Diagnostic Value of C-Reactive Protein and Total Leukocyte Count in Acute Appendicitis

Erisha Komal, Muhammad Saeed Akhtar, Khurram Niaz*, Wasif Idris Ahmed, Muhammad Ahsan Mustafa

Department of General Surgery, Combined Military Hospital Bahawalpur/National University of Medical Sciences (NUMS) Pakistan,
*Department of General Surgery, Sheikh Zayed Medical College, Rahim Yar Khan Pakistan

ABSTRACT

Objective: To find the diagnostic value of C-Reactive Protein and Total Leukocyte Count in acute appendicitis.

Study Design: Validation study.

Place and Duration of Study: Department of Surgery, Combined Military Hospital, Bahawalpur Pakistan, from Oct 2022 to Sep 2023.

Methodology: A total of 210 patients were included who underwent appendectomy. Total Leukocyte Count and C-Reactive Protein C-Reactive Protein were checked pre-operatively. Per operative findings, histopathology and duration of the start of symptoms were also noted.

Results: Out of 210 patients, 127(60.47%) were male and 83(39.53%) were female. There was a significant difference (*p*-value <0.001) in an increase of Total Leukocyte Count and C-Reactive Protein with positive operative findings. When compared with histopathological findings both show a significant difference (*p*-value<0.001). As the duration of symptoms increased there was a statistically significant difference in the values of both Leukocyte Count and C-Reactive Protein (*p*-value<0.001). The sensitivity, specificity, positive predictive value, negative Predictive Value, and accuracy of Total Leukocyte Count were (75.39%), (78.95%), (97.30%), (24.19%), and (75.71%), and for C-Reactive Protein were (72.77%), (78.95%), (97.20%), (22.39%), and (73.33%).

Conclusion: The results suggest that both C-Reactive Protein and Total Leukocyte Count have potential as diagnostic markers for acute appendicitis. The values of Both C-Reactive Protein and Total Leukocyte Count increase as the duration of symptoms increases.

Keywords: Appendicitis, Biomarkers, C- Reactive Protein, Leukocyte Count.

INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies, particularly in the pediatric population.[1] The quest for dependable and effectively available biomarkers to aid in the analysis of acute appendicitis proceeds. C-reactive protein (CRP) and absolute leukocyte count (TLC) are two generally estimated lab boundaries that have been explored for their diagnostic value in acute appendicitis.[2] These biomarkers are handily obtained from routine blood tests and may offer important diagnostic data in the assessment of acute appendicitis.[3]

The diagnostic value of CRP and TLC in acute appendicitis has been investigated in different studies. Raised CRP levels have been seen as a mark of appendiceal irritation.[4] Also, an expanded TLC, particularly neutrophilic predominance, has been seen in patients with acute appendicitis. Notwithstanding, the exact end values and the diagnostic precision of these markers remain subjects of discussion. A few studies have researched the positive predictive value (PPV) and negative predictive value (NPV) of CRP and TLC in acute appendicitis. These have revealed promising outcomes, proposing that raised CRP levels and TLC can aid in the finding of acute appendicitis, while others have found restricted diagnostic exactness.[5]

While raised CRP levels and TLC, particularly neutrophilia, have shown relationship with acute appendicitis,[6] further research is needed to determine standardized cutoff values and decide their precise diagnostic exactness. The objective of the study was to find the diagnostic value of CRP and TLC in acute appendicitis.

METHODOLOGY

The validation study was conducted at Combined Military Hospital, Bahawalpur from Oct 2022 to Sep 2023, after approval by the Institutional Ethical Review Committee (ltr No.1516/EC/05/2023).

Inclusion criteria: Patients of either gender and of all ages who presented with clinical suspicion of acute appendicitis, those who underwent blood tests,

Correspondence: Dr Erisha Komal, Department of General Surgery, Combined Military Hospital, Bahawalpur Pakistan

including C-reactive protein (CRP) and total leukocyte count (TLC) and subsequently underwent surgical exploration and histopathological examination of the appendix to confirm the diagnosis of acute appendicitis with complete medical records and available data are required for analysis were included.

Exclusion criteria: Patients with a known history of chronic inflammatory conditions, such as Crohn's disease or ulcerative colitis, which could confound the interpretation of CRP and TLC levels. Patients who had received recent immunosuppressive therapy, as this could affect the inflammatory response and laboratory parameters and those with recent infections or other acute inflammatory conditions, or those with incomplete medical records or missing data which was required for analysis were excluded.

The patients were admitted to the surgical ward. Investigations were done free of cost by the hospital laboratory. All the clinical signs and symptoms were carefully recorded. Informed written consent was taken. Serum samples for CRP and complete blood pictures were sent to the enrolled patients at admission before moving to the operating table. Emergency appendectomies were performed. The operative findings were noted accordingly as a normal appendix, inflamed appendix, and complicated appendix (gangrenous, abscess, perforated). The specimen of the appendix was sent for histopathology. The following variables were recorded for each patient: age, gender, duration of symptoms, laboratory results (CRP and TLC), operative findings, and histopathological reports.

CRP levels were measured using a standardized laboratory assay. TLC was determined through automated blood cell counting systems.

The diagnosis of acute appendicitis was based on operative findings and histopathological examination of the appendix. The surgical team and pathologists involved were blinded to the CRP and TLC results to avoid bias. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 23. Cut-off value of 10000 cells/µL and 6 mg/ml was set for TLC and CRP respectively as per previous literature. The diagnostic accuracy of CRP and TLC was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis The median and interquartile range were calculated for non-normally distributed data and, the mean and standard deviation for normally distributed data. Analysis of variance was done by non-parametric comparative test Kruskal-Wallis with post hoc analysis according to the Mann-Whitney U test for non-normally distributed data. ANOVA was used for normally distributed data. Chi-square and independent sample t tests were used for analyses of the diagnostic value of acute appendicitis for each investigation. The level of significance was set at $p \leq 0.05$.

RESULTS

A total of 210 patients with clinical suspicion of acute appendicitis were included. Out of these 127(60.47%) were male and 83(39.52%) were female. All patients underwent blood tests, including C-reactive protein (CRP) and total leukocyte count (TLC). Subsequently, the diagnosis of acute appendicitis was confirmed through surgical exploration or histopathology. The CRP data was not normally distributed, but TLC data was. The median for CRP was 11.615 with an interquartile range of 44.025–4.905. The Mean and SD for TLC was 11988.10±3036.65.

There was a significant difference in both TLC and CRP with the operative findings of a normal appendix compared with an inflamed and complicated appendix (Table–I).

Table-I: Comparison of Operative and Laboratory Findings (n=210)

Parameters	Normal appendix (n=19)	Inflamed appendix (n=160)	Complicated appendix (n=31)	p-value	p-value post hoc analysis
Age in years (median:IQR)	26.00(39.00-12.00)	24.00(31.75-16.25)	21.00(31.00-12.00)	0.430	0.673[A], 0.453[B], 0.209[C]
TLC(Mean±SD)	9178.95±2408.68	11475.00±2394.49	16358.06±2058.44	<0.001	<0.001[A], <0.001[B], <0.001[C]
CRP(median:IQR)	3.24(8.79-2.17)	9.10(28.76-4.94)	122.00(142.00-104.00)	<0.001	<0.001[A], <0.001[B], <0.001[C]

Table-II: Duration of Symptoms and Laboratory Findings (n=210)

Parameters		Normal appendix (n=19)	Inflamed appendix (n=160)	Complicated appendix (n=31)	p-value
Duration of symptoms	< 24 hours n(%)	7(3.33%)	63(30.0%)	8(3.80%)	0.831[A], 0.409[B], 0.15[C]
	>24 and <48 hours n(%)	9(4.28%)	73(34.76%)	6(2.85%)	0.885[A], 0.03[B], 0.007[C]
	>48 hours n(%)	3(1.42%)	24(11.40%)	17(8.09%)	0.928[A], 0.006[B], <0.001[C]

[A]*Normal appendix vs inflamed appendix,* [B]*Normal appendix vs complicated appendix,* [C]*Inflamed appendix vs complicated appendix*

As the duration of the start of symptoms increases; the increase in complicated appendix shows a significant difference (Table-II).

Out of 210 patients, 19 were histopathologically negative for appendicitis. Out of these negative appendectomies, 4 patients had both elevated TLC and CRP values. However, both TLC and CRP give a statistically significant value for the diagnosis of appendicitis. (Table–III).

Table-III: Laboratory Findings and Histopathology Reports of Appendices (n=210)

	Histology Positive (n=191)	Histology Negative (n=19)	p-value
TLC			
Elevated n(%)	144(68.57)	4(1.90)	<0.001
Normal n(%)	47(22.38)	15(7.14)	
Total n(%)	191(90.95)	19(9.05)	
CRP			
Elevated n(%)	139(66.19)	4(1.9)	<0.001
Normal n(%)	52(24.76)	15(7.14)	
Total n(%)	191(90.95)	19(9.05)	
Both TLC and CRP			
Elevated n(%)	130(61.90)	4(1.9)	<0.001
Not elevated n(%)	61(29.04)	15(7.14)	
Total n(%)	191(90.95)	19(9.05)	

TLC has a slightly higher sensitivity and diagnostic accuracy than CRP and both CRP+TLC for diagnosis of acute appendicitis. All three have the same specificity of (78.95%). The accuracy decreases for TLC+CRP, rather than when calculated independently (Table-IV).

Table-IV Diagnostic Value of TLC and CRP(n=210)

Parameters	CRP	TLC	Both CRP and TLC
Sensitivity	72.77%	75.39%	68.06%
Specificity	78.95%	78.95%	78.95%
Positive predictive value (PPV)	97.20%	97.30%	97.01%
Negative Predictive Value (NPV)	22.39%	24.19%	19.74%
Accuracy	73.33%	75.71%	69.05%

As the duration of symptoms increased there was a statistically significant difference in the values of both TLC and CRP (p = <0.001) as seen in Table-V.

DISCUSSION

The median for CRP was 11.615 with an interquartile range of 44.025–4.905. These findings suggest that CRP levels tend to be elevated in patients with acute appendicitis. Similarly,The mean for TLC was 11988.10±3036.650. These results indicate that TLC values can also vary in patients with acute appendicitis, which has been noted in other studies.[7-9] The duration of start symptoms has a significance change in the increase of TLC and CRP values. As the duration increases so do the values. Also, the per-operative findings became more complicated as the duration of symptoms increased.

The responsiveness, particularity, and positive predictive value (PPV) were determined to assess the diagnostic exactness of CRP and TLC. Theoretically, a CRP cutoff value of 6 mg/L yielded a sensitivity of 0.72.77%, specificity of 78.95%, and PPV of 97.20%. These values propose that CRP can be a helpful marker in diagnosing acute appendicitis, with a high probability of a positive outcome showing the presence of the condition.[10,11] For TLC, an end value of 10,000 cells/μL yielded a sensitivity of 75.39%, specificity of 78.95%, and PPV of 97,30%. These outcomes demonstrate that TLC can likewise add to the determination of acute appendicitis, with higher TLC values being related with a more prominent probability of the condition.[12-14] Recent researches reveal that normal blood parameters (total leucocyte count and neutrophil percentage) and normal ultrasonography have a high combined diagnostic accuracy for acute appendicitis.[15]

The outcomes may not precisely reflect the genuine diagnostic exhibition of CRP and TLC in acute appendicitis, owing to the small sample size and single-centre of study.[16,17] Also, the end values utilized in this study might require further perusal. Also, assessing the exhibition of these biomarkers in mix with other clinical pointers might improve the exactness of the finding.[18] Pulse rate is also an important factor for determining the severity of the disease, which was not observed in our study.

Table-V: Comparison of Laboratory Investigation with Duration of Onset of Symptoms (n=210)

	Duration of onset of symptoms				
	<24 Hours	>24 To <48 Hours	>48 Hours	p-value	p-value post hoc analysis
TLC (mean±SD)	11044.87±2649.56	11465.91±2539.47	14704.55±3078.655	<0.001	0.197[A], <0.001[B], <0.001[C]
CRP (Median:IQR)	7.15(24.23-4.33)	9.80(29.33-5.06)	49.24(123.50-20.54)	<0.001	0.150[A], <0.001[B], <0.001[C]

[A]<24 hours vs >24 to <48 hours, [B]<24 hours vs >48 hours, [C]>24 to <48 hours vs >48 hours.

CONCLUSION

In conclusion, the study suggests that both CRP and TLC have potential as diagnostic markers for acute appendicitis. The study findings indicate that elevated levels of CRP and TLC were observed in patients with acute appendicitis compared to those without the condition. The values of Both CRP and TLC increase as the duration of symptoms increases. The calculated sensitivity, specificity, positive predictive value (PPV), negative predicted value further demonstrate the potential diagnostic accuracy of CRP and TLC.

Conflict of Interest: None

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

EK & MSA: Conception, study design, drafting the manuscript, approval of the final version to be published.

KN & WIA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MAM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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