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General Surgery

# EVALUATION OF SERUM C REACTIVE PROTEIN IN ACUTE APPENDICITIS AND ITS CORRELATION WITH HISTOPATHOLOGY

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**ABSTRACT** **Background:** Acute appendicitis is the most common abdominal surgical emergency, but its diagnosis remains an enigmatic challenge, plagued by a high rate of negative explorations. There is no single reliable test with satisfactory sensitivity and specificity. Ultrasonography is not often available at a rural surgical setup. **Aim:** This study is intended to evaluate the importance of serum C-reactive protein (CRP) level estimation in diagnosis of acute appendicitis, by comparing with histopathology report. **Methods:** In a prospective study,100 patients clinically diagnosed as acute appendicitis were selected by purposive sampling method and evaluated as per criteria for serum CRP levels, leucocyte count preoperatively and were followed up postoperatively with histopathology reports. The data was analysed for finding the significance of serum CRP in the diagnosis of acute appendicitis. **Results:** CRP was positive in 75 of the 77 patients who had histologically proven acute appendicitis and in 3 with normal appendix. The sensitivity, specificity and diagnostic accuracy were 97.4%, 86.96% and 95% respectively. Leucocytosis and neutrophilia when used alone were not specific for acute appendicitis, but when combined with CRP value, diagnostic accuracy was high. Ultrasonography was useful in establishing alternative diagnoses, but had low sensitivity for acute appendicitis. **Interpretation & Conclusion:** CRP contains important diagnostic information and hence should always be included in the diagnostic workup of acute appendicitis. Since acute appendicitis is very unlikely in those patients with normal WBC count and CRP value, conservative treatment is advised.This study does not undercut the skill of an experienced surgeon in diagnosing acute appendicitis, but CRP estimation compliments clinical diagnosis.

**KEYWORDS :** Appendicitis, Appendectomy, C reactive protein, inflammatory variables

## AIMS & OBJECTIVES

### AIM

To evaluate serum c reactive protein in Acute appendicitis and its correlation with histopathology.

## METHODOLOGY

### MATERIALS AND METHODS

**Type Of Study:**

The present study is a non-randomized, prospective study. Hundred patients who reported to the surgical OPD or emergency Department S.V.S. Medical College, Mahabubnagar with history of abdominal pain in whom the clinical diagnosis was acute appendicitis participated. Their serum CRP was determined pre operatively and results were compared with histo pathology.

**Study Period**

This study was performed during the period from June-2011 to July 2013

**Source Of Data:**

Data for the study was collected from the patients attending Department of General Surgery, S.V.S. Medical College Hospital, Mahabubnagar clinically suspected to be having acute appendicitis.

**Maintenance Of Records And Collection Of Data**

All the observations during the study of each subject were recorded in an individual case proforma (CP) (annexure) signed by the investigator. The CP contained all information regarding the admission details, general particulars like name, age, sex and address, clinical history of the patients, general examination which included pulse, temperature, at the time of examination physical examination details, investigations-WBC count and ultrasound examination, operative findings, final histopathology report. The principal investigator maintained the entire record.

**Inclusion Criteria:**

1) Patients clinically suspected to be having acute appendicitis.
2) Patients aged 15 - 75 years irrespective of sex.
3) Cases with history of recurrent appendicitis
4) Cases of acute appendicitis with early pregnancy were also included in this study.

**Exclusion Criteria:**

1) All other causes of acute abdomen.
2) Cases with recurrent appendicitis not presenting with acute symptoms.
3) Cases of acute appendicitis diagnosed clinically and sonologically but not willing for further management were excluded from the study.
4) Patients with co-morbid conditions
5) Patients who were managed conservatively

**Clinical Diagnosis:**

Clinical diagnosis of acute appendicitis was made based on symptoms of pain, migration, nausea and vomiting, anorexia, fever and signs of peritoneal inflammation like right iliac fossa tenderness, rebound tenderness and guarding.

Once acute appendicitis was suspected, patient was subjected to routine investigations as per the hospital protocol.

Total leucocyte count and differential count was done in all cases.

Ultrasonography of abdomen was done in most of the cases to ruleout alternative diagnoses in accordance with the consultant's decision. Urine microscopy was performed in all cases.

Renal function and liver function parameters were evaluated in few patients.

Plain X-ray abdomen was done in some cases.

Elderly patients were subjected to further investigations as part of pre-anaesthetic work up including X-ray chest, ECG

**Serum C-Reactive Protein Estimation:**

Serum C-reactive protein estimation was done in all these cases. Two ml of whole blood was collected; serum separated. The specimen was tested within one hour of collection.

CRP was estimated by using latex agglutination slide test method using a Humatex CRP test kit (Figure 11). The test is based on immunological reaction between CRP in patients serum and anti-CRP antibodies bound to latex particle.

A positive reaction indicates a CRP content of more than 6mg/l in the serum, and is denoted by a distinctly visible agglutination of the latex particles in the test cell of the slide.

Patients with strong suspicion of acute appendicitis were advised emergency appendicectomy. After obtaining consent, patient was operated, and the appendicectomy specimen was sent for histopathological examination. The histopathology report was considered as the final diagnosis.

**CRP And Histopathological Correlation:**
Preoperative clinical findings, serum CRP status of patients with Acute appendicitis were correlated with that of Histopathological examination

**Statistical Analysis:**
The histopathologically positive cases among CRP positive group were considered true positives. The histopathologically negative cases in the same group were considered as false positives. The histopathologically positive cases among CRP negative group were considered false negatives. The histopathologically negative cases in the same group were considered as true negatives.

The evaluation of CRP estimation in the diagnosis of acute appendicitis is done as follows.

**TABLE 1**

| Acute appendicitis Histopathology | | |
|---|---|---|
| | Inflamed appendix | Normal appendix |
| CRP positive | a True positive | b False positive |
| CRP Negative | c False negative | d True negative |

$$\text{Diagnostic sensitivity} : \frac{a}{a+c} \times 100$$

$$\text{Diagnostic specificity} : \frac{d}{b+d} \times 100$$

$$\text{Predictive value of positive test} : \frac{a}{a+b} \times 100$$

$$\text{Predictive value of negative test} : \frac{d}{c+d} \times 100$$

$$\text{Diagnostic accuracy} : \frac{a+d}{a+b+c+d} \times 100$$

$$\text{False positive error rate} : \frac{b}{b+d} \times 100$$

$$\text{False negative error rate} : \frac{c}{a+c} \times 100$$

$$\text{Likelihood ratio positive} : \frac{a/a+c}{b/a+b}$$

$$\text{Likelihood ratio negative} : \frac{c/a+c}{d/b+d}$$

The patients were meticulously monitored in the post-operative period for any complications. All patients were followed up in the outpatient department for a period of two months. The case study was done as per a detailed proforma which is shown in the annexure. The hospital ethical committee clearance was obtained prior to undertaking the study.

**RESULTS**
**RESULTS AND ANALYSIS**
Before analysis of the collected data, a few assumptions were made.
1. Histopathological diagnosis was accepted as final confirmation of diagnosis.
2. Technical errors in serum CRP estimation were not assigned any significance, since all laboratory technicians were well experienced and the test kit was provided by standard manufacturers.

Considering these assumptions were true, we have analysed the data obtained, to seek the efficacy of serum C-reactive protein estimation in the diagnosis of acute appendicitis by evaluating the sensitivity, specificity, predictive values, diagnostic accuracy, error rates, and likelihood ratios of the same.

The prevalence of acute appendicitis is highest in the 15 - 19 years age group followed by the 20 - 24 years age group. There is a slight male predominance in the total number of cases.

Out of the 100 cases included in the study, 78 patients had positive serum CRP. 75 of these patients had histopathologically proven acute appendicitis, where as 3 were found to be normal histologically. Of the 22 patients with negative serum CRP, 2 patients had histological inflamed appendix and 20 had normal appendix.

**TABLE 2**

| | |
|---|---|
| CRP positive | 78 |
| CRP negative | 22 |
| Histological acute appendicitis | 77 |
| Histological normal appendix | 23 |
| Total number of cases | 100 |

**Results**
**TABLE 3**

| Histopathology | | | Total no. of cases |
|---|---|---|---|
| | Inflamed appendix | Normal appendix | |
| CRP positive | (a) True positive: 75 | (b) False positive: 3 | 78 |
| CRP Negative | (c) False negative: 2 | (d) True negative: 20 | 22 |
| Total no. of cases | 77 | 23 | 100 |

Validity refers to what extent the test accurately measures which it purports to measure. This has two components i.e. sensitivity and specificity. The sensitivity, specificity, predictive values, error rates, diagnostic accuracy and likelihood ratios of this study are given in Table 4.

**TABLE 4**

| Evaluation of serum CRP estimation | Values |
|---|---|
| Sensitivity | 97.4% |
| Specificity | 86.96% |
| Positive predictive value | 96.15% |
| Negative predictive value | 90.9% |
| Diagnostic accuracy | 95% |
| False positive error rate | 13.04% |
| False negative error rate | 2.6% |
| Likelihood ratio positive | 25.36% |
| Likelihood ratio negative | 0.03 |

This table shows the statistical significance of serum CRP estimation in diagnosis of acute appendicitis. The overall sensitivity is 97.4%, specificity is 86.96%, and diagnostic accuracy is 95%. The positive predictive value is 96.15% and the negative predictive value is 90.9% . The false positive error rate is 13.04% and the false negative error rate is 2.6%. The positive likelihood ratio is 25.36 and the negative likelihood ratio is 0.03.

Pain abdomen was the commonest clinical symptom and was present in all 100 patients. Migration of pain from the umbilical region to right lower quadrant was present in 47% cases. Nausea or vomiting was a predominant symptom which was present in 60% cases. Fever was present in only 34% of patients. Murphy's triad of symptoms i.e. pain abdomen, vomiting and fever, was seen in 28% of the cases. Anorexia was reported by 59% of patients . Other symptoms like dysuria were present in 2 cases probably due to the pelvic position of appendix, and diarrhoea in 2 cases, which can be explained due to the postileal position of appendix.

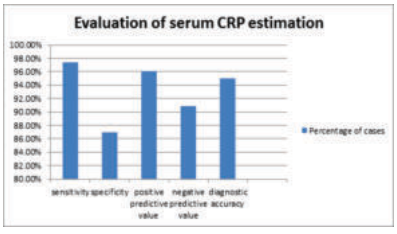


**Chart 1**

Among clinical signs, right iliac fossa tenderness was seen in all the cases. Rebound tenderness was present in 76% cases and is more specific in the diagnosis of acute appendicitis. Guarding was seen in only 50% of cases and it reflects the severity of inflammation. Other peritoneal signs like Rovsing's sign were elicited in 13% cases and Psoas sign in only 1 case. Tachycardia was seen in 54% cases. 34% cases were febrile with temperature above 99.1oF.

Urine microscopic examination showed presence of pus cells in 8% cases

Total leucocyte count revealed leucocytosis i.e. WBC count greater than 10 x

$10^9$/l, in 66% of cases. Among these, WBC count was greater than 15 x $10^9$/l in 14 cases. Differential leucocyte count showed neutrophilia in 59% cases. 15% cases had neutrophilia in the absence of appreciable leucocytosis

Evaluation of inflammatory variables like WBC count and serum CRP in combination yielded a high sensitivity and specificity of 100% and 90.48% respectively (Table 5, Chart 2).

**TABLE 5**
**Evaluation Of Inflammatory Variables**
(Combined Leucocytosis and CRP positive)

| | |
|---|---|
| Sensitivity | 100% |
| Specificity | 90.48% |

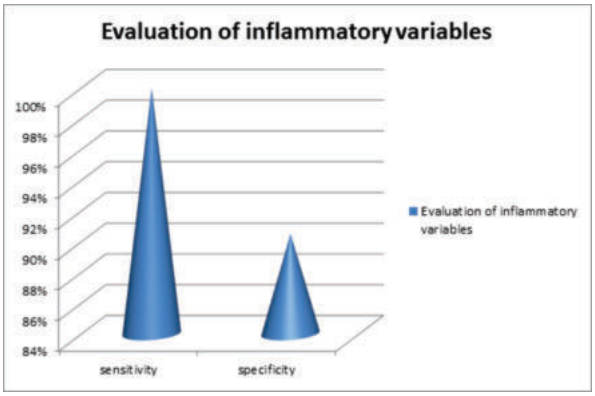


**Chart 2**

All the 100 cases underwent appendicectomy and specimens were sent for histopathological examination. The histopathology report was considered as the final confirmation of diagnosis. Table 6 elucidates the various histopathology reports obtained for all 100 cases.

**TABLE 6**

| Histopathological Diagnosis | | No. of cases |
|---|---|---|
| Acute Appendicitis | Inflamed appendix | 74 |
| | Gangrenous appendicitis | 3 |
| Normal Appendix | Chronic appendicitis with fibrosis | 7 |
| | Lymphoid hyperplasia in appendix | 7 |
| | Normal appendix | 9 |

77 cases had histologically proven acute appendicitis; 74 specimens were reported as inflamed appendix and 3 as gangrenous appendix. Of the 23 cases considered as negative for acute appendicitis, 9 were reported as normal appendix, 7 as chronicappendicitis with fibrosis and 7 as lymphoid hyperplasia in appendix.

Clinical diagnosis was correct in 77% cases and negative appendicectomy rate based on clinical diagnosis was high at 23%.

## CONCLUSION

- Serum CRP estimation has an overall sensitivity of 97.4%, specificity of 86.96%, and diagnostic accuracy of 95%.
- Increased serum CRP levels correlate well with diagnosis of Acute Appendicitis ; as proved by histopathology.
- Being an inflammatory marker, CRP may be elevated in other inflammatory conditions as well. The false positive rate was 13.04% in the present study.
- False negative rate of 2.6% is probably due to pitfalls in latex agglutination qualitative testing and can be avoided by performing qualitative assessments on serial dilutions.
- Serum CRP estimations can be a good diagnostic tool in cases of Acute Appendicitis (though it does not undercut the skill of an experienced surgeon, but compliments it in cases of diagnostic dialamma. ).

## SUMMARY

Acute appendicitis is the most common abdominal surgical emergency, but its diagnosis remains an enigmatic challenge, plagued by a high rate of negative explorations. This study is intended to evaluate the importance of serum CRP level estimation in the diagnosis of acute appendicitis, by comparing with final histopathology report. In a prospective study, 100 patients clinically diagnosed as acute appendicitis in SVS Medical College Hospital,Mahabubnagar, were selected by purposive sampling method and evaluated as per criteria for serum CRP levels, leucocyte count preoperatively and were followed up postoperatively with histopathology reports. The data was analysed for finding the significance of serum CRP in the diagnosis of acute appendicitis.

CRP was positive in 75 of the 77 patients who had histologically proven acute appendicitis and in 3 with normal appendix. The sensitivity, specificity and diagnostic accuracy were 97.4%, 86.96% and 95% respectively. Leucocytosis and neutrophilia when used alone were not specific for acute appendicitis, but when combined with CRP value, diagnostic accuracy was high. Ultrasonography was useful in establishing alternative diagnoses, but had low sensitivity (52.87%) for acute appendicitis.

CRP contains important diagnostic information and hence should always be included in the diagnostic workup of acute appendicitis. Since acute appendicitis is very unlikely in those patients with normal WBC count and CRP level, conservative treatment is recommended. This study does not undercut the skill of an experienced surgeon in diagnosing acute appendicitis, but CRP estimation is a cost-effective investigation which compliments clinical diagnosis.

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