Original Article

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The Role of Serum C - Reactive Protein, White Blood Cell Count and Neutrophils Percentage in the Diagnosis of Childhood Acute Appendicitis

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Author`s Contribution

[1,3] Concept and idea, Data collection, Methodology, Literature review, Data collection, drafting the work. [2] critically revised the important intellectual contents and reviewed the study

Funding Source: None
Conflict of Interest: None

Received: Dec 07, 2021
Accepted: June 16, 2022

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ABSTRACT

Objective: To determine the role of CRP, white cell count, and granulocytosis in accurately diagnosing acute appendicitis. The sensitivity, specificity, positive predictive value negative predictive values of these tests was calculated.

Methodology: This cross-sectional study was conducted in the immunology department of the Children's Hospital and University of Child Health Sciences, Lahore over a period of six months from July 2019 to December 2019. A total of 91 suspected patients with acute appendicitis were included. The blood samples were collected from the patients and immediately sent to the lab for estimating serum CRP, WBC count and Neutrophil Percentage (Nu %). The sensitivity, specificity, positive predictive value, and accuracy were calculated for each test, and then the combined sensitivity, specificity, positive predictive value, and accuracy were calculated.

Results: The mean values of CRP, WBC, and Nu % were 59.44 mg/L, 15.30 uL, and 76% respectively, among the 71 patients with acute appendicitis. The mean values of CRP, WBC, and Nu % in another group of patients with non-specific abdominal pain were 29.13mg/L, 9.05/uL, and 62.93 percent, respectively. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of these 3 tests 93.87%, 83.63%, 88.5%, 92% and 63.63% respectively.

Conclusion: The combination of clinical indications and symptoms, as well as tests of serum CRP, WBC count, and neutrophils percentage, can improve pre-surgical decision-making and rescue children from both negative surgery and appendix complications if left untreated.

Key Words: CRP (C - reactive protein), WBCC (White Blood Cell Count), Neutrophil percentage (Nu%), Appendix, Accuracy, Sensitivity, Positive Predictive Value (PPV), Negative Predictive Value (NPV).

Cite this article as: Sabir H, Shehzad F, Anam A. The Role of *Serum C - Reactive Protein, White Blood Cell Count and Neutrophils Percentage in the Diagnosis of Childhood Acute Appendicitis. Ann Pak Inst Med Sci. 2022; 18(2):114-118.doi. 10.48036/apims.v17i4.590*

Introduction

Acute appendicitis is one of the most common abdominal surgical conditions, with a peak incidence in the second decade of life.[1] The vermiform appendix is a vestigial part of small intestine in humans being. The inflammation of appendix is known as acute appendicitis that may be acute or chronic.[2] The worldwide prevalence of acute appendicitis is 7%.[3] The annual incidence of appendicitis is 26 per 10,000 population.[4] The male to female ratio of acute appendicitis is 3:2 and is most common in the teens.[5]

Obtaining a medical history about the pain of preverbal toddlers and preschoolers is extremely difficult. In the case of preverbal children, physicians must rely on physical examination as well as pathological symptoms, such as how the child feeds, sleeps, moves around, and plays. The patient has abdominal pain that starts in the

peri-umbilical area and moves to the right iliac fossa.[1] The patient has a flushed appearance, as well as nausea, vomiting, a dry tongue, a tight oral cavity, pyrexia, and tachycardia.[6] The complications of acute appendicitis involve appendix perforation, appendix mass, appendix abscess, gangrene of appendix with perforations. As a result, peritonitis and portal pyemia occur which lead to liver abscess and intestinal obstruction.[5] Appendectomy is a secure procedure. Morbidity and mortality are associated with the stage of the disease. The mortality rate of non - perforated appendix is 0.8 per 1000 and 5.1 per 1000 of the perforated appendix.[6] The morbidity rate of acute appendicitis is 3.1%.[4] The diagnosis of acute appendicitis is based on the patient history, physical examination, and clinical evaluation**.** It is further strengthened by laboratory investigations such as WBCC, Serum CRP and Nu%**.** These were the only diagnostic parameters for many years.[7] Although, the laboratory tests and data are useful in the diagnosis of acute appendicitis but only no single test is conclusive. Often, if ESR, WBC and CRP are within a normal range before the operation, the diagnosis of appendicitis is unlikely and the surgeon should consider other diagnostic methods to prevent the patient from undergoing negative appendectomy.[8]

Acute appendicitis is one of the most common abdominal emergencies. An accurate preoperative diagnosis is still a challenge in many cases. Patient history and clinical examination are the basis of diagnostics, but other tools are also needed in order to limit the incidence of misdiagnoses. The utilization of laboratory data and radiological imaging procedures is common, and scoring systems can aid in the risk classification of individuals with suspected appendicitis. Inpatient observation with meticulous supervision of clinical and laboratory parameters in patients with equivocal diagnoses is an effective way to reduce the frequency of negative explorations without increasing the rate of perforation or morbidity.

Methodology

A cross sectional validation study was conducted on 91 patients, aged of 2 to 16 years in the department of diagnostic immunology section, The Children's Hospital and University of Child Health Sciences, Lahore (CH, UCHS Lahore). The study was done during the period of six months after the approval of synopsis from 1st July 2019 to 31 December 2019. The 91 suspected patients of acute appendicitis were enrolled in this study. Careful history, physical examination, signs and symptom were recorded. Sample size was taken by using the WHO sample size calculator with the help of 95% confidence level anticipated population (P- 7%), and precision level of 5%.

The blood sample for the measurement of CRP, WBC count and neutrophil percentage (Nu%) were taken from the 91 patients in surgical emergency and carried out immediately in laboratory (ethical review letter is attached for permissiom for taking patients from surgery ward and doing tests from haematology lab). Out of these 91 patients, 71 were turned out of acute appendicitis on the basis of history and laboratory investigation and underwent surgery whereas 20 patients were discharge after giving initial treatment and base line investigation, as nonspecific abdominal pain. The cut off value of CRP for positive tests was 10 mg/L. The cut off value for positive tests of WBC and neutrophils percentage were 11,000/µl and 75% respectively. The post-operative finding was graded as normal appendix, acute appendicitis, perforated appendix and gangrenous appendix. Statistical data was analyzed by using this technique SPSS v25 (Statistical Package for Social Science will be applied. The sensitivity, specificity, PPV, NPV and accuracy of CRP, WBC and neutrophils were calculated and then the combined sensitivity, specificity, PPV, NPV and accuracy of these tests were calculated. The p value was calculated for each test by independent T-test and it was < 0.05, that were indicate the results are significant.

Results

Out of the 91 patients, 71 (78.02%) had acute appendicitis and 20 (21.98%) were discharged with nonspecific abdominal discomfort. The participants in the study ranged in age from 2 to 16. Patients were separated into three groups based on their age: <5 years had 12 (13.2%), 5-10 years had 47 (51.6%) and 10-16 years had 32 (35.2%) patients, respectively. There were 55 males (60.44 **%**) and 36 females (39.56 **%**) among the 91 patients. The ratio of males to females was 3:2. Out of the 71 patients who had acute appendicitis, 45 (49.5%) were males and 26 (28.57%) were females**.**

The value of CRP (>10 mg/L) was positive in 63 (69.23%) patients, and negative (<10 mg/L) in 8 (8.79%) patients with acute appendicitis. In the other group of individuals with nonspecific abdominal discomfort, 8 (8.79%) have positive CRP values, while 12 (13.18%)

have negative CRP levels. The CRP had a sensitivity and specificity of 88.73 % and 60.0 %, respectively, as well as positive and negative predictive values of 88.70 % and 60.0 %. CRP had an accuracy of 82.41% (Table I).

The WBC count was high (> 11,000/L) in 56 (61.58%) of the acute appendicitis patients and normal (11,000/L) in 15 of them (16.45 %). The WBC count was high in 5 (5.49%) and normal in 15 (16.48%) of the patients with non-specific abdominal pain (Table I). WBC count had a sensitivity of 78.87%, specificity of 75.0 %, positive predictive value of 91.80 %, negative predictive value of 50.0 %, and accuracy of 71.0 %, respectively**.** The value of neutrophil (> 70%) in patients with acute appendicitis was positive in 60 (65.95 %) patients and negative in 11 (12.08 %) patients. In the group of patients with non-specific abdominal pain, however, the Nu % was positive in 41 (4.39%) patients and negative in 16 (17.58%) individuals (Table I). The sensitivity and specificity of Nu% was 84.50% and 80.0%, whereas positive and negative predictive values were 93.75% and 59.25% respectively. The accuracy of the neutrophils% was 83.51%. Among the 71 patients of acute appendicitis, mean values of CRP, WBC and Nu% were 59.44mg/L, 15.30/uL and 76% respectively. In other group of patients with non-specific abdominal pain the mean value of CRP, WBC and Nu% were 29.13mg/L, 9.05/uL and 62.93% respectively (Table II).

The sensitivity, specificity positive predictive value, negative predictive value and accuracy of the triple test (CRP, WBC and Nu%) was 93.87%, 83.63%, 92.0%, 63.63% and 88.50% respectively.

Out of the 71 patients of appendicitis there were 46 (64.78%) patients had the acute appendicitis, 22(30.98%) patients had perforated appendicitis and 3(4.22%) patients had gangrenous appendix.

The mean value of CRP in those patients who had acute appendicitis was 37.41 mg/L and in those patients who had perforated appendix the mean value of CRP was 97.69 mg/L. The patients who had gangrenous appendix, the mean value of CRP was 116.67 mg/L. The mean value of WBC count in acute appendicitis, perforated and gangrenous patients were 13.47, 17.60, and 23.13 respectively. The mean value of Nu% in acute appendicitis patients was 74.82%, in perforated appendix patients were 78.63% and in gangrenous appendix patients was 77.56% (Table III)

Table II: Mean and p-value of CRP, WBC and Nu% in AP and NP

Pre-Operated Blood Tests	Acute Appendicitis Mean Value	Non Appendicitis Mean Value	P-Value
CRP	55.99	29.13	0.00
WBC	15.30	9.05	0.00
NU	76.12	62.93	0.021

Table III: Mean-value of CRP, WBC and Nu% in AA, PA and GA

Appendicitis	Mean CRP	Mean WBC	Mean Nu%
Acute Appendicitis	37.41	13.47	74.82
Perforated	97.69	17.60	78.63
Gangrenous	116.67	23.13	77.56

Discussion

Acute appendicitis is one of the most common abdominal surgical conditions. Due to the lack of definitive pre-operative blood tests, the rate of negative appendectomy is still very high.[9] The diagnosis of acute appendicitis is most common clinical matter in the pediatric age group[10]. Clinical accuracy in diagnosing acute appendicitis ranges between 75% and 95%, but this is dependent on the surgeon's clinical skills. This puts a burden on the healthcare system because unneeded surgery exerts a negative socio-economic impact in the form of hospital expenses and decreased productivity.[4] CRP can be regarded as a valuable test and can support the surgeon in the diagnosis of acute appendicitis. However, antibiotic therapy can cause a decrease in serum CRP levels.[10]

According to a study by Birchley *et al., in 2006*, when CRP and WBC were measured, they were not able to distinguish between acute and complicated appendicitis. Moreover, CRP had no definite value for predicting acute

Table I:Descriptive analysis study population

	CRP		WBCC		Nu%	
	+ve	-ve	+ve	-ve	+ve	-ve
Acute appendicitis	63 (69.23%)	8(8.79%)	56(61.58%)	15 (16.48%)	60 (65.95%)	11 (2.08%)
p-value	-		< 0.05		< 0.05	
Non-appendicitis	8(8.79 %)	12(13.18%)	55(5.49%)	15(16.48%)	4 (4.39%)	16(17.58%)
p-value	-		< 0.05		-	

appendicitis. So, he concluded that the different laboratory tests, such as white cell count, neutrophil count, and C-reactive protein, are more useful in supporting a clinical diagnosis of acute appendicitis[11]. The results of our study are consistent with this study as three tests were investigated and the acute appendicitis was clearly identified from nonspecific abdominal pain.

In the literature by Monsalve S *et al.,* the WBC count was helpful in the diagnosis of simple appendicitis and CRP was helpful in the diagnosis of complicated appendicitis.[12] In the current study, the WBC count along with Nu% proved to be important inflammatory markers in the diagnosis of acute appendicitis with their sensitivity of 78.87% and 84.50%. Moreover, CRP is useful in the diagnosis of acute appendicitis as well as in complicated appendix with a sensitivity of 88.73%.

In another study by Mohammed *et al., in 2004*, the sensitivity, specificity, accuracy, and positive predictive values of CRP, WBC count, and Nu% in suspected case of acute appendicitis was analyzed and he concluded that these three tests can improve the diagnostic accuracy of acute appendicitis and reduce the incidence of perforation[10]. This study is in favor of these results, indicating that the sensitivity, specificity, PPV, and NPV of these three tests are high. In this study, the sensitivity (88.73%) of CRP was very high compared to the study by Mohammed *et al.,* showing slightly low sensitivity. This may be because of difference in sample size.

Another prospective study by Hossein *et al.,* in 2006 concluded that the combination of CRP, WBC, and neutrophil count have greater diagnostic accuracy and significantly decrease false positive and false negative diagnoses, but none of these are 100% diagnostic for acute appendicitis.[13] These results are in consistent with the results of our study because in this study the sensitivity, specificity, PPV, NPV, and accuracy of these triple tests were very high but not 100%.

Furthermore, in another study by Ng KC *et al,* in 2002 there was no significant association between acute appendicitis and elevated CRP or leukocytosis; only elevated NR was a significantly related factor.[14] However, the outcomes of this study contradict those findings, revealing that CRP has a higher diagnostic accuracy than WBC and a slightly lower accuracy than Nu%. This may be because CRP levels may decline due to antibiotic use or other causes of abdominal pain, which may produce false positive or false negative results.

Conclusion

The use of a combination of clinical indications and symptoms, as well as tests of serum CRP, WBC count, and neutrophils percentage (Nu %) can improve surgeon diagnostic accuracy and reduce perforation and negative laparotomy rates.

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