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Original Article

# Relationship of C-reactive Protein to Alvarado Score and Computed Tomography Scan in Diagnosing Acute Appendicitis

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## Abstract

**Introduction:** Acute appendicitis (AA) is a common gastrointestinal disease affecting 5.7–57/100 individuals each year with the highest incidence in children and adolescents. The variation of incidence is due to variations in ethnicity, sex, age, obesity, and season of the year.

**Aim:** The aim of ours study was to correlate C-reactive protein (CRP) to Alvarado score (AS) and computed tomography (CT) scan in diagnosing AA.

**Material and Method:** This prospective and observational study was conducted in the Department of General Surgery, Indian Centre for Advancement of Research and Education (ICARE) Institute of Medical Science and Research. Kolkata. This study was conducted for a period of 2 years, September 2019–August 2021. All patients above the age of 18 years were included in this study with high clinical suspicion of an acute attack of appendicitis and patient with whole abdominal contrast-enhanced CT as a part of protocol at ICARE Institute of Medical Science and Research, Kolkata.

**Results:** About 49 (64.5%) patients had AA in CT scan finding and 12 (15.8%) patients had chronic appendicitis in CT scan finding. According to the histopathological examination finding, 64 (84.2%) patients had AA and 12 (15.8%) patients had chronic appendicitis.

**Conclusion:** The positive correlation was found between CRP with AS which was statistically significant. AS and CRP levels in combination provide us to confirm or rule out AA safely.

**Key words:** Alvarado Score, Computed tomography scan, Acute appendicitis, and C-reactive protein.

## INTRODUCTION

Acute appendicitis (AA) is a common gastrointestinal disease affecting 5.7–57/100 individuals each year with the highest incidence in children and adolescents. The variation of incidence is due to variations in ethnicity, sex, age, obesity, and season of the year.[1]

AA is the most common cause of acute surgical abdomen, with an estimated lifelong risk of 8.6% in men and 6.7% in women.[2] It is often regarded as a disease of the young population with a peak incidence in the 2nd and 3rd decades of life.[2,3] Appendectomy is generally accepted as a first-line treatment for non-complicated AA. Reports have shown that pre-operative radiographic evaluation has helped to decrease negative appendectomy rates from 20% to as low as 5%.[4] Computed tomography (CT) has been frequently used as an imaging modality in the evaluation of AA and has improved the diagnostic ability leading to a significant reduction in the number of negative appendectomies.[5] With a reported sensitivity of up to 96.5% and specificity of about 98%, CT plays a major role in the clinical decision-making process in AA and is considered as a first-line imaging modality in the diagnostic work-up for suspected AA.

C-reactive protein (CRP) is an abnormal serum glycoprotein produced by the liver during the acute inflammation.

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Because it disappears rapidly when the inflammation subsides its detection signifies the presence of a current inflammatory process.

The function of CRP is related to its role in the innate immune system. Similar to immunoglobulin G (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 proinflammatory 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 defense and leads to a proinflammatory signal and activation of the humoral and 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 apoptotic cells, protects the cells from assembly of the terminal complement components, and sustains an anti-inflammatory innate immune response.

### Aim

The aim of the study was to correlate CRP to Alvarado Score (AS) and CT scan in diagnosing AA.

### Objective

1. The objective of the study is to assess, on admission, whether CRP levels are a good predictor for AA.

## MATERIAL AND METHOD

### Study Design

This was a prospective and observational study.

### Study Site

This study was conducted in the Department of General Surgery, Indian Centre for Advancement of Research and Education (ICARE) Institute of Medical Science and Research, Kolkata.

### Sample Size

N (sample size)= zα2p (1−p)/e2 where p is proportion and e is precision

Here, $\alpha = 5\%$, hence, $z\alpha = 1.96$, p (incidence of AA) = 4.7% e = 5%. Using these values in the above formula, n is coming as 109. Hence, minimum 69 patients were included in the study 100. On adding 10% to make up for dropouts during the study, the sample size comes as 76.

### Study Period

This study was conducted for a period of 2 years, September 2019–August 2021.

### Study Population

The source of data for study was 69 patients, admitting during period of 24 months commencing from September 2019, in the Department of General Surgery, at Calcutta Medical Research Institute and Tata Motors Hospital. Adding 10% to make up for dropouts during the study, the sample size comes as 76.

### Inclusion Criteria

The following criteria were included in the study:

1. All patients above the age of 18 years
2. High clinical suspicion of an acute attack of appendicitis
3. Patient with whole abdominal contrast-enhanced CT (CECT) as part of protocol at ICARE Institute of Medical Science and Research, Kolkata.

### Exclusion Criteria

The following criteria were excluded from the study:

1. Immunocompromised patients.
2. Patients on steroids or immunosuppressants
3. Patients with other infective or inflammatory conditions in the body
4. Pregnant patients.
5. Patients with renal compromise.

### Statistical Analysis

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by SPSS 24.0 and GraphPad Prism version 5. A Chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a Chi-squared distribution when the null hypothesis is true. Without other qualification, "Chi-squared test" often is used as short for Pearson's Chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. $P \leq 0.05$ was considered for statistically significant.

## RESULT AND DISCUSSION

This prospective and observational study was conducted in the Department of General Surgery, Calcutta Medical Research Institute, Kolkata and Tata Motors Hospital, Jamshedpur, Jharkhand. This study was conducted for a period of 2 years, September 2019–August 2021. The source of data for study was 69 patients, admitting during period of 24 months commencing from September 2019, in the Department of General Surgery, at Calcutta Medical Research Institute and Tata Motors Hospital. Adding 10% to make up for dropouts during the study, the sample size comes as 76.

All patients above the age of 18 years were included in this study with high clinical suspicion of an acute attack of appendicitis and patient with whole abdominal CECT as a part of protocol at ICARE Institute of Medical Science and Research, Kolkata.

In our study, the most of the patients had AA (49 [64.5%]) and only 12 (15.8%) patients had chronic appendicitis in CT scan finding.

Our study showed that the most of the patients had acute (Superficial) appendicitis in histopathological examination (HPE) (37 [48.7%]). Rest 1 (1.3%) patient had AA in HPE, 17 (22.4%) patients had acute (Phlegmonous and non-perforated) appendicitis in HPE, 8 (10.5%) patients had acute (Phlegmonous and perforated) appendicitis in HPE, 1 (1.3%) patient had acute (Phlegmonous and Perforated) appendicitis in HPE, and 12 (15.8%) patients had chronic appendicitis in HPE.

We found that 64 (84.2%) patients had AA in HPE final and 12 (15.8%) patients had chronic appendicitis in HPE final.

Tanrıkulu *et al.*[6] (2016) found that 278 patients were included in this study. Patients were separated into two main groups as the surgery group ($n$ = 184) and non-operative group ($n$ = 94). Inflammatory parameters were not predictive for histopathologic results, although higher CRP and PCT levels were significant in perforated and necrotizing appendicitis. Multifactorial regression analyzes showed that AS was not of significant predictive value in the non-operative group. There was no superiority of AS and/or US in the diagnosis of AA.

It was found that the mean AS (mean ± S.D.) of patients was 6.9737 ± 1.9458. The mean CRP (mean ± S.D.) of patients was 21.7724 ± 9.5334. The mean total lymphocyte count (mean ± S.D.) of patients was 14240.1316 ± 4750.8176.

We found that in AA, 16 (25.0%) patients were 21–30 years old, 21 (32.8%) patients were 31–40 years old, 6 (9.4%) patients were 41–50 years old, 4 (20.3%) patients were 51–60 years old, and 8 (12.5%) patients were 61–70 years old. In chronic appendicitis, 3 (25.0%) patients were 21–30 years old, 3 (25.0%) patients were 31–40 years old, 2 (16.7%) patients were 41–50 years old, and 4 (33.3%) patients were 51–60 years old. It was not statistically significant ($P$ = 0.5626).

Our study showed that in AA, 19 (29.7%) patients were female and 45 (70.3%) patients were male. In chronic appendicitis, 4 (33.3%) patients were female and 8 (66.7%) patients were male. This was not statistically significant ($P$ = 0.8008).

Pipal *et al.*[7] (2016) found that in HPE confirmed appendicitis in 90 patients with 10 negative appendicectomies.

In our study, the most of the AA patients had febrile fever (60 [93.8%]) compared to chronic appendicitis patients (3 [25.0%]). In AA, 4 (6.3%) patients had afebrile fever and 60 (93.8%) patients had febrile fever. In chronic appendicitis, 9 (75.0%) patients had afebrile fever and 3 (25.0%) patients had febrile fever. Association of fever versus HPE final was statistically significant ($P$ < 0.0001).

It was found that the higher number of AA patients (58 [90.6%]) had nausea and vomiting compared to chronic appendicitis patients (9 [75.0%]) which was not statistically significant ($P$ = 0.1242).

We found that in AA, 26 (40.6%) patients had tachycardia. In chronic appendicitis, 7 (58.3%) patients had tachycardia. This was not statistically significant ($P$ = 0.2560).

We also found that 30 (46.9%) AA patients had tachypnea where in chronic appendicitis group, no patients had tachypnea which was statistically significant ($P$ = 0.0023).

Tanrıkulu *et al.*[6] (2016) showed that 278 patients were included in this study. Patients were separated into two main groups as the surgery group ($n$ = 184) and non-operative group ($n$ = 94). In the surgery group, clinical predictive factors for histopathologic results such as AS ≥7, AA signs on US, neutrophilia, and leukocytosis were significant. Neutrophilia and leukocytosis had the highest accuracy rate among these factors.

Wang *et al.*[7] (2012) found that participants were divided into two groups: Leukocytosis (LK group) and non-leukocytosis (non-LK group). In the first phase of the analysis, there were statistically significant differences in white blood cell count (13.5 K vs. 10.9 K per μL), neutrophilia (81.5% vs. 73.5%), and hospital stay (4.9 vs. 3.5 days) between the two groups.

In our study, neutrophilic leukocytosis was significantly higher in AA patients (48 [75.0%]) compared to chronic appendicitis patients (1 [8.3%]) and it was statistically significant ($P$ < 0.0001).

Pipal *et al.*[8] (2016) showed that AS in combination with ultrasonography is a valuable tool for diagnosing AA in spite of sophisticated investigations like CT, thus reducing the cost of the treatment and preventing negative appendicectomy rate.

Vaghela *et al.*[9] (2017) found that the correlation between appendiceal diameter and AS was 78.7% ($P$ = 0.01 <0.05).

Presence of appendiceal diameter above 6.5 mm on CT, periappendiceal inflammation, fluid, and appendicoliths should prompt the diagnosis of AA. Since patients with AA may not always show the typical signs and symptoms, CT is a helpful imaging modality for patients with relatively low AS and leukocytosis, when physical examination is confusing.

Wang *et al.*[7] (2012) found that CT scan is necessary for patients with relatively low AS when leukocytosis is noted.

Al-Faouri *et al.*[10] (2016) showed that the diagnostic performance of CT scan was superior to that of AS with sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of 94.2 versus 85.4%, 90 versus 65%, 9.42 versus 2.44, and 0.065 versus 0.224, respectively ($P < 0.05$). The overall diagnostic accuracy of CT scan was 92.6% compared to 77.5% for AS. The AS was far from good and CT scan is more accurate in diagnosis of AA in their patient population.

Our study showed that in AA, all patients (64 [100.0%]) had AA as per CT scan finding. In chronic appendicitis, all patients (12 [100.0%]) had chronic appendicitis as per CT scan finding. It was statistically significant ($P < 0.0001$).

We found that in AA, 1 (1.6%) patient had AA in HPE, 17 (26.6%) patients had acute (Phlegmonous and non-perforated) appendicitis in HPE, 8 (12.5%) patients had acute (Phlegmonous and perforated) appendicitis in HPE, 1 (1.6%) patient had acute (Phlegmonous and Perforated) appendicitis in HPE, and 37 (57.8%) patients had acute (Superficial) appendicitis in HPE. In chronic appendicitis, 12 (100.0%) patients had chronic appendicitis in HPE. Association of HPE versus HPE final was statistically significant ($P < 0.0001$).

In our study, the mean age (mean ± s.d.) of chronic appendicitis patients was higher (42.1667 ± 13.6437 years) than the AA patients (41.4688 ± 13.5892) which was not statistically significant ($P = 0.8708$).

Talabi *et al.*[11] (2021) evaluated the diagnostic value of AS, white blood cell count, and serum CRP in children with AA. The sensitivity and specificity of AS, CRP estimation, and total white blood cell count in diagnosing AA were 86.4% and 63.2%, 98.8% and 36.8%, and 51.9% and 89.5%, respectively. AS has the highest area under ROC curve analysis 0.824, 95% CI of 0.724 to 0.924 compared with CRP, 0.769. 95% CI of = 0.647 to 0.891 and WBC count, 0.765, 95% CI of 0.643 to 0.887. Both CRP and WBC count showed higher discriminatory values between complicated and uncomplicated appendicitis, $P < 0.001$.

Thirumallai *et al.*[12] (2014) showed that patients were categorized into three groups retrospectively based on the AS. Group I: Score 7–10 ($n = 155$), Group II: Score 4–6 ($n = 71$), and Group III: Score <3 ($n = 10$). Overall, 169 of 234 (72.2%) had histopathological confirmation of AA. The predicted accuracy of AS was 84.5% in Group I, 50.7% in Group II, and 25% in Group III. The PPV of high CRP and NPV of normal CRP for Group I was 88% and 36.4%, in Group II, 63% and 72%, in Group III, 33% and 86%, respectively. The AS and CRP taken together improve the predictive value of diagnosing AA.

Farahbakhsh *et al.*[13] (2020) showed that the sensitivity, specificity, positive predictive value, negative predictive

**Table 1: Association between CT Scan Finding and Neutrophilic Leukocytosis: HPE Final**

| | | HPE Final | | | | |
|---|---|---|---|---|---|---|
| | | Acute Appendicitis | Chronic Appendicitis | Total | Chi-square value | *P*-value |
| CT Scan Finding | Acute Appendicitis | 64 | 0 | 64 | 76.0000 | <0.0001 |
| | Row % | 100.0 | 0.0 | 100.0 | | |
| | Col % | 100.0 | 0.0 | 84.2 | | |
| | Chronic Appendicitis | 0 | 12 | 12 | | |
| | Row % | 0.0 | 100.0 | 100.0 | | |
| | Col % | 0.0 | 100.0 | 15.8 | | |
| | TOTAL | 64 | 12 | 76 | | |
| | Row % | 84.2 | 15.8 | 100.0 | | |
| | Col % | 100.0 | 100.0 | 100.0 | | |
| Neutrophilic Leukocytosis | Absent | 16 | 11 | 27 | 19.6080 | <0.0001 |
| | Row % | 59.3 | 40.7 | 100.0 | | |
| | Col % | 25.0 | 91.7 | 35.5 | | |
| | Present | 48 | 1 | 49 | | |
| | Row % | 98.0 | 2.0 | 100.0 | | |
| | Col % | 75.0 | 8.3 | 64.5 | | |
| | TOTAL | 64 | 12 | 76 | | |
| | Row % | 84.2 | 15.8 | 100.0 | | |
| | Col % | 100.0 | 100.0 | 100.0 | | |

value, and accuracy were 77%, 19%, 78%, 17, and 64% in Anderson, 95%, 7%, 75%, 30%, and 77% in Alvarado, and 92%, 7%, 79%, 20%, and 75% in Alvarado + CRP scoring systems, respectively. Anderson scoring system had lower diagnostic accuracy than the Alvarado system.

Alhames *et al.*[14] (2021) showed that AS categories were retrospectively calculated as low (0–4 points), intermediate (5–6 points), or high (7–10 points). The cutoff levels were >0.5 mg/dl for CRP. According to the AS, 108 (32.6%) were at low risk, 76 at (23.0%) intermediate risk, and 147 (44.4%) at high risk of AA. The AUCs of ROC were 0.76 (0.70–0.81) for AS and 0.79 (95% CI 0.75–0.84) for CRP-AS being the difference statistically significant ($P$ = 0.003). The CRP for diagnosis AA in low-risk AS group had negative predictive value of 95.8% (95%CI 87.3–98.9) and likelihood ratio negative of 0.4 (95%CI 0.2–1.0). CRP-AS has shown to increase the diagnostic accuracy of AS for AA.

Zouari *et al.*[15] (2016) conducted a study where patients were categorized into three groups based on the AS: Group I: Score 7–10, Group II: Score 5–6, and Group III: Score 0–4. The difference between predictive values of AS alone and AS with CRP was not statically significant. The PPV increased from 74.29% (AS and CRP) to 93.75% (AS and US) in Group I ($P$ = 0.001) and the NPV increased from 64.86 and 79.69% (AS and CRP) to 82.6 and 88.2% (AS and US) in Group II ($P$ = 0.01) and Group III ($P$ = 0.001), respectively.

It was found that the mean AS (mean ± s.d.) of AA patients was higher (7.6094 ± 1.3641 (than the chronic appendicitis patients (3.5833 ± 0.5149) and this was statistically significant ($P$ < 0.0001) [Table 1].

## CONCLUSION

The positive correlation was found between CRP with AS which was statistically significant.

We concluded that using AS and CRP levels in combination provide us to confirm or rule out AA safely.

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