Diagnostic Accuracy Of Total Leukocyte Count, Neutrophil Count, And C-Reactive Protein In The Diagnosis Of Acute Appendititis In Children

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KEYWORDS

Acute appendicitis, complete blood count, children, diagnostic accuracy

ABSTRACT

Objective: Diagnostic accuracy of total leukocyte count, neutrophil count, and c-reactive protein in the diagnosis of acute appendititis in children
Patients and methods: A prospective observational study conducted in the Department of Pediatric Surgery, Liaquat National Hospital, Karachi from January 2019 to January 2022. Children admitted with suspected case of acute appendicitis, age ≤16 years, and both males and females were included in this study. Included patients were subjected to carry out c-reactive proteins and complete blood picture including differential leukocyte count and neutrophil count pre-operatively. White blood cell counts of more than 11,000 cells/mm, neutrophil count of more than 75%, c-reactive protein (CRP >0.5 mg/dl were considered positive.
Results: A total of 135 patients were included and their mean age was 8.90±2.81 years with a majority of patients were males 69.6% (n = 94). Prevalence of acute appendicitis was 94.07% (n = 127) and patients with mean higher mean neutrophil count and CRP were more likely to have acute appendicitis. Receiver operator characteristics (ROC) shows diagnostic precision of CRP was highest with a sensitivity of 79.5% followed by total leukocyte count (77.2%) and neutrophil count (78.0%) in diagnosing acute appendicitis by using histology as benchmark.
Conclusion: The study concluded that there was a predominance of male patients as compared to female patients as observed in the study. CRP and TLC including neutrophilia are valuable markers in acute bacterial infections as they have a positive correlation with each other.

INTRODUCTION:

Pediatric acute appendicitis occurs secondary to the inflammatory process affecting the appendix and is the most common surgical emergency (1). The prevalence of acute appendicitis varies in different regions of the world. An international study conducted by Almaramhy HH and colleagues have shown prevalence of pediatric appendicitis was 1-2% of all pediatric surgical admissions (2). While the actual burden of pediatric appendicitis is not known in Pakistan. The diagnosis of acute appendicitis in children may sometimes be difficult and there is a high chance of misdiagnosis and it has been reported that approximately 28-57% of children of school going age are misdiagnosed (3).
Although classic/straightforward cases of acute appendicitis are easy to manage, real dilemma lies in diagnosing and managing the cases of atypical/complicated appendicitis. Clinical diagnosis alone leads to relatively unacceptable negative appendectomy rates of 15 to 30% (4).

In addition, the classic symptoms for detecting appendicitis in adults are not encountered in all pediatrics; in such young patients, the abdominal examination is more challenging due to a lack of cooperation and appropriate expressions. Among younger patients, the incidence of complicated appendicitis is common (5). Due to its complexity, missed appendicitis is a common cause of lawsuits in the emergency department (ED). Luminal occlusion due to various etiologies and bacterial infections of the appendix is typically held

responsible for the pathogenesis of this disease, which is mostly seen in children (6). Although inflammatory markers are still being studied in the presence of appendicitis, a definite conclusion has not been reached yet. The laboratory evaluation of patients with suspected appendicitis, including white blood cell count (WBC), C-reactive protein (CRP), and other serum markers, either alone or in combination, can be helpful, but the reported sensitivities and specificities for these markers are highly variable and not independently reliable for accurately excluding or confirming the diagnosis (7, 8). We still rely on imaging for the diagnosis of appendicitis in pediatrics, with the ultrasound (US) as the first modality, with its relatively low sensitivity and specificity (9). Computerized tomography (CT) is, however, sometimes necessary to rule out appendicitis.

Studies conducted previously reported sensitivity and specificity of Total leukocyte count (TLC), C-Reactive Protein (CRP) and Neutrophil count as (80.5%, 62.5%), (82.95% and 86.41%) and (83.5%, 57.7%), while one of the studies showed combined sensitivity, specificity, and positive predictive value (PPV) of Total leukocyte count (TLC) and C-Reactive Protein (CRP) 89.28%, 83.33%, 98.03 %, respectively (10). In another study reported sensitivity and specificity of combined, Total leukocyte count (TLC), C-Reactive Protein (CRP) and percentage of neutrophil count in diagnosis of acute appendicitis (11). If CRP can be added to already existing laboratory tests, the diagnosis of acute appendicitis can be made with more accuracy, and unnecessary appendectomies can be reduced.

PATIENTS AND METHODS:

This was a prospective observational study conducted in the Department of Pediatric Surgery, Liaquat National Hospital, Karachi for a period of 1 year from January 2019 to January 2022 through a convenience sampling technique. The study was approved by the hospital's ethical committee before commencement. Every parent was briefed regarding the purpose and benefits we would expect after completion of this study. Children admitted with suspected case of acute appendicitis, age ≤16 years, and both males and females were included in this study. All patients were given standard care during hospitalization course and proceeded for appendectomy where needed. Decision to operate was not influenced by the preoperative levels of these tests. All the patients were operated for appendicitis on the basis of history, physical findings and relevant clinical data. Postoperatively, the removed appendix was sent for histopathological examination. Based on histological features of the removed appendix, the patients were divided into three groups as follows: Group A: Normal appendix. Group B: Inflamed appendix (simple appendicitis). Group C: Perforated/gangrenous appendix (complicated appendicitis).

Patients included in this study were subjected to carry out c-reactive proteins and complete blood picture including differential leukocyte count and neutrophil count pre-operatively and evaluate the results. White blood cell counts of more than 11,000 cells/mm^3, neutrophil count of more than 75%, c-reactive protein (CRP >0.5 mg/dl were considered positive.

The cut-off value for white cell count was taken as 11 x 10^6/L. This value was selected arbitrarily as it corresponds to the elevated TLC. In our set up, the rapid latex agglutination slide test was the standard for the qualitative and semiquantitative in vitro determination of CRP in the sample. For semiquantitative determination, serum dilutions were prepared with the diluent provided with the commercially available CRP kit and C-Reactive protein >0.5 mg/dl were considered positive. Percentage of neutrophil was considered elevated when >75%.

All the collected data was analyzed through statistical package for social sciences (SPSS) Version 22.0. Mean ± SD was calculated for age, weight, height, and duration of symptoms. Frequency and percentages were computed for qualitative variables like gender, total leukocyte count group, neutrophils group etc. Mean ± SD were calculated for quantitative variable i.e., age, height, weight, duration of symptoms, general physical examination, pulse rate, temperature, total leukocyte count, and neutrophil percentage. Post-stratification sensitivity, specificity, positive predictive value, negative predictive values, and the diagnostic accuracy of total leukocyte group, neutrophils group were calculated taking histopathology as gold standard. The number of patients with (1) both values normal, (2) only leucocyte count raised, (3) only CRP level raised and (4) both values raised were calculated in each of the three groups. The stratification was done on gender and age to see the effect of these modifiers on outcome i.e., accuracy. Chi-square test was applied to see the association. A p value of ≤0.05 was considered as statistically significant.

RESULTS:

A total of 135 patients were included to assess the diagnostic precision of C-reactive proteins, neutrophil count, and total leukocyte count in the identifying suspected cases of acute appendicitis. The mean age was 8.90±2.81

years with a majority of patients were males as compared to females, 69.6% (n = 94) and 30.4% (n = 41), respectively. Table 1. Among all, prevalence of acute appendicitis was 94.07% (n = 127) and patients with mean higher mean neutrophil count and CRP were more likely to have acute appendicitis. Most of the patients operated for appendectomy did not have any complication (89.6%, n = 121) while wound infection was found among 6.7% (n = 9), intra-abdominal collection 3.0 (n = 4), and adhesive small bowel obstruction was observed among 0.7% (n = 1) of the patients. Graph 1.
Receiver operator characteristics (ROC) shows diagnostic precision of CRP was highest with a sensitivity of 79.5% followed by total leukocyte count (77.2%) and neutrophil count (78.0%) in diagnosing acute appendicitis by using histology as benchmark.

DISCUSSION:
Although acute appendicitis is considered as one of the commonest surgical emergencies, still the diagnosis could be difficult and appendectomy for normal appendix usually ranges from 15 to 30% (12), while our study showed the negative appendectomy rate of 5.8 %. Also, in our study, most of the study subjects were males (n = 94, 69.6%) and 4 (30.4%) were females. this finding correlates with the previously published literatures (13-15). Sensitivity and specificity of total leukocyte count, C-Reactive protein and neutrophil percentage were more, in cases of complicated appendicitis, and Patients presenting less than 5 years of age, were more likely to have complicated appendicitis. This study also shows the relationship between the duration of symptoms and the likelihood of a case being simple or complicated. It was observed that cases with a short duration of symptoms (<72 hours) were more likely to have simple acute appendicitis, whereas complicated appendicitis was more likely to have longer duration of symptoms. Bickel et al. (16) reported a duration longer than 36 h between onset of pain and surgery to carry higher risk of perforation, whereas Moon et al. found no correlation between the two (17). In current study clinical diagnosis was found to be correct in 127 (94.1%) of the patients. Our study shows that C-Reactive protein and neutrophil count are more sensitive than Total leukocyte count i.e., 80.3%,81.1% vs. 75.5%, respectively for the diagnosis of acute appendicitis. C-Reactive protein has highest specificity, and highest diagnostic accuracy, in both simple and complicated appendicitis. Studies suggest that, neutrophils highly sensitive in cases of simple appendicitis, while C-reactive protein was found to be more sensitive in cases of complicated appendicitis, C-reactive protein if specific in both simple and complicated appendicitis. Our values correlate with the literature when combined analysis is done, while on subgroup analysis between simple and complicated analysis, values differ from as previously reported in the literature. C-Reactive protein, Total leukocyte count and neutrophilia (Triple test) when used, together are moderately sensitive, while highly specific to exclude acute appendicitis. Despite multiple laboratory tests and scans, Clinical assessment remains the highly diagnostic for acute appendicitis.

CONCLUSION:
The study concluded that there was a predominance of male patients as compared to female patients as observed in the study. CRP and TLC including neutrophilia are valuable markers in acute bacterial infections as they have a positive correlation with each other. When they are measured together, it increases their diagnostic value because of their feasibility and sensitivity.

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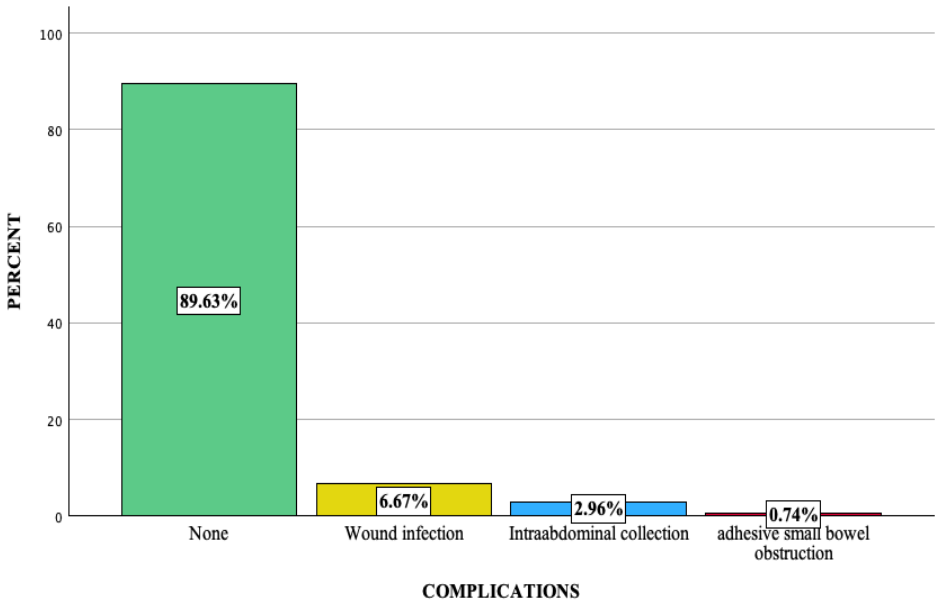
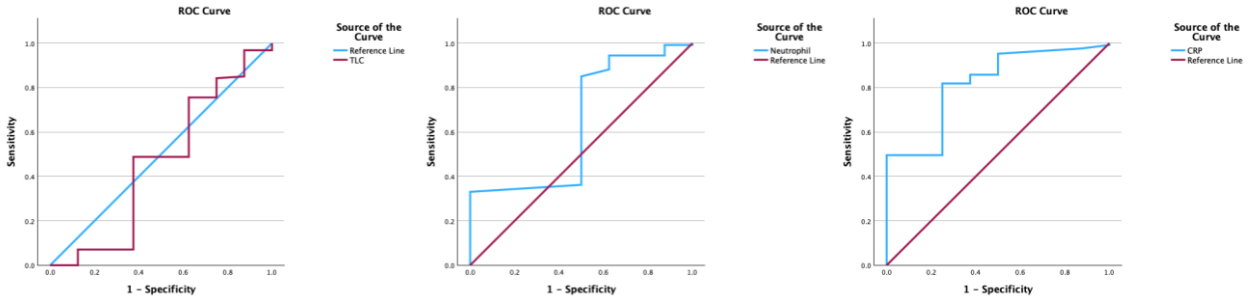
Table No. 1: Baseline and clinical characteristics of study participants
(N = 135)

Baseline & clinical characteristics	Total	Acute appendicits		p value
		Yes	No	
	(N = 135)	(N = 127)	(N = 08)	
	Mean±SD	Mean±SD	Mean±SD	
Age - years	8.90±2.81	8.96±2.84	8.0±2.33	0.35
Duration of symptoms - hours	43.14±33.62	44.06±33.80	28.50±10.06	0.2
Pulse - bpm	107.90±13.91	107.86±13.44	108.63±21.24	0.88
TLC - cells/µL	12.98±11.09	17.98±11.09	15.15±5.79	0.21
Neutrophil - %	79.44±9.08	79.84±8.61	73.0±13.85	0.03*
CRP	9.13±18.04	9.64±18.48	.98±1.55	<0.001*
	n (%)	n (%)	n (%)	
Age range - years				
<6 years	20 (14.8)	19 (14.1)	1 (0.7)	
6 - 12	100 (74.1)	93 (68.9)	7 (5.2)	0.83
≥12	15 (11.1)	15 (11.1)	0 (0)	
Gender				
Male	94 (69.6)	86 (63.7)	8 (5.9)	0.1
Female	41 (30.4)	41 (30.4)	0 (0)	
Temperature				
Afebrile	106 (78.6)	100 (74.1)	6 (4.4)	0.68
Febrile	29 (21.5)	27 (20)	2 (1.5)	

* p value <0.05 is statistically significant
TLC - Total leukocyte. Count
C-RP - C-Reactive protein

Chart 1: frequency of complications associated with appendectomy (N = 135)





(A) (B) (C)

Figure 1: ROC analysis was performed to determine the sensitivity and specificity of three inflammatory markers (a) TLC (b) Neutrophil count, and (c) CRP levels in patients suspected with acute appendicitis