may increase the ratio of negative appendectomies, while late diagnosis may lead to complications like perforation, abscess formation, peritonitis and even death.⁷ C-reactive protein (CRP) and other acute phase reactants increase after various inflammatory conditions. CRP levels can also help in differentiating uncomplicated appendicitis from gangrenous appendicitis. CRP levels are a simple latex agglutination test

that utilises specific CRP kits. Various studies have been conducted to determine the value of CRP in acute appendicitis, but the results have been variable.^{8,9} The previous studies have demonstrated a sensitivity of 40-94% and a specificity of 38-87% for CRP measurement.¹⁰ One of the latest studies revealed the sensitivity of C-reactive protein in acute appendicitis to be 85.1%, while specificity was 72%.⁴

The rationale of our study was to validate the accuracy of this simple and quick test for early diagnosis of acute appendicitis. If a strong correlation is found between acute appendicitis and raised C-reactive protein, this will become an important investigation in helping and confirming the diagnosis of acute appendicitis, and it can be used as a routine investigation. This simple, cheap, quick, and effective laboratory test will improve the diagnosis of acute appendicitis and will also decrease the number of negative appendectomies.

METHODOLOGY

The cross-sectional study was carried out after getting the approval from the Ethical Committee (No.

Correspondence: Dr Hassan Tariq, Department of Surgery, Armed Forces Institute of Pathology, Rawalpindi Pakistan

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139), at the Surgical Unit of Combined Military Hospital Gujranwala Pakistan, from February 2019 and January 2021. The sample size using the WHO calculator was calculated, with the expected sensitivity of CRP in diagnosing acute appendicitis as 85.1%.⁴

Inclusion Criteria: Patients aged 12 to 60 years, who presented in the Emergency and Trauma Bay with pain in the right lower abdomen and underwent surgeries were included.

Exclusion Criteria: Patients with upper respiratory tract infections, pregnant females, having generalised peritonitis or right iliac fossa mass and cirrhotic patients were excluded.

Informed consent was taken from all patients after thorough counselling regarding the advantages and disadvantages of this research. Each patient was assessed thoroughly by taking a complete history and performing relevant clinical examinations. A chemical pathologist assessed C-reactive protein levels in blood samples in AFIP, and the results were entered in a special Performa.

The decision regarding surgery was made after confirming clinical findings, laboratory parameters, and radiological investigations, including USG and CT scan abdomen and diagnostic laparoscopy. Two classified surgeons in the unit operated on patients. After surgery, all patients were given antibiotics for one day and discharged after two days. Complications were dealt with in different ways, with prolonged intravenous antibiotics and drains placed until the third post-op day. Postoperatively, specimens were dispatched to Histopathologists at AFIP and CMH Kharian. The histopathology report finally confirmed acute appendicitis, and these results were analysed by using and entering all data on a specific proforma.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables with normal distribution were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. The 2x2 table was used to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of C-reactive protein.

RESULTS

During our research period, 120 patients were selected. Among these 120 patients, 72(60%) were males, and 48(40%) were females. The ratio of Males to females was 1.5:1. Most of the patients were between

12 and 60 years old. The mean age was 26.12±5.32 years. The results of the study were statistically analysed to determine the relation of CRP with tissue diagnosis of the appendix by histopathology, as shown in Table-I. Amongst these 120 patients, all had a preoperative clinical diagnosis of acute appendicitis. However, postoperative histopathology revealed acute appendicitis only in 100 patients (83.33%), while 20 patients had no findings of morbidity, thus revealing a negative appendectomy ratio of 16.67%. Suppose we use CRP levels in these patients, with 10 mg/L as a reference range, the negative appendectomy rate minimised to 5.84% (7 in 120). Our research revealed the Sensitivity of CRP levels as 82%, Specificity at 65%, Negative predictive value at 41.94%, Positive predictive value at 92.13% and Diagnostic accuracy at 79.17% (Table-II).

Table-I: Contingency Table for C-Reactive Protein and Histopathology (n=120)

Comparisons of CRP and Histopathology	Histopathology of Appendix		
	Inflamed appendix	Normal appendix	
CRP levels (mg/L)	>10	True Positive (a) 82(68.33%)	False Positive (b) 7(5.84%)
	<10	False Negative (c) 18(15%)	True Negative (d) 13(10.83%)

Table-II: Diagnostic Parameters (n=120)

Diagnostic Parameters	Values		
Sensitivity	a/a+cx100	82/(82+18)x100	82.00%
Specificity	d/b+dx100	13/(7+13)x100	65.00%
Positive Predictive Value(PPV)	a/a+bx100	82/(82+7)x100	92.13%
Negative Predictive Value(NPV)	d/c+dx100	13/(18+13)x100	41.94%
Diagnostic Accuracy	a+d/(a+b+c+d)x100	(82+13)/(82+7+18+13)x100	79.17%

DISCUSSION

Acute appendicitis is a very common surgical emergency presenting in accidents and emergency centres in the whole world. If there is a clinical diagnosis of acute appendicitis, then emergency appendectomy is the treatment of choice.¹¹ Many patients have postoperative histopathological tissue diagnosis as negative amongst operated cases on account of suspicion of acute appendicitis.¹² Despite many advances in medical science, the negative operation rate is 15-20%¹¹ for acute appendicitis and

perforated cases 20-35%¹³ worldwide. The success of surgery depends upon early and robust diagnosis,¹⁴ thus decreasing the chances of perforation. Various research studies have been done to improve the diagnosis of acute appendicitis but with variable results. The differential diagnosis of acute appendicitis is so vast, especially in extreme age groups and young females.¹⁵ It remains a diagnostic challenge for surgeons. Amongst fresh studies, CRP measurements were helpful in diagnosing acute appendicitis.¹⁶

We conducted this study to determine the diagnostic accuracy of C-reactive protein in acute appendicitis. We found that measuring CRP levels for acute appendicitis improves diagnostic accuracy, thus minimising the chances of negative operation rates and complications.

Our study results were as follows: the mean age was 26 years, 72(60%) of patients were males, and 48(40%) were females. Acute appendicitis was diagnosed on histopathology tissue diagnosis (gold standard) 100(83.33%), while 20(16.67%) had no tissue findings of acute appendicitis. The diagnostic accuracy of CRP in acute appendicitis utilising histopathology as the gold standard investigation was evaluated, revealing 82(68.33%) as true positive, 7(5.84%) as false positive, 13(10.83%) as true negative and 18(15%) false negative. Sensitivity was 82%, specificity was 65%, positive predictive value was 92.13%, negative predictive value was 41.94%, and diagnostic accuracy was 79.17%.

In our study, sensitivity was 82%, almost the same as in their study, whereas the specificity of CRP was 67.86%, slightly lower.

Another study recorded a sensitivity of 94.4% and a specificity of 60.0%. According to that study, CRP was more sensitive but less specific.⁶ Our results can also be compared to this study. In our study, sensitivity was slightly lower than in this Indian population, but specificity was higher than in this study.

Another study conducted for diagnostic accuracy of serum CRP in anticipating appendicitis claimed sensitivity of this marker as 65% and specificity as 73%.⁷ They concluded that CRP can be used to augment diagnosis but could be a better indicator to use routinely. The specificity of this study was comparable to that of our study, but the sensitivity was much lower.

Another study, carried out by Hamill *et al.*, found that CRP has a diagnostic accuracy of 69.2% in acute appendicitis. They further concluded that CRP

values were higher in cases of perforated appendicitis and can be used to differentiate phlegmonous appendicitis from perforated appendicitis.⁸

Finally, results of almost the majority of the studies conducted in different populations of the world in establishing the role of CRP in acute appendicitis have shown that this test is more sensitive in diagnosing acute appendicitis, but it is not very specific.^{17,18}

The results of our study have also shown that CRP Levels are raised in the majority of cases. Considering the sensitivity and specificity of CRP, we recommend that C-reactive protein be used for early diagnosis of cases of acute appendicitis to reduce the negative operation rate.

CONCLUSION

CRP level measurement is a simple, quick, cheap and highly effective diagnostic test. It has very high sensitivity, specificity, and diagnostic accuracy, so it is a very effective tool for diagnosing acute appendicitis at a very early stage. It should be used in every case of suspected acute appendicitis, especially in the peripheral hospitals. It can be supplemented with TLC and ultrasound of the abdomen in obese females of reproductive age and in children, thus reducing negative.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WR & HT: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SK & SH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AB & MSH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Becker C, Kharbanda A. Acute appendicitis in pediatric patients: an evidence-based review. *Pediatr Emerg Med Pract* 2019; 16(9): 1-20.
2. Kulvatunyou N, Zimmerman SA, Joseph B, Friese RS, Gries L, O'Keeffe T, et al. Risk Factors for Perforated Appendicitis in the Acute Care Surgery Era-Minimizing the Patient's Delayed Presentation Factor. *J Surg Res* 2019; 238: 113-118.
<https://doi.org/10.1016/j.jss.2019.01.031>

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3. Xharra S, Gashi-Luci L, Xharra K, Veselaj F, Bicaj B, Sada F, et al. Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopathology findings in acute appendicitis. *World J Emerg Surg* 2012; 7(1): 27. <https://doi.org/10.1186/1749-7922-7-27>
4. Alotaibi AM, Moshref LH, Moshref RH, Felemban LS. Analysis of 190 Female Patients after Appendectomy. *Obstet Gynecol Int* 2021; 2021: 8036970. <https://doi.org/10.1155/2021/8036970>
5. Vaughan-Shaw PG, Rees JR, Bell E, Hamdan M, Platt T. Normal inflammatory markers in appendicitis: evidence from two independent cohort studies. *JRSM Short Rep* 2011; 2(5): 43. <https://doi.org/10.1258/shorts.2011.010114>
6. Hawkins AT, Wise PE, Chan T, Lee JT, Glyn T, Wood V, et al. Diverticulitis: An Update From the Age Old Paradigm. *Curr Probl Surg* 2020; 57(10): 100862. <https://doi.org/10.1016/j.cpsurg.2020.100862>
7. Lo Bianco S, Cavallaro D, Provenzano D, Stracqualursi A, Leonardi A, Basile G, et al. Open mini-incision vs laparoscopic appendectomy A retrospective single Centre study. *Ann Ital Chir* 2021; 92: 1-5.
8. Hamill JK, Hill AG. A history of the treatment of appendicitis in children: lessons learned. *ANZ J Surg* 2016; 86(10): 762-767. <https://doi.org/10.1111/ans.13627>
9. Pedram A, Asadian F, Roshan N. Diagnostic Accuracy of Abdominal Ultrasonography in Pediatric Acute Appendicitis. *Bull Emerg Trauma* 2019; 7(3): 278-283. <https://doi.org/10.29252/beat-0703011>
10. Akhtar-Danesh GG, Doumouras AG, Flageole H, Hong D. Geographic and socioeconomic predictors of perforated appendicitis: A national Canadian cohort study. *J Pediatr Surg* 2019; 54(9): 1804-1808. <https://doi.org/10.1016/j.jpedsurg.2018.10.065>
11. Kim MJ, Choi WH, Cheong JC, Choi SY, Kim JW, Park JH. Delta neutrophil index and symptomatic time are effective factors for predicting perforated appendicitis. *Medicine* 2021; 100(20): e25935. <https://doi.org/10.1097/MD.00000000000025935>
12. Castro ADAE, Skare TL, Yamauchi FI, Tachibana A, Ribeiro SPP, Fonseca EKUN, et al. Diagnostic value of c-reactive protein and the influence of visceral fat in patients with obesity and acute appendicitis. *Arq Bras Cir Dig* 2018; 31(1): e1339. <https://doi.org/10.1590/0102-672020180001e1339>
13. Klein TT, Kohn E, Klin B, Ziv-Baran T, Kozer E, Berkovitch M, et al. sTREM-1 as a diagnostic biomarker for acute appendicitis in children. *Asian J Surg* 2021; 44(9): 1172-1178. <https://doi.org/10.1016/j.asjsur.2021.02.025>
14. Kaya B, Sana B, Eris C, Karabulut K, Bat O, Kutanis R, et al. The diagnostic value of D-dimer, procalcitonin and CRP in acute appendicitis. *Int J Med Sci* 2012; 9(10): 909-915. <https://doi.org/10.7150/ijms.4733>
15. Dadeh AA, Puitong K. Predictive Factors to Diagnose Appendicitis in Children in the Emergency Department. *Open Access Emerg Med* 2021; 13: 363-372. <https://doi.org/10.2147/OAEM.S323960>
16. Schuppisser M, Khallouf J, Abbassi Z, Erne M, Vettorel D, Paroz A, et al. Abdominal Mondor disease mimicking acute appendicitis. *Int J Surg Case Rep* 2016; 20: 37-40. <https://doi.org/10.1016/j.ijscr.2015.12.031>
17. Msolli MA, Beltaief K, Bouida W, Jerbi N, Grissa MH, Boubaker H, et al. Value of early change of serum C reactive protein combined to modified Alvarado score in the diagnosis of acute appendicitis. *BMC Emerg Med* 2018; 18(1): 15. <https://doi.org/10.1186/s12873-018-0166-5>
18. Sushruth S, Vijayakumar C, Srinivasan K, Raj Kumar N, Balasubramanian G, Verma SK, et al. Role of C-Reactive Protein, White Blood Cell Counts, Bilirubin Levels, and Imaging in the Diagnosis of Acute Appendicitis as a Cause of Right Iliac Fossa Pain. *Cureus* 2018; 10(1): e2070. <https://doi.org/10.7759/cureus.2070>