



ROLE OF C-REACTIVE PROTEIN AND WHITE BLOOD CELL COUNT IN DIAGNOSIS OF ACUTE APPENDICITIS IN CHILDREN

Clinical Research

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ABSTRACT

Acute Appendicitis (AA) is the most common cause of abdominal emergency requiring surgical intervention and should be differentiated from other conditions mimicking its signs and symptoms. Delay in diagnosis can lead to complicated appendicitis and may become difficult to manage. WBC and CRP are routinely-used laboratory parameters that strengthen the diagnosis of AA. **Material And Methods:** History, meticulous physical examination, complete hemogram test, C-reactive protein, ultrasound of whole abdomen done and all patients were taken up for emergency open appendicectomy. The resected specimens were sent for HPE and divided into 2 groups based on HPE (complicated and uncomplicated appendicitis). The data were collected, analysed. **Results:** Study included 190 patients, 97 males and 93 females. CRP and WBC values of the complicated group were higher than those of uncomplicated group (p-value <0.001). The Mean (SD) of NLR in the complicated group is 15.43 (10.79) while in uncomplicated group it is 4.76 (5.04) and the P-value showing < 0.001. The ROC curve analysis demonstrated that CRP and WBC values were sensitive and specific to differentiate between uncomplicated and complicated appendicitis. **Conclusion:** The study demonstrated that CRP, WBC and NLR could be used as diagnostic markers for complicated appendicitis.

KEYWORDS

Appendicitis, White blood cell count, C-Reactive protein, NLR, Paediatric appendicitis score

INTRODUCTION

Acute Appendicitis (AA) is the most common cause of abdominal emergency requiring surgical intervention and should be differentiated from other conditions mimicking its signs and symptoms.¹⁻³ It carries a lifetime risk of 6 to 7 % in general population, peaking in the second decade of life.⁴ Depending on the definition and detection method, there are some reports of increased incidence of AA (22.71/10000) while the perforation rate is similar (2.9/10000).³ In cases diagnosed with uncomplicated AA, surgery provides recovery. However, delay in diagnosis can lead to complicated appendicitis and may become difficult to manage. Mortality rate is increased when the patients have perforation (6%), while it is low in uncomplicated AA patients (0.3%).⁵ Successful outcome depends on early diagnosis followed by appendicectomy before development of any complications such as gangrene or perforation. Nevertheless, definite diagnosis can only be made after the operation, and by histopathological examination of the specimen.⁶

Imaging is vital for accurate and prompt diagnosis when clinical presentation is equivocal. Imaging modalities like Ultrasound and Computed Tomography play an adjunctive role in improving the diagnostic accuracy of Acute Appendicitis.⁷ Computed Tomography (CT) provides a more accurate diagnosis of appendicitis than ultrasound and has high sensitivity (87%-100%), specificity (83%-93%), and negative predictive value (NPV). However, it exposes the patient to higher lifetime risk of radiation induced cancer especially in paediatric patients because of both increased dose per milliamperesecond, and greater lifetime risk per unit dose.^{8,9}

White blood cells (WBC) and C-reactive protein (CRP) are routinely-used laboratory parameters that strengthen the diagnosis of AA. Although several studies have assessed several parameters recently, such as Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), Mean Platelet Volume (MPV), Platelet to Lymphocyte Ratio (PLT) and serum bilirubin, still there is no definitive parameter that can be used to differentiate AA and perforated appendicitis. A few studies reported that these laboratory parameters are useful in the diagnosis of complicated appendicitis, but could not reach a satisfactory level. The lack of a marker in this field raised an interest to look for new parameters.⁵

The white blood cell count (WBC) and C-reactive protein (CRP) are now often used to guide clinical assessment, but past studies have

demonstrated sensitivities of CRP measurements ranging from 40% to 94%, and specificities of 38–87%.¹⁰⁻¹²

Some groups have reported more specific findings that raised CRP values have been shown to correlate with complications such as perforation or appendicular abscess.¹³⁻¹⁵ These studies have, however, all been retrospective, focusing on blood tests done on patients who have had appendectomy.

The aim of my study is to assess the level of C-reactive protein (CRP) and white blood cell count (WBC) and to correlate their values in predicting the severity of AA in children.

MATERIAL AND METHODS

A cross-sectional study was conducted in the Department of General Surgery, Jawaharlal Nehru Institute of Medical Sciences, Imphal. The study was conducted over a period of 1 year and 9 months from 1st September 2022 to 31st June 2024. All cases of Acute Appendicitis less than 18 years of age who were willing to undergo emergency open appendectomy were included in the study. Exclusion criteria were patients with age above 18 years, patients having blood dyscrasias, Koch's Abdomen, patients with chronic liver disease, chronic renal failure, malignancies and other concomitant bowel inflammatory lesions like ulcerative colitis. History, meticulous physical examination, Complete Haemogram test, serum C-reactive protein and ultrasonography of the whole abdomen were done and all patients were taken up for emergency open appendicectomy. The resected specimens were sent for Histopathological examination and divided into two groups based on HPE (complicated appendicitis and uncomplicated appendicitis). The data were collected and analysed.

Biochemical Analysis

5ml of blood was collected and centrifuged at 4000 rpm for 10 minutes. The separated sera was aliquoted into Eppendorf tubes and was stored at minus 80 degree Celsius until the time of analysis of CRP by immuno-nephelometric method using its relevant reagent was done. Normal value for CRP was accepted as 0-6 mg/dl. Another 5ml blood sample was collected in EDTA vial and Total white cell count (reference range, 4,000–11,000 per microliter) was determined using 5 parts automated cell counter (ABX Pentra ES 60). The histogram was analysed. A peripheral blood smear was also prepared and analysed for confirmation of the automated cell counter findings.

Statistical Analysis

Statistical analysis was done by the software SPSS IBM Statistics version 26. Continuous variables were represented as Mean (SD), and categorical variables were represented as Frequency (percentage). Data was also represented using appropriate diagrams like pie diagram. Patients were divided into two groups based on histopathological examinations: complicated group (Acute Appendicitis with perforation, gangrenous appendicitis, necrotizing Acute Appendicitis) and uncomplicated group (Acute Appendicitis, subacute appendicitis, recurrent appendicitis). Chi-square test or Fisher's exact tests were used to assess differences in categorical data. Student unpaired T-test were used for differences in means of independent data. Using CRP and WBC (TLC) in predicting HPE was assessed by Receiver Operating Curve Analysis (ROC). Area under the ROC curve along with 95% Confidence Interval and p-value were presented. The p value <0.05 were considered as significant.

RESULTS

A total of 190 people were included in the study. Among the 190 patients, 97 were males and 93 were females, with 51.05 % and 48.95 % respectively, showing slight male predominance over female patients. Among the 190 patients, it is shown that 76 of them fell under the age group of 11-15 years of age which is carried the highest percentage of Acute Appendicitis cases (40%) among the given age groups. While 0-5 years of age group had the lowest frequency with percentage of 2.11%. The mean (SD) CRP value for the complicated group is 41.01 (27.21) while for uncomplicated group it is 7.91 (6.92), with p-value <0.001 indicating statistically significant difference in CRP value between complicated and uncomplicated group.

The mean (SD) WBC for the complicated group is 14092.09 while for uncomplicated group it is 10543.88, with p-value <0.001 indicating statistically significant difference in WBC between complicated and uncomplicated group. The Mean (SD) of NLR in the complicated group is 15.43 (10.79) while in uncomplicated group it is 4.76 (5.04) and the p-value showing < 0.001, indicating a statistically significant difference in NLR between the two groups. Table no. 5 suggested a strong association of elevated WBC and higher CRP levels, with significant sensitivity, specificity and overall accuracy. The p-value <0.001 indicates that this association is statistically significant. The AUC for the complicated group is 0.827, which indicates a high level of accuracy in distinguishing between complicated and uncomplicated group. The ROC curve for the complicated group showing that WBC has good discriminative ability for identifying the complicated group with an AUC of 0.827 and statistically significant (p < 0.001). Whereas for the uncomplicated group WBC has no role in the diagnosis. The ROC curve analysis specifically for HPE findings with CRP in the study population showed that in the complicated group, the AUC of 0.929 indicated excellent diagnostic value of CRP and P-value showing < 0.001 showing statistically significant, affirming the test's effectiveness in this group.

Table 1: Descriptive analysis of Gender Distribution in study population (N=190)

Gender Distribution	Frequency	Percentage
Male	97	51.05%
Female	93	48.95%
Total	190	100

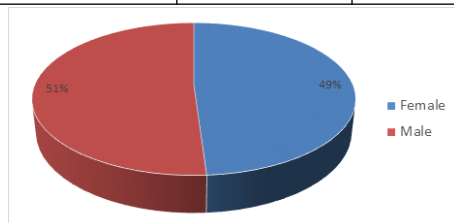


Figure 1: Pie chart of Gender Distribution (N=190)

Table 2: Descriptive analysis of Age Distribution in study population (N=190)

Age Distribution	Frequency	Percentage
0 to 5	4	2.11%
6 to 10	38	20%
11 to 15	76	40%
16 to 17	72	37.89%
Total	190	100

Table 3: CRP comparison with HPE findings in study population (N=190)

HPE Findings	Study population	CRP			P-Value
		Mean (SD)	Median	Range	
Complicated	43	41.01(27.21)	37	2.3 to 113	<0.001*
Uncomplicated	147	7.91(6.92)	6.67	0.5 to 53.54	

Student Unpaired t test

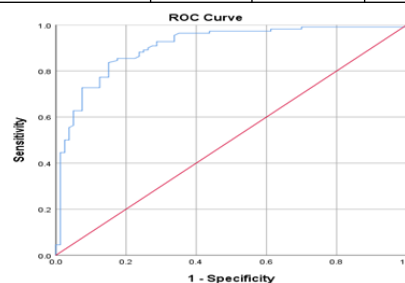
Table 4: WBC with HPE findings in study population (N=190)

HPE Findings	Study population	WBC			P-Value
		Mean(SD)	Median	Range	
Complicated	43	14092.09 (3008.833)	14200	5400 to 23200	<0.001*
Uncomplicated	147	10543.88 (2955.573)	10700	4140 to 19200	

Student Unpaired t test

Table 5: ROC curve for WBC with CRP in study population (N=190)

CRP	WBC			P-Value
	Less than 11,000/ μ L	More than 11,000/ μ L	Total	
Less than 6 mg/L	58	10	68	<0.001*
Percentage	72.5	9.09	35.79	
More than or equal to 6 mg/L	22	100	122	
Percentage	27.5	90.91	64.21	
Total	80	110	190	



Statistic	Value	95% CI
Sensitivity	90.91%	83.92% to 95.55%
Specificity	72.50%	61.38% to 81.90%
Positive Likelihood Ratio	3.31	2.30 to 4.74
Negative Likelihood Ratio	0.13	0.07 to 0.23
Positive Predictive Value (*)	81.97%	76.01% to 86.70%
Negative Predictive Value (*)	85.29%	75.98% to 91.40%
Accuracy (*)	83.16%	77.06% to 88.19%

Table 6: ROC curve for HPE findings with WBC in study population (N=190)

95% CI				
Variable	AUC	Lower Bound	Upper bound	P-Value
Complicated	0.827	0.756	0.899	<0.001*
Uncomplicated	0.173	0.101	0.244	<0.001*

Table 7: ROC curve for HPE findings with CRP in study population (N=190)

95% CI				
Variable	AUC	Lower Bound	Upper bound	P-Value
Complicated	0.929	0.874	0.984	<0.001*
Uncomplicated	0.071	0.016	0.216	<0.001*

DISCUSSION

The most frequently encountered entity of acute abdomen of the paediatric age group which requires urgent surgery is Acute Appendicitis. Atypical clinical symptoms are present in nearly one third of the appendicitis cases. And it is very difficult to establish a diagnosis specially in the paediatric age group. Many have started using computed tomography and ultrasonography for the diagnosis but it only decreases the incidence of negative appendectomy slightly. Also, since there's less prominent body fat in the paediatric age group, sometimes it is difficult to differentiate inflamed appendix and the bowel. Therefore, computed tomography has got higher sensitivity

and specificity in adults while in children it is less sensitive and got lower diagnostic accuracy. Besides when it comes to cost effectiveness computed tomography is costly and also there is exposure to radiation.¹⁶

At the Avery laboratory of the Rockefeller institute in 1930, C-Reactive protein (CRP), an acute phase reactant, was first discovered by W.S. Tillett and T. Francis. When there is inflammation and tissue damage, CRP level increases.¹⁷ For cases of acute abdominal pain including children, CRP test is often used by general practitioners but the diagnostic accuracy of CRP for Acute Appendicitis has not been determined in primary care.¹⁸

In our study, we aimed to determine the diagnostic accuracy of the two modalities, CRP and WBC count for Acute Appendicitis. The study also determined the diagnostic accuracy of NLR (Neutrophil to Lymphocyte Ratio) testing for Acute Appendicitis. It has been established by different authors that male sex predominates over females in Acute Appendicitis. Similarly in our study male: female ratio was 1.04:1. Whereas in study conducted by Peter Mekhail et al¹⁹, the male: female ratio was 1:1. Korner H et al²⁰ reported a male: female ratio of 1.15:1 and Lewis et al²¹ reported male: female ratio of 3:2 in their study. In our study, among the 190 patients 40 % of them fell under the age group of 11-15 years, carrying the highest percentage among the given age groups, while 0-5 years age group had the lowest frequency with 2.11 %. A Study by Peter Mekhail et al¹⁹ showed that the median age for Acute Appendicitis in children was 12(12-16), 53 % were below 12 years and 47% were between 12 and 16 years of age. Similar findings were also seen in a study conducted by Ukoha Agwu Kalu et al²², where aged 8 to 11 years accounted for the greater percentage of 41.9% of patients in the study population.

A Study conducted by Sevgi Buyukbese Sarsu et al¹⁶ had 144 cases out of 163 appendicitis patients with raised CRP level, whereas in the remaining Acute Appendicitis patients the CRP level was not raised. The predictive value of a positive test was 88%. There were 29 patients who had normal CRP value in which 15 were Acute Appendicitis cases and the remaining were non- appendicitis cases and the predictive value of a negative test was 48%. In this study it was shown that CRP had the highest diagnostic accuracy in complicated appendicitis with AUC of 0.887. In our study all participants were cases of Acute Appendicitis and there was statistically significant difference in CRP value of complicated and uncomplicated appendicitis.

There are many studies that have shown that WBC counts are always elevated in complicated appendicitis such as perforated appendicitis or gangrenous appendicitis²³. In the literature the sensitivity and specificity of WBC counts have been reported as 19%-88% and 53% to 100% respectively. In the study by Sevgi Buyukbese Sarsu et al¹⁶, the sensitivity and specificity of WBC counts were 73.4 % and 80.0 % respectively. A similar study was conducted by MN Khan et al²⁴, where 259 patients participated to find out the role of WBC count in the diagnosis of Acute Appendicitis. In our study, in the complicated appendicitis group, the mean (SD) for WBC was 10492.09 while for the uncomplicated appendicitis group it was 10543.88 with P value <0.001, showing statistically significant difference between the two groups, with complicated appendicitis group having high mean WBC than the uncomplicated group. In the ROC curve analysis of WBC count with HPE findings, it was indicated that the test was reliably accurate for the diagnosis of complicated appendicitis. Uncomplicated appendicitis group had AUC of 0.173, suggesting poor diagnostic accuracy.

In the ROC curve analysis of WBC with CRP in our study, the AUC for the complicated appendicitis group was 0.906, suggesting that CRP and WBC have got diagnostic value in complicated appendicitis. Our study also showed a strong association between WBC and CRP values, with significant sensitivity and specificity of 90.91% and 72.50 % respectively. Similar study was also conducted by Tolga Dinc et al²⁵ in 2022. While a study by L Van Den Worm et al²⁶ demonstrated that CRP is superior to WBC count in differentiating between complicated appendicitis and uncomplicated appendicitis.

A study by Hajibande S et al²⁷ demonstrated that NLR can predict both diagnosis and severity of Acute Appendicitis. NLR for the complicated appendicitis showed sensitivity and specificity of 76.92% and specificity of 100% with AUC of 0.91. While a study by Nelly Esquivel et al²⁸ assessed the diagnostic accuracy of NLR for Acute Appendicitis,

where NLR alone was not sufficient to exhibit diagnostic usefulness or to rule out presence of Acute Appendicitis. In our study mean NLR of the complicated appendicitis group was higher with a wider confidence interval, showing a significant difference between the two groups with p-value of <0.001.

CONCLUSION

Acute Appendicitis is the leading cause of abdominal surgery in the paediatric age group and the most prevalent abdominal surgical emergency worldwide. An accurate, prompt, safe and non-invasive approach for the diagnosis of Acute Appendicitis and its complication is essential to avoid adverse outcome. We need a timely diagnosis in children, since children have got higher incidence of perforation of appendix. The diagnosis of AA should be primarily based on clinical examination and more specifically on systemic inflammatory markers such as CRP, WBC and NLR. Combined use of WBC and CRP has got significant sensitivity, specificity and overall accuracy in the diagnosis of complicated appendicitis and could be used as diagnostic markers for complicated appendicitis. So, if there are elevated CRP, WBC and NLR in appendicitis patients, then an immediate and proper management should be done since there is a high probability of complicated appendicitis such as appendicular perforation, gangrenous appendicitis etc. especially in the paediatric age group. Thus, estimation of CRP, WBC and NLR can aid in timely intervention and prevention of further complication in paediatric patients with acute complicated appendicitis.

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