

Role of C-reactive Protein in Acute Appendicitis

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ABSTRACT

Background

Acute appendicitis is the common surgical emergency. This study analyzed the value of C-reactive protein as the diagnostic marker of acute appendicitis.

Objective

To assess the level of C-reactive protein in acute appendicitis and to relate the quantitative measurement with degree of inflammation of appendix.

Method

A cross sectional study was done with consecutive patients diagnosed with acute appendicitis that underwent appendectomy over six months period. Peroperative findings and histopathology report were compared and analyzed with the level of C-reactive protein.

Result

A total of 54 patients were enrolled in this study. 94.40% were proved as acute appendicitis in histopathology. The level of C-reactive protein was significantly raised among highly inflamed appendix. C-reactive protein showed 84.31% sensitivity, 66.66% specificity, 97.72% positive predictive value and 20% negative predictive value in diagnosing acute appendicitis.

Conclusion

With degree of inflammation of appendix, value of C-reactive protein was raised. Quantitative assessment can predict severity of inflammation. Raised level of C-reactive protein is an aid for diagnosing acute appendicitis.

KEY WORDS

Acute appendicitis, C-reactive protein, Histopathology

INTRODUCTION

Acute Appendicitis is one of the common surgical emergencies and appendectomy is the most widely performed emergency operation worldwide.^{1,2} An adequate history and clinical examination supported by laboratory investigations and imaging is usually enough to make a diagnosis of acute appendicitis. Nevertheless, the rate of negative appendectomies is between 15 and 50%. Although leucocyte count and ultrasonography of abdomen provides a valuable aid, diagnosis depends mostly upon the clinical judgment.³⁻⁶

Several scoring system like Modified Alvarado Score, Lintula, RIPASA has been developed to make the diagnosis of acute appendicitis but each system has its own limitations.⁷⁻⁹

C-reactive protein (CRP) is an acute phase reactant produced in the liver, controlled by interleukin-6. Its normal serum concentration is less than 10 mg/l. Its concentration is increased in infection, autoimmune disorders, neoplasia and ageing.¹⁰⁻¹³ The evaluation of this protein is simple and its quantitative assessment aids in the diagnosis of acute appendicitis.¹⁴ However, Amalesh T et al. have concluded that neither raised nor normal CRP value is helpful in diagnosing acute appendicitis.¹⁵

The aim of this study was to assess the level of C-reactive protein in acute appendicitis and to relate the quantitative measurement with degree of inflammation of appendix.

METHODS

A single center, cross-sectional observational study was conducted from 15th September 2014 to 15th March 2015 at Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu, Nepal. The study included fifty-four consecutive patients diagnosed with acute appendicitis who underwent appendectomy. Based on institutional protocol, the diagnosis was based on history, clinical judgment, total leucocyte count, and ultrasonography of abdomen.

Fifty four patients posted for emergency appendectomy were sent for C-reactive protein test. The decision to operate was not influenced by the level of C-reactive protein. However, it was made by the attending surgeon based on the above mentioned institutional protocol. Level of C-reactive protein less than 6 mg/dl was reported as negative. According to the study done by Gurleyik E, value of C-reactive protein less than 6 mg/dl was found as negative, value of 6-35 mg/dl was found in inflamed nonperforated appendix and value of more than 84 mg/dl was found in perforated appendix.¹⁰ Based on these findings we have categorized the value of C-reactive protein.

Appendectomy was done and the appendix was sent for histopathological examination. The pathological criterion for diagnosis of acute appendicitis was neutrophilic

infiltration of all layers of appendicular wall. Based on the histopathological features of the removed appendix, the patients who underwent surgery were divided into three groups.^{16,17}

- Normal appendix (Negative in microscopic and macroscopic findings for acute appendicitis)
- Inflamed appendix (Simple appendicitis)
- Gangrenous/ perforated appendicitis (Complicated appendicitis)

IBM SPSS Statistics version 20 was used to analyze the data. The levels of C-reactive protein were correlated with per-operative and histopathological findings of appendix. Specificity, sensitivity, positive predictive value and negative predictive value of C-reactive protein were calculated.

RESULTS

A total of 54 patients were enrolled in the study. Out of 54 patients, 34 (62.96%) were male and 20 (37.04%) were female. Most common age of presentation was between 16-60 years. 11(20.37%) patients were from paediatric age group i.e. < 15 years and only 2 (3.70%) patients were elderly.

Table 1. Age Distribution of patients with acute appendicitis who underwent appendectomy, n=54.

Age (Years)	Number
<15	11
16-60	41
>60	2
Total	54

Histopathologically proven acute appendicitis was seen in 94.40% of patients and negative appendectomy was seen in 5.60% of patients. C-reactive protein was raised in 81.50% of patients. Of those with raised C-reactive protein, 2.27% of patients had normal appendix on histopathology whereas 84.09% had inflamed appendix and 13.63% had gangrenous appendix. C-reactive protein was negative in 18.51% of patients.

Table 2. Correlation of degree of inflammation noted preoperatively with level of C- Reactive protein

	CRP (mg/L) <6	6-34	35-84	>84	Total
xHPE					
Group A (Normal Appendix)	2	0	1	0	3
Group B (Inflamed Appendix)	8	7	14	16	45
Group C (Perforated/ Gangrenous Appendix)	0	0	1	5	6
Total	10 (18.52%)	7 (12.96%)	16 (29.62%)	21 (38.88%)	54

Table 3. Correlation of C- Reactive Protein with histopathologically proven acute appendicitis

	HPE	Acute Appendicitis	Normal	Total
CRP				
Positive (>=6 mg/L)	43	1	44	
Negative (<6 mg/L)	8	2	10	
Total	51	3	54	

From the table,

Sensitivity (True Positive): $(43/51) \times 100 = 84.31\%$

Specificity (True Negative): $(2/3) \times 100 = 66.66\%$

False Positive: $(1/3) \times 100 = 33.33\%$

False Negative: $(8/51) \times 100 = 15.68\%$

Predictive Value of Positive Test: $(43/44) \times 100 = 97.72\%$

Predictive Value of Negative Test: $(2/10) \times 100 = 20\%$

Table 4. Correlation of ultrasound with histopathologically proven acute appendicitis

	HPE	Acute Appendicitis	Normal	Total
USG				
Acute Appendicitis	35	0	35	
Normal	16	3	19	
Total	51	3	54	

Sensitivity: $(35/51) \times 100 = 68.62\%$

Specificity: $(3/3) \times 100 = 100\%$

Predictive Value of Positive Test: $(35/35) \times 100 = 100\%$

Predictive Value of Negative Test: $(3/19) \times 100 = 15.78\%$

DISCUSSION

In our series, all patients underwent ultrasound of abdomen by radiologist as an institutional protocol. The objective of doing abdominal sonogram was to rule out other differential diagnosis and to reduce negative appendectomy rate rather than diagnosing appendicitis.^{18,19}

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In this study, the sensitivity and specificity of ultrasound in detecting acute appendicitis was found to be 68.62% and 100% respectively compared to studies conducted by Douglas CD et al. with sensitivity and specificity of ultrasonography was 94.7% and 88.9%, respectively.²⁰ Puylaert JB et al. with the sensitivity of ultrasound 75% and specificity 100%.¹⁹

Different studies have shown C-reactive marker as not a good indicator in acute appendicitis. Al-Abed YA et al. has shown sensitivity and specificity as 76.4 % and 55.7% respectively.¹⁴ Amalesh T et al. showed the sensitivity and specificity of C-reactive protein was 91% and 42%.¹⁵

Negative C-reactive protein was found in 18.52% of patients among whom 14.81% of patients were histopathologically proved as acute appendicitis. Compared to the study conducted by Peltola et al. negative C-reactive protein was more useful to exclude acute appendicitis.²¹

Strongly positive C-reactive protein i.e >85 mg/dl was seen in 38.88% of patients. Among them, most were histopathologically gangrenous type.

The sensitivity and specificity of C-reactive protein was 84.31% and 66.66% respectively. Similar findings of sensitivity of 53-88% and specificity of 46-82% was noted in a meta analysis by Chung JL et al.²²

The level of C-reactive protein with per-operative findings and histopathology reports was not statistically significant but majority of patients with significantly raised C-reactive protein level (>85 mg/dl) had severely inflamed or gangrenous appendix. Similar findings was noted in another study done by Xharra S et al.¹⁶

In this study, the relation of CRP level with the severity of acute appendicitis was found to be positive. Yokoyama S et al. and Exadactylos A et al. also suggested a similar relation as in this study.^{23,24}

CONCLUSION

Accuracy of C-reactive protein in diagnosing acute appendicitis was low in our study. However, significant rise in the level of C-reactive protein suggests severe inflammation of appendix.

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