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Original Research Article

# Role of C- reactive protein in addition of Alvarado score as a diagnostic toll in diagnosing acute appendicitis

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**Abstract:** Appendicitis the most common surgery performed by a surgeon. Many scoring system helps us to guide if it is truly a appendicitis or not, to help us avoid negative appendectomies. C- reactive protein is an acute phase reactant, which rises rapidly in response to inflammation. Along with the Alvarado score it is a helpful to diagnose acute appendicitis.
**Keywords:** C- reactive protein: CRP, Appendicitis, inflammation

## INTRODUCTION:

In an age accustomed to early and accurate preoperative diagnosis acute appendicitis remains an enigmatic challenge. The goal of surgical treatment is removal of an inflamed appendix before perforation with a minimal number of negative appendectomies[1]. Many scoring system like Alvarado's score and Bayesian scoring have been used in diagnosing acute appendicitis[2]. C- reactive protein is an acute phase reactant, which rises rapidly in response to tissue injury and can be measured in serum 6-12 hours after the onset of inflammation. Many studies have investigated the role of CRP in improving the diagnosis of acute appendicitis, with promising results[3-5].

Claudius Amyrand in 1736 performed the first appendectomy on an 11 year old boy. Laurence heister in 1755 suggested the possibility of inflammation arising and abscess formation in the appendix. Lawson Tait in 1880 performed the first abdominal appendectomy[1].

Tillet and Francis in 1930 first described C-reactive protein. They demonstrated that CRP could bind to C-polysaccharide of streptococcus in acute phase sera. CRP was discovered in the Avery laboratory of Rockefeller institute.

C – Reactive protein has been a measure of the acute phase reaction to inflammation for the last 20 years recently improved highly sensitive and standardized quantitative assay in serum and CSF have allowed a reevaluation of its potential as a diagnostic laboratory test[4].

C-reactive protein is an abnormal serum glycoprotein produced by the liver during the acute inflammation. Because it disappears rapidly when the inflammation subsides its detection signifies the presence of a current inflammatory process.

CRP production is a non-specific response to disease and it can never on its own be used as a diagnostic test. However if CRP results are interpreted in the light of full clinical information on the patient, then it can provide exceptionally useful information.

CRP is a cyclic pentameric protein composed of five non-covalently bound, identical 23.5 kDa subunits, arranged in a doughnut-shaped polymer. The main function of this pentamer is related to the ability to bind biologically significant ligands in vivo. Tillet and Francis first described protein in 1930. They concluded that sera of patients suffering from acute &reactive infection precipitated with a non-proteic pneumococcus extract called C polysaccharide in the presence of calcium ions. The protein that caused this reaction was therefore called C reactive protein•

The function of CRP is related to its role in the innate immune system. Similar to immunoglobulin IgG, it activates complement, binds to Fc receptors and acts as an opsonin for various pathogens. Interaction of CRP with Fe receptors leads to the generation of pro inflammatory cytokines that enhance inflammatory response. Unlike IgG, which specifically recognizes distinct antigenic epitopes, CRP recognizes altered self and foreign molecules based on pattern recognition.

Thus, CRP is thought to act as a surveillance molecule for altered self and certain pathogens. This recognition provides an early defence and leads to a pro inflammatory signal and activation of the humoral, adaptive immune system. CRP binds to molecular groups found on a wide variety of bacteria and act as an opsonin.

CRP may also be important in the recognition of necrotic tissues. CRP binds to apoptotie cells, protects the cells from assembly of the terminal complement components, and sustains an anti-inflammatory innate immune response.

In man, the only CRP gene coding sequence is found on Chromosome 1. The liver synthesizes CRP. Synthesis of CRP and other acute phase proteins by hepatocytes is modulated by cytokines. Interleukins l b and 6 and tumour necrosis factor are the most important regulators of CRP synthesis. After stimulation with IL-6, IL-l b, TNF and INF, the hepatocytes receive signals to start transcription of DNA coding for CRP. CRP begins to rise in bacterial infections within 4-6 hours, peaks at 36-50 hours, closely parallels acute response with 4-7 hour half-life, allowing to normal 3-7 days after the stimulus is withdrawn.

**Why Measure CRP?**

- Levels of CRP increase very rapidly in response to trauma, inflammation and infection and decrease rapidly with the resolution of the condition. Since an elevated CRP level is always associated with pathological changes, determination of CRP is of great value in diagnosis, treatment and monitoring of inflammatory conditions.
- CRP is a more sensitive and reliable indicator of inflammatory processes than ESR and leucocyte count.
- The serum CRP concentrations increase faster than that of ESR and falls very quickly when the condition subsides.

Rises in CRP are only one part of a number of intricate changes in serum proteins and enzymes but it happens to be one that is earliest to measure because it increases so dramatically.

**Clinical applications:**

1. Screening of organic diseases.
2. Monitoring the extent and activity of disease
3. Predictor of cardiovascular event
4. Detection and management of intercurrent infection.

Drugs that may cause false-positive results include oral contraceptives.

Drugs that may cause false-negative results include NSAIDS/steroids/salicylates.

**Normal values**

Adult serum: 0.07 to 8 ug/ml
Neonatal serum: 0.01 to 0.35ug/ml

**CRP in Acute Appendicitis**

C- reactive protein (CRP) is an acute phase reactant, which rises rapidly in response to inflammation and can be measured in serum 6-12 hours after the Onset of the inflammatory process. Many studies have illustrated the role of CRP in improving the diagnosis of acute appendicitis[3-5].

C-reactive protein levels are elevated in bacterial and protozoal infections, neonatal sepsis, and acute appendicitis. Since an elevated CRP level is always associated with pathological changes, determination of CRP is of great value in diagnosis, treatment and monitoring of inflammatory conditions.

CRP is a more sensitive and reliable indicator of inflammatory processes than ESR and leucocyte count. The serum CRP concentrations increase faster than that of ESR and falls very quickly when the condition subsides. False negative results generally only occur early in Infective episodes.

**MATERIAL AND METHOD:**

The study includes all cases of the right iliac fossa pain presenting themselves in the emergency department of the hospital over a time span of 1 year. The study is a prospective study; each patient will be studied in detail preoperative intraoperative and postoperative period of the patient. Patients will be treated with appendectomy (open/laparoscopically)

**Inclusion Criteria:**

1. Admission to the emergency department with possibility of acute appendicitis.
2. informed consent

**Exclusion Criteria:**

1. HIV seropositivity
2. Patients on cortico steroid therapy
3. Patient with inflammatory bowel diseases or sickle cell disease.
4. Waiting interval appendectomy

Since CRP is a marker of acute inflammation, confounding factors like HIV steroid therapy and inflammatory bowel conditions are excluded.

**METHODS:**

- Clinical history of all patients will be taken in detail.
- Complete examination of all systems will be done
- Laboratory and other investigations will be done as and when required

- Management of appendicitis with appendectomy (open/laparoscopy)
- Examine intra operative condition of appendix and assess the specimen obtained
- Follow and treat the patient post operatively
- Study and discuss the data obtained statistically and reach to an inference

| | **INFLAMMED APPENDIX** | **NORMAL APPENDIX** |
|---|---|---|
| **RP POSITIVE** | a<br>True Positive | b<br>False Positive |
| **RP NEGATIVE** | c<br>False Negative | d<br>True Negative |

Diagnostic sensitivity: a/ (a+c) X 100
Diagnostic specificity: d/ (b+d) X 100
Predictive value of positive test: a/ (a+b) X 100
Predictive value of negative test: d/(c+d) X 100
Diagnostic accuracy: (a+d)/ (a+b+c+d) X 100
False positive error rate: b/ (b+d) X 100
False negative error rate: c/ (a+c) X 100

**RESULT AND ANALYSIS**

Before analysis of the collected data few assumptions were made:-

- Histopathological diagnosis was accepted as final confirmation of diagnosis.
- Though clinical examination and surgical decision involved a large no of consultants in the Department of Surgery, no significance was attached to inter observer variation, as all the consultant were well qualified and had good experience
- Technical errors in CRP estimation were not assigned any significance, since all laboratory technicians were experienced and the test kit was provided by standard manufacturers.
- Considering these assumptions were true, we have analyzed the data obtained, to seek the efficiency of CRP estimation in the diagnosis of acute appendicitis by evaluating the sensitivity specificity predictive values, diagnostic accuracy, error rates and likely hood ratios of same

Sex distribution in the sample is illustrated in Table 1. There is a female predominance in the total number of cases.

The distribution of cases in different age group is shown in Table 2. The prevalence of acute appendicitis is highest in the 21 - 30 years age group followed by the <20 years age group.

Pain abdomen was the commonest clinical symptom and was present in all 100 patients (Table 3). Nausea or vomiting was a predominant symptom which was present in 50% cases. Fever was present in only 69% of patients. Anorexia was reported by 76% of patients (Table 3).

Rebound tenderness was present in 91% 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% case and Psoas sign in 1 case .tachycardia was seen in 98% of cases.

Total leucocyte count revealed leukocytosis i.e. WBC count greater than 10X 109/1,in 59 % of cases differential leukocyte count showed neutrophilia in 36% cases. Abdominal sonography was positive for acute appendicitis in 40 % cases.

Out of 100 cases of histologically proven acute appendicitis, 65 patients had positive serum CRP and 35 patients had normal CRP. These results are given in table 4.

The CRP was elevated in 66.15% patients with acute appendicitis with adhesions. It shows specificity of 57.69% and a sensitivity of 89.58%. It showed a positive predictive value of 66.15% and a negative predictive value of 85.71%. The diagnostic accuracy turned out to be 0.47

The CRP was elevated in 36.92% patients with acute appendicitis with collections. It shows specificity of 45.33% and sensitivity of 96%. It showed a positive predictive value of 36.92% and a negative predictive value of 97.14%. The diagnostic accuracy turned out to be 0.17.

The CRP was elevated in 66.15% patients with acute appendicitis with perforation. It shows a specificity of 38.04% and sensitivity of 100%. It showed a positive predictive value of 12.31% and a negative predictive value of 100%. The diagnostic accuracy turned out to be 0.09.

The cases of acute appendicitis with adhesions and collections were found mostly in the range of 15 to 50mg/dL of CRP and cases of acute appendicitis with perforation were found in the CRP ranging >50mg/dL

**Table-1:Gender wise distribution:**

| Gender | No. of Patients | Percentage (%) |
|---|---|---|
| **Male** | 36 | 36.00 |
| **Female** | 64 | 64.00 |
| **Total** | 100 | 100.00 |

**Table-2: Age Wise Distribution of Patient**

| Age Group | Number Of Patients | Percentage (%) |
|---|---|---|
| ≤20 | 39 | 39.00 |
| 21-30 | 45 | 45.00 |
| 31-40 | 8 | 8.00 |
| 41-50 | 5 | 5.00 |
| 51-60 | 2 | 2.00 |
| ≥60 | 1 | 1.00 |
| TOTAL | 100 | 100.00 |

**Table-3: Distribution of patients with respect to CRP levels**

| CRP | Number of patients | Percentage |
|---|---|---|
| Normal | 35 | 35.00 |
| Abnormal | 65 | 65.00 |
| Total | 100 | 100.00 |

**Table-4: Distribution of patients with respect to CRP level and Acute Appendicitis Adhesion (AAA)**

| CRP | AAA | AAA | Total | P-value |
|---|---|---|---|---|
| | Present | absent | | |
| Normal | 5(14.29%) | 30(85.71%) | 35 | <.001 |
| Abnormal | 43(66.15% | 22(33.85%) | 65 | |

By chi- square test p-value<0.05 therefore there is association between the occurance of acute appendicitis adhesion and CRP level

**Table-5: Distribution of patients with respect to CRP level and Acute Appendicitis Adhesion + Collection (AAC)**

| CRP | AAA | AAA | Total | p-value |
|---|---|---|---|---|
| | Present | absent | | |
| Normal | 1(2.68%) | 34(97.14%) | 35 | <0.001 |
| Abnormal | 24(36.92%) | 41(63.08%) | 65 | |

By chi- square test p-value<0.05 therefore there is association between the occurance of acute appendicitis +collection and CRP level

**Table-6: Distribution of patients with respect to CRP level and Acute Appendicitis + Perforation (AAP)**

| CRP | AAA | AAA | Total | p-value |
|---|---|---|---|---|
| | Present | absent | | |
| Normal | 0 | 35(100%) | 35 | 0.048 |
| Abnormal | 8(12.31%) | 57(87.69%) | 65 | |

By chi- square test p-value<0.05 therefore there is association between the occurance of acute appendicitis +perforation and CRP level

**Table-7: Distribution of patients with respect to CRP level and Acute Appendicitis with collection (AAC)**

| CRP | AAC | AAC | Total | p-value |
|---|---|---|---|---|
| | Present | absent | | <0.001 |
| 0-6 | 1 | 34 | 35 | |
| 6.01-15.00 | 6 | 26 | 32 | |
| 15.01-50.00 | 15 | 13 | 28 | |
| >50 | 3 | 2 | 5 | |

By chi- square test p-value<0.05 therefore there is association between the occurance of acute appendicitis +collection and CRP level

**Table-8: Distribution of patients with respect to CRP level and Acute Appendicitis with perforation (AAP)**

| CRP | AAP | AAP | Total | p-value |
|---|---|---|---|---|
| | Present | absent | | <0.001 |
| 0-6 | 0 | 35 | 35 | |
| 6.01-15.00 | 1 | 31 | 32 | |
| 15.01-50.00 | 3 | 25 | 28 | |
| >50 | 4 | 1 | 5 | |

By chi- square test p-value<0.05 therefore there is association between the occurrence of acute appendicitis +perforation and CRP level

## DISCUSSION

CRP is a member of the class of acute phase reactants as its levels rise dramatically during inflammatory process occurring in the body.

It is thought to assist in the complement binding to foreign and damaged cell and affect the humoral response to disease.

Appendicitis is the most common abdominal surgery emergency and appendectomy is one of the most frequently performed abdominal operations.

Some, indicating that patients who do not have recurrent episodes of appendicitis within 3 to 6 months may never need an appendectomy, has called the traditional practice of an interval appendectomy into question.

Therefore a clinician always wonders whether a patient with appendicitis needs to receive surgical management or a medical management. After a patient is diagnosed with appendicitis the clinician generally wants to determine the severity before they can select the optimal treatment. If the clinician can predict the severity of appendicitis, one could the therapeutic method and the timing of the operation.

A surgical indication marker such as WBC, neutrophil percentage or CRP would be useful for deciding between treating the patient with surgery or antibiotics. The aim of this study was to evaluate whether blood inflammatory markers predict the severity of appendicitis and to identify an independent marker for the surgical indication of acute appendicitis.

Our novel findings give additional information for surgical indication for appendicitis. Numerous previous studies have shown that the CRP level enhance the precision of diagnosis of acute appendicitis but not surgical indication[6-9].

A large retrospective study has documented that the sensitivity of CRP in these patients is greater than 90%. Furthermore the negative appendectomy rate is reduced by approximately 8% if the surgery is cancelled in patients with CRP levels and WBC within the reference range.

Another prospective study has shown that it is important to measure serial CRP level and WBC counts in patients with suspected appendicitis. The sensitivity of CRP level in predicting appendicitis was 60% on admission and increased to 100% by fourth blood specimen. Conversely, WBC count exhibited a sensitivity of 95% on admission, but dropped to 75% by th fourth specimen. Other studies confirm that an elevated CRP serves as a systemic marker of focal inflammation and infection.

## CONCLUSION

This study clearly suggested that CRP leads to precise prediction of the severity of acute appendicitis for treatment.

Elevated CRP has a higher sensitivity for complications of acute appendicitis than specificity.

Therefore before using our system for surgical indication, clinicians interpreting must depend on their subjective experience and modalities such as computed tomography, ultrasonography to establish a diagnosis of appendicitis and must exclude other causes of symptoms

The cut off level at around 6mg/dL needs to be handled carefully and may need much higher patient number to reach the confidant level.

If clinical symptoms and image examinations indicate that a person has appendicitis, a person with high CRP should undergo surgery immediately and if CRP level is negative then the patient could be managed non-surgically.

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