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Predictive Value of TLC and CRP in Children With Clinically Suspected Acute Appendicitis

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ABSTRACT

Acute appendicitis represents one of the most common abdominal emergencies in children. Initially inflammation is localized to appendix but if untreated can lead to generalized peritonitis. It is often difficult and challenging even for the most experienced surgeon to make a definite diagnosis in paediatric patients. Inflammatory markers like Total Leukocyte count (TLC) and C-reactive protein (CRP) can help in making an early and accurate diagnosis in difficult cases. **Objective:** To evaluate the predictive value of TLC and CRP in children with clinically suspected acute appendicitis in whom physical findings were equivocal. **Study Design:** Cross sectional analytical.: **Setting:** This study was conducted in Pediatric Surgery Department of Shaikh Zayed Postgraduate Medical Institute, Lahore. **Subjects and Methods:** All patients from 5-14 years of age fulfilling the inclusion criteria were admitted for this study. Preoperative blood samples for total leukocyte count and CRP were collected and submitted to hematology and microbiology laboratories. Postoperatively, specimen of appendix was sent to histopathology laboratory of Shaikh Zayed Hospital. The histological results of report were differentiated into non-inflammed and inflamed appendix. **Results:** The mean age of the patients was 9.9±2.2 years. The mean TLC of the patients was 14.1±6.4 (10^9/L). The mean CRP of the patients was 19.0±8.7 mg/dl. Histopathology showed that 70 (69.4%) patients had inflamed appendix. The sensitivity of TLC & CRP was 82%, specificity 75% and diagnostic accuracy was 79%. The positive predictive value of TLC & CRP was 83% and negative predictive value was 73%. **Conclusion:** It is concluded from the results of this study that TLC and C-reactive protein can provide help in making accurate diagnosis of acute appendicitis. There monitoring enhances the diagnostic accuracy of acute appendicitis thus reducing the morbidity associated with delay in diagnosis and negative explorations.

Key Words: Acute appendicitis, Total leukocyte count, C-reactive protein.

Introduction

Acute appendicitis represents one of the most common abdominal emergencies in children. Initially inflammation is localized to appendix but if untreated can lead to generalized peritonitis. It is often difficult and challenging even for the most experienced surgeon to make a definite diagnosis in paediatric patients. [1] Clinical diagnosis is the corner stone in the management, although laboratory & radiological investigations can provide significant complimentary help.[2]

In classic description of the disease, the first symptom is peri-umbilical pain, followed by nausea, right iliac fossa pain, later on vomiting and fever. This sequence of events can only be seen in 50% of adult cases and even less commonly in children.[3]

The classic signs and symptoms are often not present in children making the diagnosis more difficult which may lead to missed diagnosis with significant morbidity and mortality. The risk of perforation in children is high as compared to adults which ranges from 20 to 50% and on the other hand rate of negative appendectomy is as high as 40%.[3]

The possibility of perforated appendicitis increases with time. After more than 48 hours from the onset of symptoms, most appendices will be perforated resulting in abscess, phlegmon or

generalized peritonitis.[4]

To improve diagnostic accuracy, modern sophisticated investigations including computerized tomography, ultrasonography and laparoscopy can be used but these investigations have their own demerits. CT scan is not freely available and exposes the child to excessive radiation. Ultrasound does not carry the risk of radiations but is highly operator dependent.[5]

Total leukocyte count (TLC) and C-reactive protein (CRP) are easily available tests and inexpensive. They can be done in almost all laboratories round the clock. [6] In less than 50% of the cases, history and examination lead to a definite diagnosis, and no supportive investigation is required.[7] In rest of the patients, physical findings are equivocal, in this group role of inflammatory markers becomes significant in making a definite diagnosis.[7]

The aim of the study was to evaluate the predictive value of preoperative TLC and CRP in those patients of acute appendicitis in whom physical findings were equivocal and a definite diagnosis could not be made at the time of initial presentation.

PATIENTS AND METHODS

This study was conducted in Pediatric Surgery Department of Shaikh Zayed Postgraduate Medical Institute, Lahore. The sample size of 101 cases was calculated with 90% confidence level with expected sensitivity of 74%, specificity of 92% and expected frequency of 80% inflamed appendicitis cases.

All the patients from 5-14 years of age who presented in the pediatric emergency and outpatient clinic with right iliac fossa pain and other signs and symptoms of suspected acute appendicitis were included. The patients in whom diagnosis of acute appendicitis was made confidently at initial presentation, patients with localized peritonitis and appendicular mass were excluded. Those patients in which duration of pain was more than 5 days were also excluded. The patients meeting inclusion criteria were admitted in pediatric surgery ward at Shaikh Zayed Hospital Lahore. Detailed history and thorough physical examination of the patients were performed. Preoperative blood samples for total leukocyte count and CRP were collected and submitted to hematology and microbiology laboratories of Shaikh Zayed Hospital.

The result of TLC was reported using impedance method or light scattering method by the help of one of the two available machines in hematology laboratory, which are sysmax18001 and Abacus. On the other hand, the result of CRP was reported using slide agglutination semi quantitative reporting method.

The patients in whom pain settled after 6 hours of admission were discharged. Other patients who continued to have symptoms were operated.

Postoperatively, specimen of appendix was sent to histopathology laboratory of Shaikh Zayed Hospital. The histological results of report were differentiated into non inflamed and inflamed appendix. All the information was collected through a predesigned proforma.

Data analysis was done on computer package SPSS version 15.0. Data for age, TLC and CRP were reported by using mean and standard deviation. Inflammation confirmed by histopathology was reported by using frequency and percentage. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of TLC and CRP were calculated against histopathological findings and reported in percentage with 95% confidence interval.

Comparison of TLC and CRP between two groups was performed by using Mann Whitney U test. P value <0.05 was considered as statistically significant.

RESULTS

Among 101 patients 65 (65.4%) were male and 36 (35.6%) were females. The mean age of the patients was 9.9±2.2 years. Distribution of patients in different age groups is shown in Table 1. Most of the patients 73 (72.3 %) were younger than 10 years

The mean duration of pain was 1.5±0.8 days. In majority of the patients (89.1%) duration of pain was less than 2 days.

There were 97 (96.0%) patients who had right iliac fossa pain, 2 (2%) patients had umbilical region pain and 2 (2%) patients had generalized

abdominal pain.

Table 1: Distribution of patients by age (n=101)

Age (Years)	No. of patients	Percentage
5-7	15	14.8
8-10	48	47.5
11-12	25	24.8
13-14	13	12.9
Mean±SD	9.9±2.2	

Key:
n=No. of patients
SD=Standard deviation

Table 2: Distribution of patients by hemoglobin (n=101)

Hemoglobin (mg/dl)	No. of patients	Percentage
8.0-10.0	11	10.9
10.1-12.0	48	47.5
12.1-14.0	41	40.6
14.1-16.0	1	1.0
Mean±SD	11.8±1.3	

Only 3 (3.0%) patients had shifting of pain. The character of pain was dull ache in 91 (90.1%) patients and 10 (9.9%) patients had colicky pain. Anorexia was noted in 58 (57.4%) patients.

The color of vomiting was white in 39 (38.6%) patients, 9 (8.9%) patients had yellow color and 53 (52.5%) patients had no vomiting. Out of 48 patient who had vomiting, majority (77.0%) had 1-2 episodes of vomiting per day.

Fever was noted in 43 (42.6%) patients. The mean hemoglobin of the patients was 11.8±1.3 mg/dl, details of hemoglobin range are given in Table 2.

In 36 (35.6%) patients TLC was less than 11000 and in 65(64.35%) patients TLC was more than 11,000.

The mean CRP of the patients was 19.0±8.7 mg/dl. There were 40 (39.6%) patients who had CRP less than 6.0 and 61 (60.4%) patients had CRP more than 6.0.

Histopathology finding were non inflamed appendix (lymphoid Follicular Hyperplasia) in 31 (30.6%) patients and acutely inflamed appendix in 70 (69.4%) patients.

In the comparison of TLC & CRP combined, with histopathology findings for acute appendicitis, 50 (49.5%) patients were true positive, 10 (9.9%) patients false positive, 11 (10.9%) patients false negative and 30 (29.7%) patients were true negative (Table 3).

The sensitivity of TLC & CRP combined, taken by histopathology finding as gold standard was 82%, specificity 75% and diagnostic accuracy was 79%.

Table 3: Comparison of TLC & CRP versus histopathology finding (n=101)

	Histopathology findings (Gold Standard)		Total
	Positive	Negative	
True positive	50	0	50
False positive	0	10	10
False negative	11	0	11
True negative	0	30	30
Total	**61**	**30**	**101**

The positive predictive value of TLC & CRP by histopathology finding as gold standard was 83% and negative predictive value was 73%.

DISCUSSION

Appendectomy for acute appendicitis is a common procedure. The rate of normal appendices unnecessarily removed remains high at 15-30% despite several techniques and investigations used to improve the diagnostic accuracy.[8]

Many studies have investigated the role of raised C-reactive protein in improving the diagnosis of acute appendicitis. In majority of patients with histopathologically proven acute appendicitis both the white blood cell (WBC) count and serum CRP level were significantly raised as reported by Asfar et al.[8]

Total leukocyte count is one of the helpful investigations in diagnosis of acute appendicitis. Mild leukocytosis ranging from 10,000 to 18,000 is usually present in patients with acute, uncomplicated appendicitis and is often accompanied by a moderate polymorphonuclear predominance.[9]

Various studies have been published on the

evaluation of role of leukocytosis in the diagnosis of acute appendicitis. The diagnostic accuracy of TLC is increased further if combined with CRP, absolute neutrophil count, shift to the left, sequential leukocyte count and neutrophil lymphocyte ratio.[10,11]

Yang et al reported that TLC and C-reactive protein were helpful in the diagnosis of acute appendicitis and patients with normal values of these tests were highly unlikely to have acute appendicitis in adults.[12] The sensitivities of leukocyte count, neutrophil percentage, and CRP in the diagnosis of acute appendicitis were 71.4 per cent, 88.3 per cent, and 90 per cent, respectively, while the specificities were 37.5 per cent, 25 per cent, and 37.5 per cent, respectively as reported by Yang et al[2]

Wu et al reported that TLC may serve as predictive parameter for early diagnosis of acute appendicitis in children.[13]

Various studies evaluating TLC in diagnosis of acute appendicitis have variable results. 80-85% patients with acute appendicitis will have TLC count of more than 10,000/cmm.[14] A raised TLC is regarded as sensitive test for diagnosis of acute appendicitis but is not diagnostic because of its lower specificity.[15]

The mean age of our patients was 9.9±2.2 years which is comparable with the study of Beltran et al[4] in which mean age of patients was 9.8±3.2 years.

In our study 64.4% patients were male and 35.6% patients were females. As compared with the study of Kamal and Shafiullah[3] there were 55.5% male and 44.5% female patients. In another study conducted by Kamran et al[6] there were 58% male and 42% female patients.

Leukocytosis was found in 64.4% the patients. As compared with the study of Kamal and Shafiullah[3] the TLC was raised in 80% of their patients, which was more than our study.

In our study, CRP was high in 60.4% patients. According to Iqbal [16] CRP was high in 61%. In another study by Fernando et al [17] CRP was raised in 78% of their cases. So our results are nearly comparable with the above studies. The number of patients with higher TLC and CRP was lower in our study than reported by others. The reason for this may be that we included only those patients in whom diagnosis of acute appendicitis could not be made at initial presentation and sample were drawn at the same time. We did not include patients with perforated appendicitis or appendicular mass and abscess. This may also explain the reason for high negative appendectomy rate (30%) in our study. If all the patients with acute appendicitis had been included then negative appendectomy rate would had been less than 10%. Secondly acute appendicitis is an ongoing inflammatory process. Even if initial sample is within normal limits, subsequent sample after 8-12 hours may be raised above normal thus increasing the utility of these investigations. In a study by Amlesh et al the specificity and sensitivity of serum CRP was 42% and 91% respectively. The predictive value of a positive (raised CRP) and negative (normal CRP) test was 88% and 48% respectively.[18]

In our study, the TLC and C-reactive protein sensitivity was 82%, specificity was 75%, positive predictive value was 83%, negative predictive value was 73% and accuracy was found to be 79%. As compared with the study of Kamal and Shafiullah[3] the TLC sensitivity was 92%, specificity 74%, positive predictive value 95%, negative predictive value 60 and diagnostic accuracy of 76.8%, which is comparable with our study.

In another study conducted by Kamran et al [6] the sensitivity of TLC was 76.5%, specificity 73.7% and positive predictive value was 92.5%.

The diagnostic value of TLC is increased when combined with neutrophilia and raised C-reactive proteins. Neutrophilia of more than 75% occurs in 78% of patients with acute appendicitis.[19, 20]

TLC was also evaluated by Khan et al and Shoshatan et al and found helpful in increasing the diagnostic accuracy in patients with suspected acute appendicitis.[21, 22]

CONCLUSION

It is concluded from the results of this study that TLC and C-reactive protein provides a rapid, cost effective and accurate diagnosis of acute appendicitis. If a patient with suspected appendicitis had normal TLC and CRP, then it is highly unlikely

that patient had appendicitis. TLC & CRP monitoring enhances the diagnostic accuracy of acute appendicitis thus reducing the morbidity associated with delay in diagnosis and negative explorations.

REFERENCES

1. Stefanutti G, Ghirardo V, Gamaba P. Inflammatory markers for acute appendicitis in children. Are they helpful? J Pediatr Surg 2007; 42: 773-9.
2. Mekhail P, Naguib N, Yanny F, Izzidien A. Appendicitis in paediatric age group: Correlation between preoperative inflammatory markers and postoperative histological diagnosis. Afr J Pediatr Surg 2011; 8:309-12.
3. Kamal A, Shafiullah. Significance of total leukocyte count in the diagnosis of acute appendicitis in children. Gomal J Med Sci 2011; 9:90-93.
4. Beltran MA, Almonacid J, Vicencio A, Guitierrez J, Cruces KS, Cusmsille MA. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. J Pediatr Surg 2007; 42:1208-14.
5. Siddique K, Baruah P, Bhandari S, Mirza S, Harinath G. Diagnostic accuracy of white cell count and C-reactive protein for assessing the severity of paediatric appendicitis. R Soc Med Sh Rep 2011; 2:1-6.
6. Kamran H, Naveed D, Nazir A, Hameed M, Ahmad M, Khan U. Role of total leukocyte count in the diagnosis of acute appendicitis. J Ayub Med Coll Abbottabad 2008; 20:70-71.
7. Kwan KY, Nager AL. Diagnosis pediatric appendicitis: usefulness of laboratory markers. Am J Emerg Med 2010; 28:1009-15.
8. Asfar S, Safar H, Khoursheed M, Dashti H, al-Bader A. Would measurement of C-reactive protein reduce the rate of negative exploration for acute appendicitis? J R Coll Surg Edinb 2000; 45: 21-4.
9. Ho HS. Appendicectomy. In: Wilmore DW, Cheung LY, Harden AL eds. ACS Surgery, Principle & Practice. Web MD, 2002:815–23.
10. Thomson C, Underwood M, Dookeran K, Lloyd D, Bell P. Role of sequential Leukocyte count and CRP in the diagnosis of acute appendicitis. Br J Surg 1992;79: 822–4.
11. Goodman D, Goodman C, Monk J. use of neutrophil: lymphocyte in the diagnosis of appendicitis. Am Surg 1995; 61:257–9.
12. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Role of leukocyte count, neutrophils percentage and C-reactive protein in the diagnosis of acute appendicitis. Am Surg 2005;71:344–7.
13. Wu HP, Chang CF, Lin CY. Predicitive inflammatory parameters in the diagnosis of acute appendicitis in children. Acta Paediatr Taiwan 2003;44:227–31.
14. Bener A, Suwaidi MH, Ghazawi IE. Diagnosis of appendicitis. Can J Rural Med 2002;7:26-9.
15. De Carvalho BR, Diogo FA, Fernandes C. Barra CB. Leukocyte count, C-reactive protein, alpha-1 acid glycoprotein and erythrocytes sedimentation rate in acute appendicitis. Arch Gastroenterol 2003;40:25–30.
16. Iqbal S. Role of C-reactive protein in diagnosis of acute appendicitis. [Dissertation] FCPS 2006: 78.
17. Fernando A, Rivera CMD, Wheeler H, Lindberg G, Munford KG. Regional and Systemic Cytokine Response to Inflammation of Vermiform Appendix. Annal Surg 2003; l237: 408-16.
18. Amalesh T, Shankar M, Shankar R. CRP in acute appendicitis — is it a necessary investigation? Int J Surg 2004; 2: 88-9.
19. Rasmussen OO, Haffman J. Assessment of reliability of the symptoms and signs of acute appendicitis. J Roy Coll Surg Edinb 1991;36:372–6.
20. Clifford PC, Chan M, Hewett DJ. The acute abdomen, management with microcomputer aid. Ann Roy Coll Surg Engl 1986;68:182–4.
21. Khan MN, Daue E, Irshad K. The role of white cell count and C-reactive protein in the diagnosis of acute appendicitis. J Ayub Med

Coll Abbottabad 2004;16:17-9.
22. Shoshatan MHS, Askarpur S, Alamshah M, Elahi A. Diagnostic value of qualitative CRP measured in patients with acute appendicitis. Pak J Med Sci 2006;22:300-3.

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