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# Diagnostic role of C-Reactive Protein in Acute Appendicitis

**Ashis pun,[1] Amit Dhungana,[2] Ramjee Bastola[1]**
[1]Department of General Surgery, [2]Department of Anaesthesiology, Bharatpur Hospital, Bharatpur-10, Chitwan, Nepal.

## ABSTRACT

### Introduction

Acute appendicitis is the common surgical disease however, accurate diagnosis and exclusion of acute appendicitis always remains challenge to the surgeons. Although diagnoses rely mostly on clinical examination but C- reactive protein (CRP) can be of valuable armamentarium. Hence, this study was conducted to find the diagnostic role of C-reactive protein in Acute Appendicitis

### Methods

A retrospective cross sectional study was conducted among 100 respondents in the Department of Surgery, Bharatpur Hospital from September 2019 to August 2020. Ethical approval was taken from the Institutional Review Committee (IRC) Bharatpur Hospital. Statistical analysis was done by using SPSS version 16 using descriptive statistics.

### Results

Total of 100 patients was included in study with mean age 31 years old.Out of which 60% were male and 40% were female. CRP value was raised (>6) in 87 (87%) cases and normal in 13(13%) cases. Among those with raised CRP, three patients had normal appendix histopathologically and 57 had uncomplicated appendicitis and 27 had complicated appendicitis histopathologically with sensitivity, specificity, positive predictive value and diagnostic accuracy rate of 95.45 %, 75 %, 96.55 % and 93% respectively. When white blood count (WBC) and CRP level were combined with HPE findings, its sensitivity, specificity and diagnostic accuracy rate were 100%, 80% and 93.83 % respectively.

### Conclusions

CRP improves the diagnostic accuracy of Acute appendicitis. The adjunct use of CRP and leucocyte count can effectively reduce the negative appendectomy rate.

**Keywords:** acute appendicitis; C-reactive protein; leucocyte; white blood cell.

**Correspondance:** Dr. Ashis Pun, Department of Surgery, Bharatpur Hospital, Bharatpur-10, Chitwan, Nepal. Email: ashis_pun@hotmail.com, phone: +977-9851094189.

## INTRODUCTION

Acute appendicitis is the most frequent cause of abdominal pain requiring surgery. An estimated 16% of people in western world require appendectomy at some stage during their life.[1,2] Over the years, many studies have been done to improve the diagnostic accuracy in appendicitis but its accurate preoperative diagnosis still remains elusive.[2,3,4] The diagnosis of acute appendicitis relies largely on clinical assessment, although both ultrasound and computed tomography (CT) can be helpful.

At any site of injury or inflammation macrophages and monocytes release soluble cytokines including IL-1, IL-6 and TNF-alpha. Some of these cytokines enter the circulation and exert pressure on bone marrow to increase production and release of leucocytes and on liver to increase production of CRP to combat infection.[5]

C-reactive protein is produced form liver to combat against the infection. CRP level help monitor inflammation/infection. Normal value is <8mg/l. Like ESR, it is raised in many inflammatory conditions, but changes more rapidly; increases in hours and falling within 2-3 days of recovery. Therefore it can be used to follow the response to therapy or disease activity. CRP value in mild inflammation 10-15 mg/l; active bacterial infection 50-200 mg/dl; severe infection or trauma >200mg/l.[6]

The purpose of this study is to correlate the preoperative diagnostic accuracy and the predictive value of CRP in patients with acute appendicitis which can help the surgeon to come to an accurate diagnosis.

## METHODS

A hospital based retrospective cross sectional study was conducted in the Department of Surgery, Bharatpur Hospital, Chitwan Nepal from June 2019 to May 2020. Ethical approval was taken from the institutional review committee (IRC) Bharatpur Hospital (Ref No.17/076/77) and written consent was taken from all the study respondents. Sample size was calculated using pre-determined value of sensitivity using the formula $n= Z^2Pq/d^2$. Pre-determined value of sensitivity or specificity was taken as 95.6 from the study conducted by Shafiet[7] with 5% margin error. The minimum sample size of this study was found to be 64. By adding extra 10% non response error, study was conducted among 100 respondents. Respondents were selected by using non probability sampling technique. Patients of aged ≥ 14 years who presented with right lower quadrant pain and clinically diagnosed of acute appendicitis were included in study. Patients with diagnosis of recurrent appendicitis, appendicular lump and alternative diagnosis on intraoperative finding were not subjected to study. Similarly patients who were already on antibiotics before the blood sample was sent for laboratory analysis and patient with other systemic illness that effects WBC and CRP level like musculoskeletal disorders, pancreatitis etc were not enrolled in the study.

All the appendix were sent for histopathological reports. On the basis of operative findings and histopathological reports patients were categorized in Group A: normal (uninflamed appendix),Group B: uncomplicated (inflamed appendix) and Group C: complicated (perforated/gangrenous) CRP value is considered normal if ≤ 6 mg/dl and cut off value for increased leucocyte count is 11000/mm.[8] Self designed questionnaire was used to collect the data from the patients. Collected data were check for completeness and entered in Microsoft excel then analyzed using SPSS version 16. Data were analyzed by using descriptive. In the descriptive statistics frequency, percent mean and SD were used. By using cross tabulation sensitivity, specificity, positive and negative predictive values were calculated among the various parameters.

## RESULTS

A total of 100 respondents were included in the study in which 63% were aged below 30 years age and37% were more than 30 years of age. The mean ± SD of age of respondents was 31±15.31 years. Also, 60% patients were male and 40% patients were female by gender. Histopathologically normal appendix was found in 12% cases, uncomplicated appendicitis in 61% cases and complicated appendicitis in 27% cases. White blood cell count (WBC) was increased (>11,000cells/mm$^3$) in 86% of cases and normal in 14%cases. CRP level was normal among 13% respondents and abnormal among 87% cases (Table 1).

**Table 1.** Baseline characteristics of the respondents.

| | | n=100 |
|---|---|---|
| **Variables** | **Frequency** | **Percent** |
| **Age** | | |
| <30 | 63 | 63.0 |
| ≥30 | 37 | 37.0 |
| Mean(SD) | 31±15.31 years | |
| **Gender** | | |
| Male | 60 | 60.0 |
| Female | 40 | 40.0 |
| **IO** | | |
| Gangrenous | 17 | 17.0 |
| Inflamed | 70 | 70.0 |
| Normal | 7 | 7.0 |
| Perforated | 6 | 6.0 |
| **HPE** | | |
| Normal | 12 | 12.0 |
| Uncomplicated | 61 | 61.0 |
| Complicated | 27 | 27.0 |
| **TLC** | | |
| Normal | 14 | 14 |
| Increased | 86 | 86 |
| **CRP** | | |
| Normal | 13 | 13 |
| Increased | 87 | 87 |

Among those with increased WBC count, 27 patients (100%) had complicated appendicitis with raised WBCs and 53 patients (86.89%) of patients had histologically proven uncomplicated appendicitis with raised WBCs as in (Figure 1).

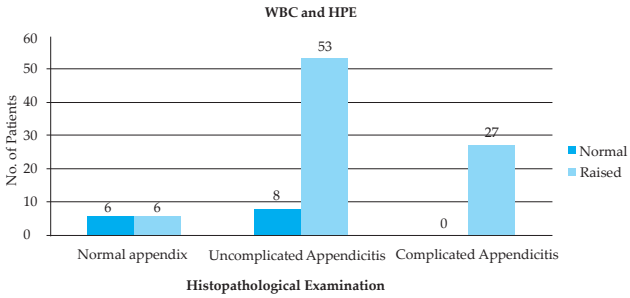


**Figure 1.** WBC and HPE of respondents.

CRP value was raised (>6) in 87 (87%) cases and normal in 13(13%) cases. Among those with raised CRP, three patients had normal appendix histopathologically and 57 patients (93.44%) had uncomplicated appendicitis and 27 patients (100%) had complicated appendicitis histopathologically with raised CRP (Figure 2).

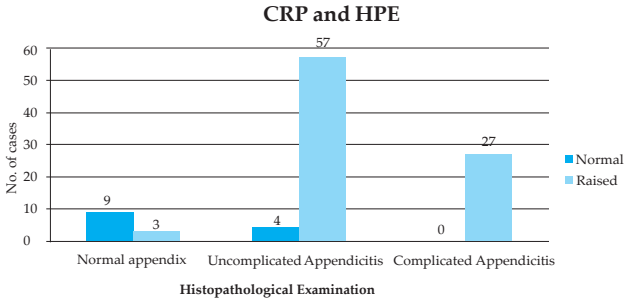


**Figure 2.** CRP and HPE of respondents.

The sensitivity, specificity, positive predictive value, negative predictive value , diagnostic accuracy rate of CRP was 95.45%, 75%, 96.55% , 69.23% and 93% respectively with P value: <0.001 (Table 3).

**Table 3.** The sensitivity, speci icity, positive predictive value, negative predictive value, of CRP.

| Serum C-reactive Protein | Histologically Appendicitis | Histologically Normal Appendix | Total |
|---|---|---|---|
| Raised | 84 (TP) | 3 (FP) | 87 |
| Normal | 4 (FN) | 9 (TN) | 13 |
| Total | 88 | 12 | 100 |

*TP: true positive; TN: true negative; FP: false positive; FN: false negative*

WBC and CRP were both raised in 79 cases, out of which 76 patients had positive HPE findings and three patients had negative HPE findings. In four cases both WBC and CRP were normal and HPE findings also showed normal appendix. There was no histologically proven appendicitis when both WBC and CRP were normal as in (Table 4).

**Table 4.** Relationship between CRP value and WBC with HPE findings.

| WBC / CRP | HPE | | Total |
|---|---|---|---|
| | Appendicitis | Normal Appendix | |
| Normal | 0 | 4 | 4 |
| Raised | 76 | 1 | 77 |
| Total | 76 | 5 | 81 |

When both CRP and WBC was combined and compared with HPE, sensitivity, specificity and diagnostic accuracy rate were100 %, 80 % and 93.83 % respectively

## DISCUSSION

The diagnosis of appendicitis can be very challenging due to its wide variety in clinical presentation. To overcome this diagnostic dilemma modern diagnostic tools like ultrasonography, Computed tomography (CT) and various scoring system like Alvarado, modified Alvarado, Tzanaki, Lintula, Paediatric Appendicitis Score (PAS), Raja IsteriPengiranAnakSaleha Appendicitis (RIPASA) and Appendicitis Inflammatory Response (AIR) are introduced. Implementation of these diagnostic tools and scoring systems hasshown some improvement but these modern tools are not easily available at all hospitals. Although various studies have been conducted,here we attempt to evaluate CRP which can be easily performed in most of the hospitals and compare it with leucocyte count and HPE report to see its diagnostic essence.

In our study, the sensitivity and specificity of CRP level is 95.45 % and 75% respectively. The positive predictive value of CRP is 96.55 % and negative predictive value is 69.23%. The diagnostic accuracy rate is 93 % and P value is <0.001 which is statistically significant. This finding is comparable to the study done by Gurleyik E. et alwhere the sensitivity, specificity and accuracy of serum CRP measurements were calculated as 93.5%, 80% and 91% respectively.[9] Whereas our results were superior to that by Shafi S.M and collegues where sensitivity, specificity and positive predictive value were 98.9%,38.88% and 89.21%.[8] In a double blind study by Asfar S. et al,[10] the specificity and sensitivity of CRP level was 86.6% and 93.6% concluding that normal CRP level in suspected appendicitis is most likely to be associated with normal appendix. In contrary, study done by Agrawal C.S et al[11] and Jangjoo A et al[12]CRP level was not found to be a good indicator of appendicitis with sensitivity and specificity of 78.8% and 66.7% by Agrawal CS and sensitivity and specificity of 59% and 68% by Janjoo A. However in a meta-analysis done by Hallan S et al it showed that CRP performed is better and statistically significant.[13] Similarly john S.K et al also found CRP better with sensitivity of 98% and specificity of 87% with P value <0.0001 comparable to our study.[14]

At present study, when both leucocyte count and CRP were combined and compared with HPE positive finding, sensitivity increased to 100% and specificity increased to 80 % and diagnostic accuracy of 93.82%. This showed that normal leucocyte and CRP level patients subjected for operative management should be thought twice and planned for other diagnostic modalities like CT scan. Our result was comparable with study done by Mohammed A.A et al[15] with sensitivity and specificity of 86% and 90.7% and John S.K et al[14]with sensitivity of 100% and diagnostic accuracy of 92% . In a cross sectional study done by Siddique K et al[16]combined sensitivity of

WBC and CRP increased to 95% and 100% for diagnosis of uncomplicated appendicitis and complicated appendicitis respectively.

In this study, total complicated appendicitis cases were found in 27 patients and WBC was raised in all cases (100%). Likewise CRP was also raised in all cases of complicated appendicitis (100%). In all cases (61 cases) of uncomplicated appendicitis WBC count was raised by 86.89% and CRP was raised by 93.4 %. This showed that WBC and CRP also help to estimate the severity of the disease. This present study is comparable to the study done by Sulberg D et al[17] where it showed strong CRP correlation with respect to the grade of inflammation and perforation. Similar finding was also observed in study by Vaugh-Shaw PG et alwhere CRP, WBC and neutrophil combined were able to differentiate between normal, uncomplicated and complicated appendicitis.[18]

## CONCLUSIONS

Although the diagnosis of acute appendicitis mostly relies on clinical evaluation, we suggest CRPlevel measurement is useful in assessment of acute appendicitis. Besides, we also found that combined analysis of CRP and WBC parameters can spare a group of patients from unnecessary surgical procedure.

**Conflict of interest:** none

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