Journal of Diabetic Association Medical College 2022;6(2)11-15

Original Article

Diagnostic Value of Inflammatory Markers in Acute Appendicitis

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Abstract

Background: Appendicitis in children is a common surgical emergency and its diagnosis remains challenging. Diagnosis using blood inflammatory markers is still debatable. The purpose of this study was to determine the effectiveness of blood inflammatory markers obtained during routine blood tests in diagnosing acute appendicitis in childrenin addition to respondent's demographic data as well.

Methods: This was a descriptive cross-sectional study conducted between January 2018 to June 2019 at the Department of Surgery of Sylhet MAG Osmani Medical College Hospital to determine the value of blood inflammatory markers in the diagnosis of acute appendicitis. The study enrolled 246 patients who underwent surgery for acute appendicitis based on clinical/ultrasonographic diagnosis. Prior to surgery, white blood cell (WBC) count and C-reactive protein (CRP) levels of the patients were measured, and their sensitivity was analyzed based on histopathological diagnosis.

Results: The mean age of the 246 study participants was 28.31±10.12 years. Histological confirmation of acute appendicitis was obtained in 212 cases. The male-female ratio was 2.21:1 in 212 cases of confirmed appendicitis. WBC counts had a sensitivity of 84% and CRP 76% while those were elevated alone. But the sensitivity and specificity increased to 91% and 75%, respectively when both the WBC counts and CRP levels were raised.

Conclusion: When only the WBC count or CRP is performed, no additional information can be obtained to help the diagnosis of acute appendicitis. However, the diagnostic sensitivity increases when both WBC count and CRP level are raised.

Keywords: Acute appendicitis, Laboratory diagnosis, Children, White blood cell, C-reactive protein

Introduction

Diagnosis of acute appendicitis is challenging especially when the patient presents with atypical signs and symptoms.[1-3] On the other hand, failure to diagnose acute appendicitis promptly increases the risk of perforation and associated complications.[4] As a result, surgeons are more likely to operate when the diagnosis is probable than when it is certain.[5] Consequently, a normal appendix is removed in 15 to 30 percent of cases as a result of a clinical decision to operate.[6,7] While observing ambiguous cases for an extended period appears to be safe for the majority of patients, it is unacceptable to decrease "unnecessary" operations while increasing perforations.[6,8]

Several diagnostic aids have been suggested over the past years ranging from ultrasonography, computed tomography, magnetic resonance imaging (MRI) and laparoscopy.[9-11] But in resource poor settings like in Bangladesh, it is not feasible in most centers to perform these tests for diagnostic confirmation. Several blood inflammatory markers have been suggested as well to aid the diagnosis such as white blood cell (WBC) counts, C-reactive protein (CRP), phospholipase A2, serum amyloid A, leukocyte elastase, and several interleukins and cytokines.[5,12-15] However, the majority of these tests are not available in the majority of centers in Bangladesh, with the exception of the WBC count and CRP, which are inexpensive and can be repeated if necessary.

Several recent studies suggest that in the absence of specific clinical signs and symptoms, reference levels of WBC and CRP can be used to rule out the possibility of acute appendicitis to a large extent.[5,16–18] In such cases, negative appendicectomy can be reduced by up to 25%.[17] However, the utility of WBC and CRP counts in diagnosing acute appendicitis is still debatable and there is limited data available in Bangladesh regarding the role of WBC and CRP counts in assisting surgeons in making the decision for appendicectomy. The purpose of this study was to determine the diagnostic accuracy of WBC counts and CRP levels in diagnosing acute appendicitis in addition to the demographic data of the respondents as well.

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Materials and Methods

This descriptive cross-sectional study was conducted at Sylhet MAO Osmani Medical College Hospital in Bangladesh from 1st January 2018 to 30th June 2019. The study population consisted of 246 consecutive patients admitted with clinical and ultrasonographic findings consistent with acute appendicitis. A consecutive sampling technique was used to include all eligible patients who met the inclusion criteria and were admitted to the hospital during the study period.Ethical approval for the study was obtained from the Institutional Review Board of Sylhet MAG Osmani Medical College Hospital. Written informed consent was obtained from all the patients before the study. A structured questionnaire was used to collect demographic data.Demographic data was collected using a structured questionnaire which included questions about age, sex, occupation, and other relevant factors. Blood samples were collected from each patient before the surgery, and standard laboratory procedures were used to perform complete blood count (CBC) and C-reactive protein (CRP) tests. Tests were performed by the hospital laboratory. Total white blood cell (WBC) count and CRP levels were recorded for each patient from the CBC and CRP reports, respectively.After surgery by standard appendectomy technique, histopathology was performed on the appendix specimen.Additionally, surgical findings of the appendix were noted. If an appendix with pathological confirmation showed signs of abscess or perforation during surgery, it was classified as complicated; otherwise, it was classified as uncomplicated.Postoperative management and follow-ups were performed on each patient in accordance with appropriate guidelines.

Categorical data were summarized as mean standard deviation. The Chi-square test, and sensitivity and specificity tests were performed on the lab reports. SPSS Version 21.0 was used to analyze the data (IBM Statistical Package for the Social Sciences for Windows. IBM Corp., Armonk, New York, USA). P values <0.05 were considered significant.

Results

A total of 246 patients were enrolled who had clinical or ultrasonographic diagnosis of acute appendicitis. About 86% patients had acute appendicitis confirmed by histopathology, while 14% had other diagnoses.

Table 1: Demographic characteristics of the patients (n = 246)

Characteristics	Diagnosis		*p-value*
	Acute appendicitis n = 212	Others n=34	
Age group (years)			
11-20	91 (42.9%)	8 (23.5%)	0.166
21-30	77 (36.3%)	15 (44.1%)	
31-40	18 (8.5%)	4 (11.8%)	
>40	26 (12.3%)	7 (20.6%)	
mean(±SD) age= 28.31(±10.12) years			
Sex			
Male	146 (68.9%)	22 (64.7%)	0.234
Female	66 (31.1%)	12 (35.3%)	

Table-1 shows that the mean(±SD) age of the patients was 28.31(±10.12) years. The majority (42.9%) of patients with a confirmed diagnosis of acute appendicitis were between the ages of 11 and 20 years followed by 36.3% in the age group of 21-30 years. Majority(68.9%) of the participants were male. The male-to-female ratio of confirmed appendicitis patients was 2.21:1. However, the age and sex difference did not have any statistical significance.

Figure 1: Surgical findings of complications during appendicectomy.

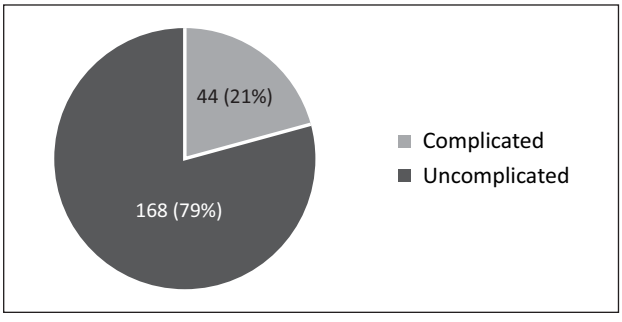

Figure 1 shows that during surgery, out of 212 patients with acute appendicitis, 20.75% had complicated appendicitis with either abscess or perforation.

Table 2: WBC counts and CRP levels of patients underwent appendicectomy compared on histopathological and surgical findings (n = 246)

	Histopathological confirmed appendicitis (n = 212)				Histopathological normal appendix (n=34)
	Complicated (n = 44)	Uncomplicated (n = 168)	P value	Total	
WBC count ($\times 10^9$/L, mean ± SD)	16.15 ± 5.21	13.87 ± 5.78	0.01	16.02 ± 5.52	9.75 ± 5.34
CRP (mg/L, mean± SD)	104.5 ± 69.1	62.4 ± 52.2	<0.01	67.8 ± 68.3	18.7 ± 17.8

Table 2 shows that the mean WBC count of the patients with histopathological diagnosis of appendicitis was $16.02 \pm 5.52 \times 10^9$/L and the CRP level was 67.8 ± 68.3mg/L. For histopathological normal appendix, the WBC counts and CRP levels were

9.75 ± 5.34×10^9/L and 18.7 ± 17.8mg/L, respectively. Both WBC counts and CRP level for complicated and uncomplicated appendicitis had statistically significant difference.

Table 3: Sensitivity and specificity of elevated WBC counts and CRP levels in diagnosing appendicitis

Variables	Sensitivity	Specificity	PPV+	PPV-
Elevated WBC counts	84.21%	41.18%	89.80%	28.00%
Elevated CRP levels	76.19%	45.45%	64.00%	60.00%
Elevated both WBC counts and CRP levels	91.43%	75.00%	86.49%	83.33%
**PPV+: Positive predictive value, PPV-: Negative predictive value*				

Table 3 summarizes the sensitivity and specificity of elevated WBC count and CRP levels in patients with histopathological diagnosis of appendicitis alone and in combination. Elevated WBC count has a sensitivity of 84.21% but the specificity is low as 41.18%. For elevated CRP level, the sensitivity is 76.19% and specificity is 45.45%. When WBC counts and CRP levels are elevated the sensitivity and specificity increases to 91.43% and 75% respectively that corresponded to a positive predictive value of 86.49% and negative predictive value of 83.33% respectively.

Discussion

Acute appendicitis is diagnosed primarily clinically, with a thorough medical history and physical examination.[9] However, appendectomy rates remain high in patients with normal appendices, ranging between 15% and 30%.[6]

Apart from WBC counts and CRP, several inflammatory markers have been proposed to aid in the diagnostic procedure, including phospholipase A2, serum amyloid A, leukocyte elastase, and several interleukins and cytokines.[5,12-15] However, in Bangladesh and other resource-scarce countries, the WBC counts from CBC and CRP are the most feasible and can be repeated multiple times if required.[19] Although CRP, WBC count can easily be performed in medical centers or primary care settings, their diagnostic value remains debatable.[20–23]

Male predominance was also suggested by Humes et al. and other researchers, as were the most common age groups of 10-20 years.[3,9,24]

The utility of routine blood inflammatory markers in the diagnosis of appendicitis is still being debated. Several studies suggest that in combination with specific clinical features, elevated WBC count and CRP level in combination can be helpful to diagnose acute appendicitis.[5,17,25-28] Peltola et al. and others observed that combining positive CRP and WBC tests had a predictive value of greater than 93% for diagnosing acute appendicitis in children.[29,30]Gronroos et al. also suggest that low or normal WBC counts and CRP levels in women of reproductive age have a 100% predictive value for ruling out acute appendicitis.[31]

However, Jasper et al. argue that no WBC count or CRP level can safely and adequately confirm or exclude the suspected diagnosis of acute appendicitis in patients with abdominal pain lasting ≤5 days.[32] Taylor et al. also found that an elevated total WBC count was statistically associated with appendicitis. But it had extremely low sensitivity and specificity and thus concluded that elevated WBC count almost has no clinical utility in diagnosing appendicitis.[33] This study also confirms a statistically significant association between acute appendicitis, elevated WBC counts ($p = 0.01$) and elevated CRP levels ($p < 0.01$). Our findings corroborate the fact that elevated WBC counts and CRP levels alone do not provide sufficient specificity to aid in the diagnosis of acute appendicitis, despite their high sensitivity. However, when both the WBC counts and CRP levels increased, it demonstrated high sensitivity (91%) and specificity (75%), as well as a positive predictive value of greater than 86%.In conjunction with clinical findings, routine CBC for WBC counts and CRP levels may be considered for additional confirmation of acute appendicitis, potentially reducing the number of unnecessary surgical interventions.

Limitation

The study was conducted in a single center and sampled a small number of participants. Our findings warrant further investigation in a multicenter study with larger sample sizes.

Conflict of interest: No

Conclusion

This study findings suggest that routine testing of blood inflammatory markers in admitted patients may aid in the diagnosis of appendicitis. Patients with increased white blood cell counts and CRP levels have a higher risk of having appendicitis, helping the decision-making process for surgical interventions.

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