



ORIGINAL RESEARCH PAPER

General Surgery

ROLE OF ELEVATION OF C-REACTIVE PROTEIN (CRP) AS AN INDEPENDENT MARKER FOR SURGICAL INTERVENTION IN ACUTE APPENDICITIS

KEY WORDS: Acute appendicitis; pre operative CRP; C-reactive protein; Appendicectomy.

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ABSTRACT

Background: The treatment of acute appendicitis has been primarily by surgery. The rate of negative Appendicectomy still remains at 15–30%. This study is designed to investigate effectiveness of CRP as a surgical indication marker as well as to analyze the levels of elevation in CRP so as to identify cut offs for deciding between surgical and conservative management in Acute Appendicitis. **Method:** 200 patients who underwent emergency Appendicectomy were subjected to clinical examination and routine investigations including pre operative CRP and imaging studies on admission. Intra operative findings and post operative histopathology report of the specimen were also used for analysis. The HPR of each Appendicectomy specimen was used to distinguish between inflamed appendix and negative Appendicectomy and this was correlated to the pre operative levels of serum CRP of each patient to assess the level of elevation. **Results:** Among the 200 patients who underwent Appendicectomy, 85.5% had elevated CRP levels above 10mg/dL and the sensitivity and specificity of CRP was found to be more than those of USG and Alvarado score in diagnosing the disease. Also among the 12 patients who underwent negative Appendicectomy, CRP was normal (below 10) in more than 83%. Hence CRP is effective as a marker for surgical intervention in acute appendicitis. The best cut off value for CRP to serve this function was calculated to be 10mg/dL according to this study. **Conclusion:** Pre operative serum CRP value can be used as an independent marker for surgical intervention and the cut off value for this function is 10mg/dL.

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen and it is a surgical emergency^{1,3}. Diagnosis is usually made by an adequate history followed by clinical examination and supporting laboratory and imaging studies. But in spite of all the advances in surgery and investigation modalities, acute appendicitis remains one of the most common diagnostic problems in emergency surgery. Even though various scoring systems have been introduced for the diagnosis such as Alvarado scoring and RIPASA, they are not without limitations.

Also atypical presentations are not uncommon in case of appendicitis and various other inflammatory and non-inflammatory conditions can mimic the presenting features. Acute appendicitis has been primarily managed by surgical intervention⁴. A delay in surgical intervention can lead to abscess formation and perforation in case of a complicated appendicitis⁵. Hence the decision on whether to operate in a case of acute appendicitis is always difficult in clinical practice.

Various investigations have been used to guide this decision such as total leukocyte count and Ultrasonography findings⁶. One among them is an acute phase reactant C-reactive protein^{4,8,9}. CRP is synthesised in liver in response to inflammation and infection and its normal level is less than 10mg/L in blood^{7,10}. The relation between acute appendicitis and CRP have been extensively analysed in various studies in the past but the results have been contradictory. This study also tries to analyse the same.

OBJECTIVES

- a) To investigate the effectiveness of elevation of CRP measured at the time of presentation, as a marker for surgical intervention in Acute Appendicitis.
- b) To analyze the levels of elevation in CRP so as to identify cutoffs for deciding between surgical and conservative treatment approach for Acute Appendicitis

METHODOLOGY

Study setting

Department of General Surgery, Government Medical College, Thrissur, Kerala, India.

Study design

Cross sectional study.

Study population

Patients who attended Casualty in General Surgery department and underwent emergency Appendicectomy in Govt. Medical College, Thrissur.

Inclusion criteria

Patients undergoing emergency Appendicectomy in Department of Surgery, Govt. Medical College, Thrissur.

Exclusion criteria

Patients who are not willing to participate in the study.

Study period

30/11/2021 to 30/12/2022 (till the sample size was reached)

Sample size calculation

The formula for calculation of sample size is

$$n = \frac{Z^2 pq}{d^2}$$

Where n is the sample size Z is the z score = 1.96 p is the prevalence in previous study = 13% (0.13)

q is (1-p) = 1-0.13 = 0.87 d is the margin of error = 0.05

$$\text{Hence, } n = \frac{1.96^2 \times 0.13 \times 0.87}{0.05^2} = 174.$$

200 patients who presented to General Surgery Casualty and underwent emergency Appendicectomy during the study period were included.

Study tools

- Pre operative examination and blood routine evaluation reports
- Pre operative serum CRP levels
- Pre operative Ultrasound abdomen report
- Post operative histopathology report

Study Method

All were subjected to clinical examination and routine investigations including pre operative CRP and imaging studies on admission. Decision for surgery was taken on the basis of Alvarado score and ultrasound findings in each

patient. Intra operative findings and post operative histopathology reports were followed up and used for analysis. The HPR of each case was correlated to the pre operative CRP to assess the level of elevation. The data was collected using a proforma and tabulated and analysed.

Statistical analysis

The data of study subjects and the outcome were statistically analysed using the version 25 of Statistical Package for Social Sciences (SPSS) software for Windows. Student t-test will be used to compare the serum CRP levels with the HPR findings.

Conflicts of interest

None

RESULTS

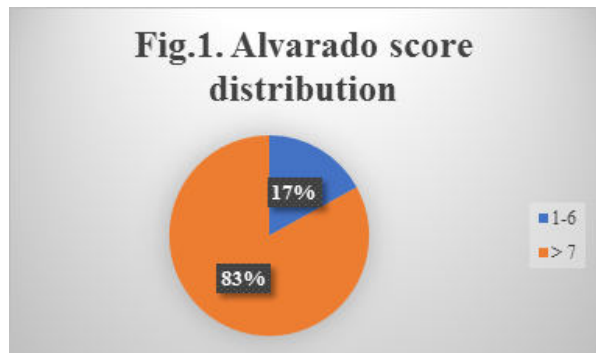


Table 1. Ultrasonography findings

Ultrasound	Frequency	Percentage
Inflamed Appendix not visualized	28	14.0
Inflamed Appendix visualized	172	86.0
Total	200	100.0

Pre operative CRP levels were estimated for the study population and here, for 29 (14.5%) participants C - reactive protein values were <10 mg/dL, 112 (56.0%) had values between 10-15 mg/dL, 34 (17.0%) were 15-20 mg/dL and 25 (12.5%) were having values >20 mg/dL. The mean CRP value in our study was 15.00 ± 8.80.

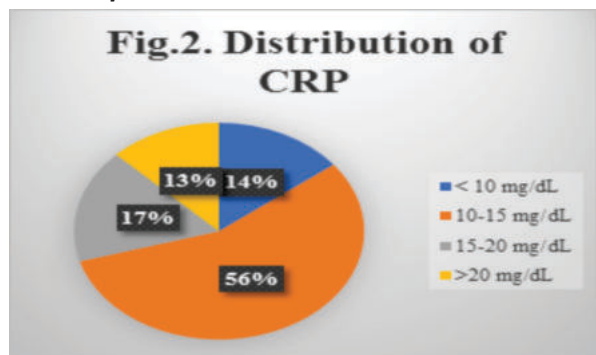


Table 2. Histopathological examination findings

Histopathology	Frequency	Percentage
Negative Appendicectomy	12	6.0
Uncomplicated Appendicitis	144	72.0
Complicated Appendicitis	44	22.0
Total	200	100.0

As Alvarado score and ultrasound findings were used to decide the treatment modality, each were co related to the histopathology findings separately.

Table 3. Comparison of Alvarado score with HPR

Alvarado Score	Histopathology				Total
	Positive		Negative		
	n	%	n	%	
>6	158	84.0	8	66.7	166

Alvarado Score	Frequency	Percentage	Total
1-6	30	16.0	4
Total	188	100.0	12

In this study, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Alvarado score for detecting acute appendicitis was 84.0%, 33.3%, 95.2%, 11.8% and 81.0% respectively.

On co relating the Ultrasonography findings with the HPR, in this study, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasound for detecting acute appendicitis was 88.3%, 50.0%, 96.5%, 21.4% and 86.0% respectively.

Table 4. Comparison of USG with HPR

USG	Histopathology				Total
	Positive		Negative		
	n	%	n	%	
Positive	166	88.3	6	50.0	172
Negative	22	11.7	6	50.0	28

Similarly, CRP values were also compared to the histopathology findings and on analysing the data, it was found that CRP yielded the best ROC characteristics (cut off value-10) with an AUC of 0.961 (95% CI, 0.928- 0.995) in differentiating appendicitis with Sensitivity of 89.9%, Specificity of 83.3%, Positive Predictive Value of 98.8%, NPV of 34.5% and accuracy of 89.5%.

Table 5. Comparison of CRP with HPR

CRP	HPE				Total
	Positive		Negative		
	n	%	n	%	
> 10	169	89.9	2	16.7	171
≤ 10	19	10.1	10	83.3	29
Total	188	100.0	12	100.0	200

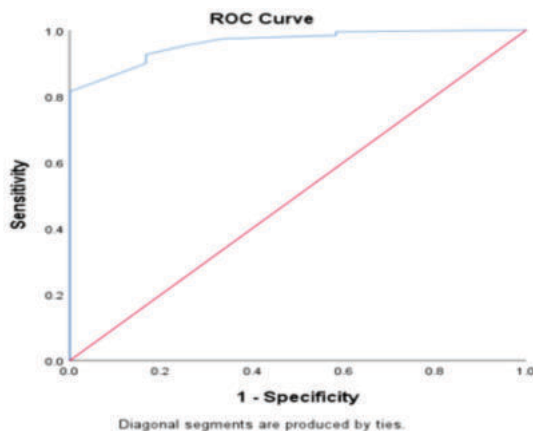
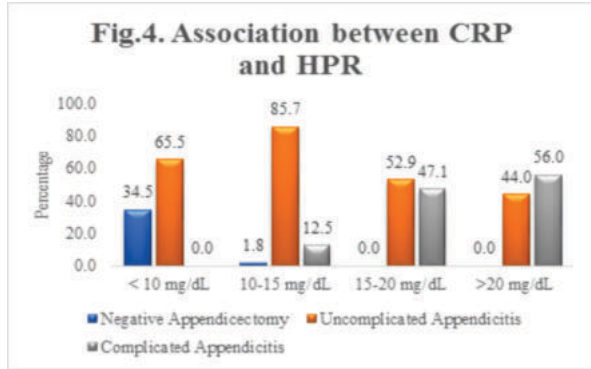


Fig.3. ROC curve for CRP (cut off point 10)

The association of CRP with Histopathological findings were done and it was found that :

1. Among the 29 patients with CRP < 10 mg/dL, none of them had complicated appendicitis and 19 had uncomplicated appendicitis.
2. 10 patients had negative appendicectomy.
3. Among the 110 with value between 10-15 mg/dL, 14 (12.5%) had complicated appendicitis and 96 (87.5%) had uncomplicated appendicitis.
4. Among those with CRP 15-20 mg/dL, 16 (47.1%) had complicated appendicitis and 18 (52.9%) had uncomplicated appendicitis.
5. Among those with CRP >20 mg/dL, 14 (56.0%) had complicated appendicitis while 11 (44%) had uncomplicated appendicitis.
6. The p value showed that CRP was statistically associated with Histopathology (p<0.001).



DISCUSSION

This is a cross sectional study conducted in the Department of General Surgery, Government medical college, Thrissur. The study population includes 200 participants who presented to the general surgery casualty with Acute Appendicitis and underwent emergency Appendicectomy. The primary objective of this study was to assess the effectiveness of CRP as a marker for surgical intervention in acute appendicitis. For this we can co relate the CRP levels with the histopathology findings. Among the 200 patients recruited in the study, among those with CRP values more than 10, 44(26%) had complicated appendicitis and 125(74%) had uncomplicated appendicitis. The p value was calculated which showed that CRP was statistically associated with the histopathology findings. Also, the sensitivity and specificity of CRP in differentiating appendicitis was found to be more than those seen with Ultrasound findings and Alvarado score.

It was noted that among the 44 patients with complicated appendicitis, 42(95%) had pre operative CRP values more than 10. Also, on comparing the histopathology reports of the 200 Appendicectomy specimens, 6%, i.e., 12 patients were found to have normal appendix (hereafter called negative Appendicectomy). Among these, 10 patients had CRP values less than 10. That is, if CRP values were also included in the diagnosis and for decision of treatment modality, about 80% of negative Appendicectomies could have been avoided.

The secondary objective of this study was to identify cut off values in pre operative CRP for deciding between surgical and conservative management. For this, after data analysis, ROC curve was drawn and it was found that the cut off value of CRP was found to be 10 with the AUC of 0.961 for predicting appendicitis. So, 10 can be taken as an independent marker for surgical intervention in a patient with acute appendicitis and those with pre operative CRP levels above 10 should be taken up for surgical intervention.

The results of this study are in accordance with the conclusions of most of the studies mentioned in the review of literature.⁹¹⁰¹¹

CONCLUSIONS

CRP is an effective tool for the diagnosis of Acute Appendicitis.

CRP has been found to be significantly elevated in most cases of complicated appendicitis while, low in those that underwent negative Appendicectomies. Hence, CRP can be used as an independent marker for surgical intervention acute appendicitis.

The cut off value for CRP as a marker for surgical intervention is 10mg/dL.

REFERENCES

1. Josef E. Fischer. Fischer's mastery of surgery. 2018;7(2)
2. Terry W Du Clos. Function of C-reactive protein. Annals of Medicine 2000; 32(4):274-278.
3. Charles J. Yeo. Shackelford's surgery of the Alimentary tract. 2019;8(2).

4. Townsend, Beauchamp, Evers, Mattox. Sabiston textbook of surgery : The biological basis of modern surgical practice. 2021;21.
5. Norman S. Williams, P. Ronan O'Connell, Andrew W. McCaskie. Bailey and Love's short practice of surgery. 2022;28(2).
6. O. Yildirir, Cem Solak, B. Koçer, et al. The role of serum inflammatory markers in acute appendicitis and their success in preventing negative laparotomy. J of Investigative Surg. 2006; 19(6):345-352.
7. M. Zimmerman, C. Selzman, C. Cothren, et al. Diagnostic implications of C-reactive protein. Arch of Surg 2003; 138(2):220-224.
8. Sami Asfar, Hussein Safar, et al. Would measurement of C-reactive protein reduce the rate of negative exploration for acute appendicitis? J of Royal College of Surgeons of Edinburgh 2000; 45(1):21-24.
9. Han-Ping Wu, Ching-Yuang Lin, et al. Predictive value of C-reactive protein at different cutoff levels in acute appendicitis. The Am J of Emerg Med 2005; 23(4):449-53.
10. T. Amallesh, M. Shankar, R. Shankar. CRP in Acute Appendicitis : Is it a necessary investigation? Int. J of Surg 2004; 2(2):88-89.
11. Horng-Ren Yang, Yu-Chun Wang, Ping-Kuei Chung, et al. Role of leukocyte count, neutrophil percentage and C-reactive protein in the diagnosis of acute appendicitis in the elderly. The American surgeon 2005; 71(4):344-347.