International Surgery Journal
Jaiswal AK et al. Int Surg J. 2020 Aug;7(8):2662-2667
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20203252

Original Research Article

Prospective study of accuracy of C-reactive protein and leucocyte count in diagnosis of acute appendicitis in comparison with histopathology

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Received: 17 May 2020
Revised: 20 June 2020
Accepted: 29 June 2020

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ABSTRACT

Background: Acute appendicitis is one of the most common surgical emergencies. Approximately 7.0% of the population will have appendicitis in their lifetime with the peak incidence occurring between the age of 10 and 30 years. The classical history of peri umbilical pain at beginning and later shifting to right iliac fossa is present in only 50% cases. C-reactive protein is an acute phase reactant synthesized by liver in response to tissue injury. Serial measurement of CRP can improve the accuracy of diagnosing acute appendicitis.
Methods: A prospective study of 70 cases with clinical diagnosis of acute appendicitis admitted in the department of surgery, B. R. D. Medical College Gorakhpur during a period of one year.
Results: There was young age predominance (54.2%) and commonest presenting symptom was RIF pain (100%) followed by nausea/vomiting (66%) and fever (60%). Among 48 cases of histopathology proven appendicitis, CRP was raised in 44 cases (91.6%).
Conclusions: Serial measurement of CRP is more sensitive and specific than TLC count and the raised value of CRP is directly related to the severity of inflammation. Combining the TLC and CRP increases the diagnostic accuracy and therefore may reduce rate of negative appendectomy.

Keywords: Appendicitis, C-reactive protein, Histopathology, Total leucocyte count

INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies and the most common source of infection in community-acquired intra-abdominal infection.[1] Approximately 7.0% of the population will have appendicitis in their lifetime with the peak incidence occurring between the age of 10 and 30 years.

Abdominal pain is the most common clinical presentation. Anorexia, nausea and vomiting with tenderness or guarding rigidity in right iliac fossa on examination. However, these are not very specific for appendicitis.[2] In 70.0% of the cases the clinical presentation is typical and there is no difficulty in making a diagnosis. The remaining 30.0% have atypical clinical presentation and present a diagnostic dilemma for the surgeons especially in the extreme of age, in women of reproductive age and with abnormal position of the appendix and thus have an uncertain preoperative diagnosis leading to unnecessary laparotomy and appendectomy.[3]

A negative appendectomy ranging from 10.0 to 44.0% has been considered acceptable by various authors with view to minimize the incidence of perforation and associated morbidity and mortality. Various diagnostic modalities have been reported to influence the negative appendectomy. This includes radiological, laparoscopy and laboratory methods of investigation. Leucocyte has

long been known to be a useful adjunct to the diagnosis of appendicitis; however, the utility of this test has been poorly characterized as it can be very non-specific at times.[4] A more recently suggested laboratory evaluation is determination of C-reactive protein level. C-reactive protein (CRP) is an acute phase reactant synthesized by liver in response to tissue injury. A multivariate analysis showed that the serial measurement of CRP can improve the accuracy of diagnosing acute appendicitis.[5] Fortunately, it's easy and economical as well. Negative appendectomy, as any other operation, results in socio-economic impact in the form of lost working days and declined productivity.

CRP is a non-specific inflammatory marker that is used routinely in many hospitals as an aid in the diagnosis of patients with an acute abdomen. An acute phase protein is produced in the liver. Normal serum concentration is less than 10 mg/dl 8-12 hours after infection or trauma; the increase of acute phase protein in liver CRP is more important in clinical practice. Production of CRP is controlled by Interleukin-6 and in a few minutes increase from 10 to 1000 times.

There is no single reliable test with satisfactory, sensitivity and specificity.

The objective of the study was to evaluate the role of few known and proven investigations for appendicitis like CRP and leucocyte count in diagnosing acute appendicitis. The comparison of the same with histopathological study will be considered gold standard. Also a study on whether combining these investigation would improve the diagnostic accuracy to avoid negative appendectomies will be done.

METHODS

This was a prospective non randomized, comparative study conducted in the Department of surgery, Nehru Hospital, BRD Medical College, over a period of 12 months from 1 January 2018 to 31 December 2018. A total number of 70 cases with a clinical diagnosis of acute appendicitis were studied.

A detailed clinical history and thorough clinical examination was done by the surgeon on duty. Relevant investigation like haemoglobin, leucocyte count, urine albumin, sugar and microscopic examination were done in all cases.

Blood sample for estimation of C-reactive protein (CRP) was taken before operation. CRP was estimated by semi quantitative method-Latex Fixation Slide Test (Rhekax CRP- Tulip Diagnostic, India).

The decision of operation was made independent of CRP and TLC level. The laboratory staffs were also not aware of the clinical findings, decision and the outcomes. Normal CRP level was taken as equal or less than 6 mg/dl and the level above 6 mg/dl was considered as raised for this study. Similarly, TLC value more than 11000 cells/mm^3 was considered raised for this study.

Patient was operated and operative findings were noted. Appendix was removed and sent for histopathological examination in The Department of Pathology.

Ultrasonography was also done pre operatively. Informed consent was obtained from all registered cases. Result of all the investigations were correlated with HPE reports to evaluate their role in diagnosis of acute appendicitis which was considered gold standard.

Sample size and design

First 70 patients of appendicitis admitted in surgery ward and subjected to hematological and radiological investigations.

Ethical approval

Study was approved by the ethical committee of B. R. D. Medical College, Gorakhpur.

Statistical analysis

All categorical variables are reported as number (%) compared across groups using Chi-square test for independence of attributes.

Inclusion criteria

All patients diagnosed clinically to have acute appendicitis and subjected for appendectomy in Nehru Hospital, B. R. D. Medical College Gorakhpur in Department of Surgery during a period of one year from 01 January 2018 to 31 December 2018.

Exclusion criteria

Patients with co-morbid condition were not included in the study; patients who were managed conservatively were also excluded from the study; patients admitted for interval appendectomy following recurrent appendicitis or appendicular mass previously treated conservatively, were also excluded; concomitant conditions where CRP/leucocyte count is elevated in acute appendicitis patients with associated diseases like rheumatoid arthritis, SLE, glomerular nephritis, gout, inflammatory bowel diseases, any other condition where CRP was raised, were also excluded.

The histopathology report was considered as the final diagnosis. On basis of the histopathological result two groups were formed: a) acute appendicitis; b) other (acute on chronic, sub-acute, chronic).

TLC>11000 cells/mm^3 was considered raised. CRP>6 mg/dl was considered raised.

True positive (TP)- patients with TLC/CRP values above the reference range and HPE report of excised appendix specimen shows acute appendicitis

False positive (FP)- patients with TLC/CRP value above the reference range but HPE results are other than acute appendicitis.

True negative (TN)- patients with TLC/CRP value below the reference range and HPE report of excised appendix shows results other than acute appendicitis.

False negative (FN)- patients with TLC/CRP values below the reference range but HPE report shows acute appendicitis.

Sensitivity SN=(TP/TP+FN)×100

Specificity SP=(TN/TN+FP)×100

Positive predictive value PPV=(TP/TP+FP)×100

Negative predictive value NPV=(TN/TN+FN)×100

Diagnostic accuracy =(TP+TN/TP+FN+TN+FP)×100.

RESULTS

Case distribution according to age and sex

Majority of patients in the study were male 42 out of 70 (60%) and then female 28 out of 70 (40%).

30% of patients (21 out of 70) were in the age group 11-20 years followed by 24.2% in the age group 21-30 years followed by 17% in the age group 31-40 years.

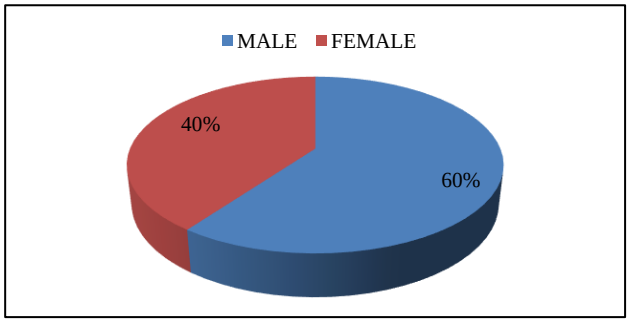

Figure 1: Graph showing sex ratio.

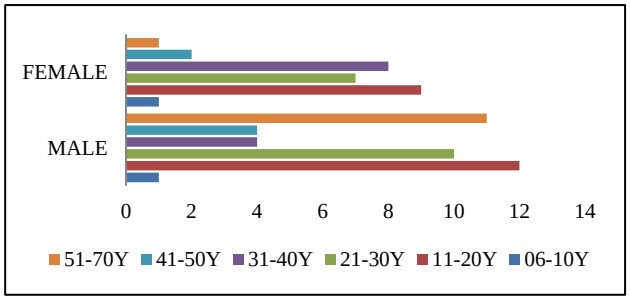

Figure 2: Graph showing age group.

Case distribution according to clinical signs and symptom

Commonest clinical presenting symptom age RIF pain was found in all the 70 patients (100%) followed by tenderness in RIF in 68 patients (97.1%) followed by nausea and vomiting 66 out of 70 patients (94.2%) followed by fever (85.7%), anorexia (78.5%) abdominal distended (60%), diarrhea/constipation (45.7%).

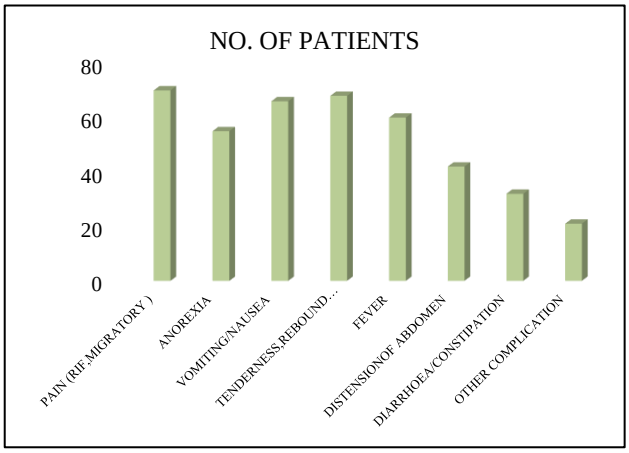

Figure 3: Graph showing clinical signs and symptom.

Case distribution according to histopathological report

Out of total suspected cases of acute appendicitis (n=70), Histopathology report revealed acute appendicitis in 68.5% (n=48) cases, while 31.5% (n=22) had report other than acute appendicitis like sub-acute, chronic, acute on chronic, neuro endocrine tumour etc.

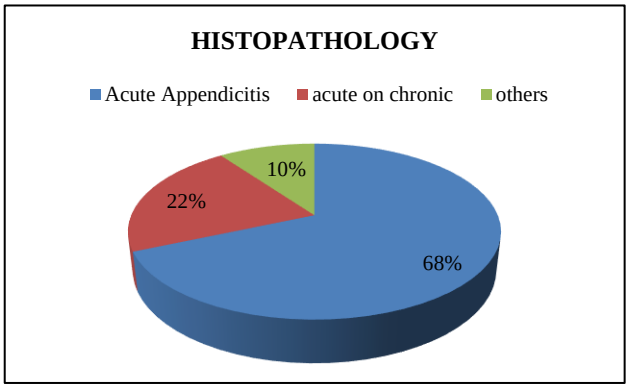

Figure 4: Graph showing histopathological correlation.

TLC and histopathology correlation

Among 48 cases of acute appendicitis on TLC was and histopathology correlation, TLC was found to be raised in 87.5% (n=42) cases and normal in 12.5% (n=6) cases.

While in case other than acute appendicitis TLC was raised in 22.7% (n=5) and normal in 77.3% (n=17) cases.

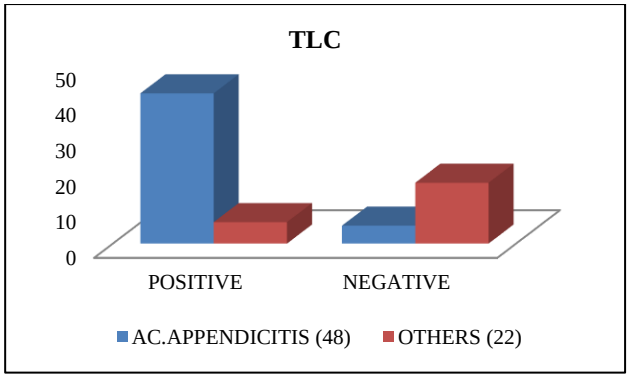

Figure 5: Graph showing TLC correlation.

CRP and histopathology correlation

Among 48 cases (HPE proven), on CRP and histopathology correlation, CRP was found to be raised in 91.6% (n=44) and normal in 8.4% (n=4).

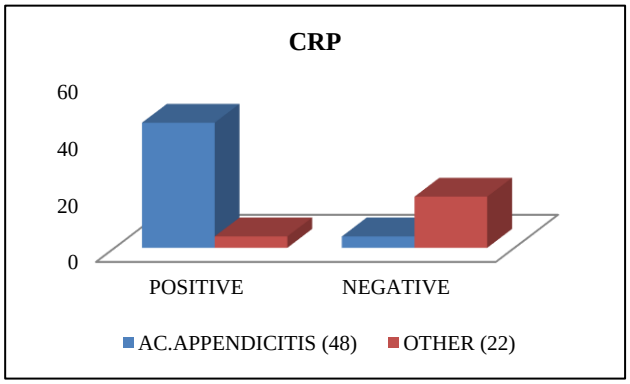

Figure 6: Graph showing CRP correlation.

Among 22 cases of other than acute appendicitis, CRP was raised in 18% (n=4) and normal in 82% (n=18).

Table 1: Final result.

Parameters	TLC	CRP	TLC+CRP
Sensitivity	87.5	91.6	93.1
Specificity	77.2	81.8	88.2
PPV	89.2	91.6	95.3
NPV	73.9	81.8	78.9
Diagnostic accuracy	84.2	88.5	90.3

DISCUSSION

A total of 70 patients were included in this study. Patients with extreme age, pregnancy, immune compromised status, pre-existing disease and patients suffering from other acute inflammatory condition were excluded from the study.

Out of 70 patients, 28 (40%) were female and 42 (60%) were male. Maximum group of patients belonged to 11-20 years (21 patients i.e., 30%).

Appendicitis is mainly a disease of adolescents and young adult.[6]

Clinical diagnosis for frank acute appendicitis was found to be correct in 68.5% of cases and negative appendectomy rate was 31.5% in this study. However , if the HPE report suggesting acute on chronic appendicitis (n=15) which demand emergency appendectomy is taken into account, negative appendectomy rate falls to 10% which is comparable to Jawed et al (7%), Alvi et al (10.97%) A high degree of accuracy is required to reduce the incidence of negative appendectomies which still remain around 20%.[7,8]

CRP and acute appendicitis

In this study, the CRP has a sensitivity of 91.6%, specificity of 81.8% .This comparable to the study done by Asfar et al where sensitivity and specificity were 86.6% and 93.6% respectively.[9]

Study found sensitivity of 93.5% and specificity of 80% and pointed that normal CRP is mostly associated with normal appendices, deferring surgery would probably reduce unnecessary appendicectomies.[10]

In this study, none of the case with appendicular perforation had normal CRP. This observation is supported by the study done by Grönroos.[11]

In this study, 4 (8.3%) cases has normal CRP level seven though HPE was positive. So, it was advised by Thimsen et al in his study that if the symptoms are present for more than 12 hours and CRP is negative, acute appendicitis is unlikely.[12]

False negative reactions usually occur early in the infective episode, the reasons are due to technical pitfalls in laboratory testing. Because CRP levels can increase very rapidly and dramatically, the latex agglutination assay is subject to false negative reactions due to a prozone-type phenomenon in which all of the antibody combining sites on the latex particles are bound to as excess of CRP, so no cross linking (agglutination) can occur.

Thus, at the end it should be stressed that serum CRP estimation does not replace clinical diagnosis but is useful adjunct in diagnosis of acute appendicitis. Serum CRP value should be interpreted in combination with clinical findings and leucocyte count.

TLC and acute appendicitis

The sensitivity, specificity, predictive value of positive test and predictive value of negative test of TLC in our study is 87.5%, 77.2%, 89.2% and 73% respectively. These result are in accordance with study by Yang et al indicating high association between TLC and acute appendicitis.[13]

According to study done by Grönroos et al TLC is the test of choice in diagnosing uncomplicated acute appendicitis, however it's a poor predictor of protracted inflammation.[14] This is supported in study by David et al.[15]

The TLC count when done individually distinguishes normal appendix from uncomplicated acute appendicitis. But does not distinguish uncomplicated from complicated appendicitis. Colemen et al reported that TLC is a poor predictor of severity of disease.[16]

Vermenum et al after evaluating 221 patients concluded that TLC count did not significantly influence the surgical decision making.[17]

The rationale of combining TLC and CRP in diagnosis of acute appendicitis

In this study correlation between the TLC and CRP in combination with histopathology and found sensitivity and specificity of 93.1% and 88.2% respectively. This had better significance than individual TLC or CRP.[17]

When combined value of CRP. WBC and raised neutrophil count tests is taken into consideration negative value was important.

Avoiding surgery in these cases can reduce negative appendectomy rate considerably.

Marchand et al in their study suggested that combination of these tests has 100% sensitivity and 50% specificity in the diagnosis of acute appendicitis[12,18,19]

CONCLUSION

Appendicitis is one of the commonest surgical emergency in children and adult. In the present study TLC is more sensitive and specific for its diagnosis but serial measurement of CRP is more sensitive and raised value of CRP is directly related to severity of inflammation. Combining TLC and CRP increases the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy and therefore may reduce the rate of negative appendectomy.

In the present study association of CRP and acute appendicitis has shown to be significant, but it cannot replace surgeon's clinical acumen.

It seems rational to use active observation which should identify most patients with non specific pain and reserve operation for those who need it most.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Study was approved by the ethical committee of B. R. D. Medical College Gorakhpur

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Cite this article as: Jaiswal AK, Rai RK, Chandra A. Prospective study of accuracy of C-reactive protein and leucocyte count in diagnosis of acute appendicitis in comparison with histopathology. Int Surg J 2020;7:2662-7.