EFFECTIVENESS OF TOTAL LEUKOCYTE COUNT (TLC) AND C-REACTIVE PROTEIN (CRP) IN THE DIAGNOSIS OF ACUTE APPENDICITIS

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Abstract: *Acute appendicitis is a typical surgical emergency. Diagnosing it can be challenging due to variable symptoms. Total leukocyte count (TLC) and C-reactive protein (CRP) are commonly used to assess inflammation and guide treatment. This study evaluates the diagnostic accuracy of TLC and CRP in acute appendicitis to determine appropriate management.* **Objective:** *This study aimed to assess the diagnostic accuracy of TLC and CRP in predicting acute appendicitis and their role in determining the proper management approach, either conservative or surgical.* **Methods:** *This prospective observational cohort study was conducted in the Department of General Surgery at Dow University of Health Sciences (DUHS), Ojha Campus, from July 2023 to March 2024. A total of 87 adult patients with clinical signs of appendicitis and an Alvarado score of greater than 4 were enrolled. Data was analyzed using SPSS version 22. Variables included socio-demographic characteristics, clinical presentations, and levels of TLC and CRP. Both conservative and surgical management approaches were analysed, with laparoscopic appendectomy being the most common procedure.* **Results:** *Among the 87 patients, most were male. TLC and CRP levels were similar across genders, with notable variations in socio-demographic characteristics. CRP levels were more frequently elevated in patients managed conservatively compared to those managed surgically. Both TLC and CRP were elevated in 43 patients (49.4%), highlighting the value of using both markers together. Surgical intervention, primarily laparoscopic appendectomy, was the preferred treatment, with suppurative inflammation being the most common histopathological finding.* **Conclusion:** *The combination of TLC and CRP significantly improves the diagnostic accuracy for acute appendicitis. TLC correlates more strongly with the need for surgical intervention, whereas CRP did not show a significant association with management type. Both markers are useful in assessing the duration of the complaint, but they are not substitutes for clinical judgment. Further research is warranted to refine their diagnostic utility and evaluate their impact on surgical care availability in resource-limited settings.*

Keywords: Acute appendicitis, C-reactive protein, CRP, Inflammatory markers, Laparoscopic appendectomy, Total leukocyte count, TLC, Suppurative inflammation, Conservative management.

Introduction

Acute appendicitis is amongst the most common general surgical emergencies that need prompt surgical intervention to prevent complications. Its annual incidence is 1/1000 individuals (1). The peak incidence of acute appendicitis is between the ages of 10 to 20 years. The male-to-female ratio is 1.4:1. Lifetime incidence of acute appendicitis is 7% (2). A third of patients with appendicitis are found to have complicated cases at presentation involving gangrene, abscess formation, and appendiceal perforation. (3). Furthermore, diverse results have been documented from various regions across the globe. Perioperative mortality is reported to range from 2.4 per 1000 appendectomies in South Asia to 54 per 1000 appendectomies in Central sub-Saharan Africa, likewise in other low-income countries (4). Despite being very common and with the advances in diagnostic tools, its diagnosis is still arduous. Diagnosis as well as management of acute appendicitis is mired in controversies and contradictions even today (5). A 10-point clinical scoring system, commonly referred to by the acronym MANTRELS, was developed by Alvarado in 1986 to diagnose acute appendicitis in patients who present with suspected cases based on symptoms, signs, and diagnostic tests (6). The American College of Emergency Physicians recently released a clinical policy paper that discusses the importance of utilising clinical findings to inform decisions while treating acute appendicitis (7). Many medical professionals have turned to radiological modalities as clinical algorithms have proven to be unsatisfactory (8). Additional investigations, such as ultrasound (US) and computed tomography (CT) scanning, are also suggested for the confirmatory diagnosis of appendicitis (6). MRI can be the next step for pediatric and pregnant patients whose initial USG results are inconclusive (5). Nowadays, clinicians have started planning the management of acute abdomen, including acute appendicitis, based more on imaging correlation than on laboratory markers to support their clinical judgement (5).

Studies conclude that sensitivity, specificity, and positive and negative predictive values of total leukocyte count (TLC) and C-reactive protein (CRP) are better than either TLC or CRP alone—very high levels of CRP either alone or coupled with raised TLC warrant mandatory explorations. The studies recommend that CRP should be done as a routine laboratory test along with TLC in the doubtful diagnosis of acute appendicitis (9). Leukocyte count (TLC) and CRP together can be used to predict the inflammatory response score of appendicitis (5).

Interestingly, the sensitivity to diagnose acute appendicitis is improved to 97%–100% when combined with an elevated CRP, elevated WBC, or neutrophilia greater than 75%. Consequently, there would be little chance of acute appendicitis in patients whose values for all three investigations were average. (10). As demonstrated in one of the literature, using both in combination has increased the specificity and positive predictive value to 88.04% and 98.7%, respectively (11).

More than 300,000 appendectomies are performed annually in the USA, demonstrating the widespread acknowledgement of surgery as the only treatment since the nineteenth century (12). According to available data, laparoscopic appendectomy is the most successful surgical procedure; it is linked to a decreased risk of wound infection and post-intervention morbidity, a shorter hospital stay, and higher quality of life ratings than open appendectomy (13). At the same time, several studies have also challenged the aphorism that "the sun should not rise and set on appendicitis", concluding that conservative management of acute appendicitis with antibiotics is associated with fewer complications (14).

We aim to evaluate the diagnostic accuracy of TLC and CRP in acute appendicitis. This study will not only help to elude gratuitous lab investigations that are in practice but will also assist in managing patients with comorbidities conservatively in whom there is a high risk of complications of surgery. It will also help manage pregnant females in whom the fetus will be at risk during surgical procedures. Overall, we believe this study will help further understand current acute appendicitis diagnosis/management and possibly build upon it. In low-income countries like Pakistan, it will help reduce the cost of other diagnostic tests and radiological scans.

Methodology

This study was conducted as a prospective observational cohort at the Department of General Surgery, Dow University of Health Sciences (DUHS), Ojha campus, between July 2023 and March 2024. Dow University Hospital, a tertiary care facility, provided the setting with seven general surgeons capable of performing both laparoscopic and open appendectomies. After a thorough literature review and the development of the study protocol, the study received approval from the DUHS Institutional Review Board (IRB Reference Number: IRB-2992/DUHS/Approval/2023/245).

Participants included adult patients aged between 12 and 65 years, including pregnant women, who presented with clinical signs of appendicitis, such as right lower quadrant abdominal pain, nausea, vomiting, and anorexia, with an Alvarado score greater than 4. Patients with signs of generalised peritonitis or radiological evidence of perforation were excluded from the study due to the need for immediate surgical intervention, which was beyond the study's scope.

Data collection was carried out using a structured questionnaire developed from the review of relevant literature identified through searches on PubMed and Google Scholar. The terms "C-reactive protein (CRP)," "total leukocyte count (TLC)," and "acute appendicitis" were used to guide the development of the data collection tool, which was divided into three parts. The first part

gathered socio-demographic details such as the patient's name, age, gender, and medical record number. The second part focused on clinical presentation and laboratory or radiological findings. This section included symptoms, their duration, TLC and CRP levels, and radiological investigations such as ultrasound for appendiceal diameter and the presence of fecolith, as well as CT scans when necessary. The final part centred on patient management, whether conservative or surgical. It detailed the duration of management, antibiotic regimens, type of surgical incision, operative findings, and postoperative outcomes, including complications, length of hospital stay, and surgical site infections. The study concluded with a review of histopathology reports, which is essential for assessing whether conservative management or surgical intervention was appropriate, given the diagnostic accuracy of TLC and CRP levels.

The study's sample size was calculated using OpenEpi Software Version 3.01, similar to research conducted in India. A 10% margin of error and a 90% confidence level were used, determining that a minimum sample size of 87 participants was required. Resident doctors in the General Surgery department at Dow University Hospital, who also supervised patient care, collected the data.

For data analysis, IBM SPSS Statistics Version 22 was used. Categorical variables, such as gender, were summarised as frequencies and percentages, while continuous variables, including age and the duration of symptoms, were presented as medians with interquartile ranges. The Mann-Whitney U and Kruskal-Wallis tests were applied to determine differences in median TLC and CRP levels across various socio-demographic and clinical presentation groups. Qualitative variables were compared between groups using the Chi-square test, with statistical significance set at a p-value $\leq$ 0.05. This methodological approach ensured a rigorous analysis, enabling the study to accurately assess the relationship between CRP, TLC levels, and clinical outcomes in acute appendicitis.

Results

Overall, 87 acute appendicitis patients were a part of this study. Among all the patients, 73.5% (64) were males and 26.4% (23) were females. The average age of patients was 30.9 (median = 31) years and ranged between 12 to 52 years, which highlights that the disease is more prevalent in the middle-aged group. It was noted that median TLC and CRP were identical in both genders. Although statistically significant TLC and CRP differences were found between categories of socio-demographic characteristics (Table 1). The TLC (P-VALUE=.00004) has shown a substantial value in male patients compared to CRP (P-VALUE=.09551). Similarly, higher CRP 18 (P-VALUE=.54463) levels were assessed in female patients as compared to TLC 13 (P-VALUE=.56932) levels, which were not statistically significant. The duration of the symptoms that patients experienced was measured in days. It was evaluated that patients whose symptoms were less than 3 days had a higher CRP (P-VALUE =.00001) and TLC (P-VALUE =.00001) compared to those whose symptoms lasted for more than 3 days. However, a statistically significant correlation was found between inflammatory markers and the duration of symptoms. The fundamental descriptive analysis also shows that (Table 2)

the majority of the patients, 76 (88%) (Figure 1), were managed through surgical treatment, with Laparoscopic Appendectomy 53 (60.9%) being the most common surgery type as compared to Open Appendectomy 17 (19.5%) opted for by the patients.

Table 2 shows that the TLC/WBC count is <11 for 43.7% (n=38) of the population in which the majority was categorised in surgical group 29 (76.3%). There is a significant association at the 5% significance level between the treatment type and TLC/WBC counts (Chi-Square = 7.96, P > 0.047). About 11 (12.6%) of the patients have TLC/WBC count levels more than 17. Twenty-four (27.6%) of the patients have a CRP level between 11-75, followed by a group with a CRP level over 150 (29%). It was also observed that in conservative management, CRP was significantly higher in 8 (72.7%). The data did not show any association between management type and CRP level (Table 3). Collectively TLC and CRP were elevated in 43 (49.4%) patients, which highlighted the significance of using both inflammatory markers together in such cases, as illustrated in Table 4.

Operative findings, along with the levels of TLC and CRP of appendicitis, are reported in Table 5 and Figure 2,

histopathology report, it was noticed that 56 (73.7%) were uncomplicated cases (like Catarrhal, Suppurative Appendix), whereas 20 (26.3%) were complicated (which includes Gangrenous and Perforated Appendix), in which low-grade Appendiceal Mucinous Neoplasm (n=1) and Benign Follicular Lymphoid Hyperplasia (n=2) of the appendix were also seen.
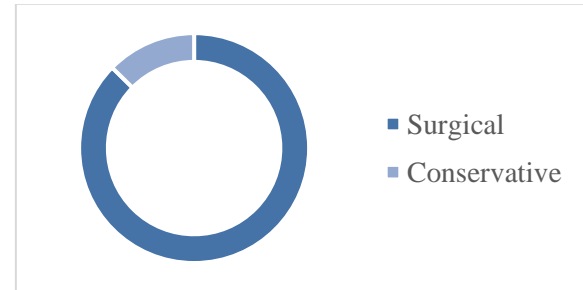

Figure 1. Surgical accounts for the majority of 'Management'.

proving suppurative inflammation to be the most common finding in the patients. When compared with the

Table 1. Socio-demographic characteristics of patients based on raised TLC and CRP (n=87)

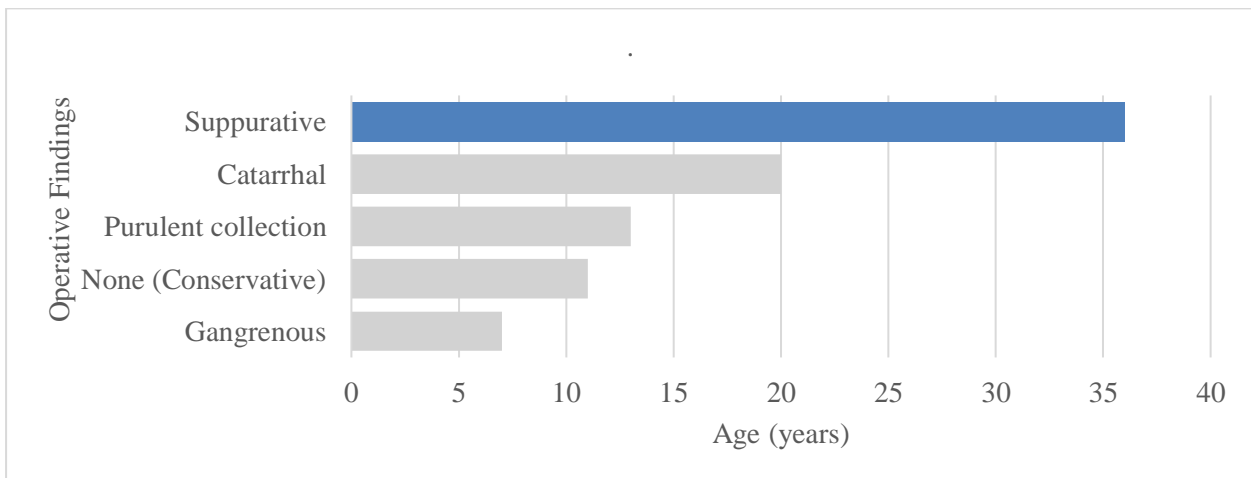| Characteristics		Total n (%)	TLC Median (Q$_1$ - Q$_3$)	p-value	CRP Median (Q$_1$ - Q$_3$)	p-value
Age (years)						
	(mean)	30.9	15 (12-15)	<.00001	113 (43-150)	<.00001
Gender						
	Male	64 (73.5)	12 (12-15)	.00004	113 (43-150)	.09551
	Female	23 (26.4)	12 (12-15)	.56932	113 (43-150)	.54463
Duration of Symptoms						
	≤ 3	51 (58.6)	12 (12-15)	.00001	113 (43-150)	<.00001
	> 3	36 (41.3)	12 (12-16)	.75085	113 (43-150)	.00533
*p-value was calculated by Mann-Whitney/ Kruskal-Wallis test, Total leukocyte count (TLC), C-reactive protein (CRP)						

Figure 2. Operative Findings, Suppurative appears most often

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Table 2: Association Between Management and TLC/WBC (Total leucocyte count) Level

Management	TLC/WBC LEVEL				Total (%)
	< 11	11-13	14-17	>17	
	N	N	N	N	
Conservative	9	1	0	1	11(12.6)
Surgical	29	20	17	10	76(87.4)
Total (%)	38 (43.7)	21 (24.2)	17 (19.5)	11 (12.6)	87 (100)

Chi-Square = 7.96, P > 0.047

Table 3: Association Between Management and CRP (C-reactive protein) Level

Management	CRP LEVEL				Total (%)
	< 10	11-75	75-150	>150	
	N	N	N	N	
Conservative	0	2	5	4	11 (12.6)
Surgical	17	22	16	21	76 (87.4)
Total (%)	17 (19.6)	24 (27.6)	21 (24.1)	25 (28.7)	87 (100)

Chi-Square = 5.49, P > 0.139

Table 4: Association Between TLC (Total leucocyte count) and CRP (C-reactive protein) Level

	CRP Level				
TLC/WBC Count	>10	11-75	75-150	<10	Grand Total
<11	8	9	10	11	38
11-13	7	8	3	3	21
14-17	5	5	6	1	17
>17	5	2	2	2	11
Grand Total	25	24	21	17	87

Table 5: Grouping Of The Patients As Per The Histology Of The Removed Appendix

Group	Operative finding	Total No. of patients	TLC raised	CRP raised	Both normal	Both raised
A	Uncomplicated Appendix	56	5	13	10	28
B	Complicated Appendix	20	1	4	1	14
Grand Total		76	6	17	11	42

TLC - Total leucocyte count, CRP - C-reactive protein

Discussion

Acute appendicitis is the most common cause of urgent abdominal surgery. Clinical diagnosis of acute appendicitis is a bit challenging; hence, it can be a false positive, and the chances of negative appendectomy being performed are high, up to 15–25% of the cases (11).

Most of the patients with acute appendicitis present with right-sided lower abdominal pain, nausea, and vomiting, but these symptoms are very nonspecific. Thus, one must perform laboratory tests like CBC (TLC) and CRP before proceeding with surgery.

False-positive decisions were made for patients who had signs and symptoms like those of appendicitis patients [appendicitis score 5.7 (95% CI = 5.2 to 6.1) vs 6.5 (95% CI = 6.4 to 6.7)]. Female patients had an increased risk of false-positive surgery (2.3 OR 95% CI = 1.5 to 3.4) (15).

This leads to misdiagnosis of these patients, which can cause complications. Furthermore, these patients could be treated with conservative management.

Our study aimed to evaluate the diagnostic effectiveness of total leukocyte count (TLC) and C-reactive protein (CRP) in identifying acute appendicitis.

We took data from 87 patients in our study and studied thoroughly all the labs and radiological reports from 10-50 years. The total number of patients was 87, of which 76 were surgically performed and 11 were conservatively performed.

This descriptive analysis revealed that a large proportion of the patients are between the ages of 12 and 52, indicating that middle-aged groups are more likely to experience this issue (Figure 1). We considered TLC <11 and CRP <10 average, non-inflamed values in our hospital's laboratory setting. About 38% of the patients have TLC/WBC count levels lower than 11. Seventeen (17%) per cent of the patients have a CRP level of less than 10 (Table 1).

Table 1. shows that the majority of the treatment (86%) was managed through surgical treatment. Table 2. shows that the TLC/WBC count is between 14 and 17 for 17% of the population, while most of the patients in the surgical group have TLC/WBC counts. There was no association between the treatment type and TLC/WBC counts (Chi-Square = 7.96, P > 0.047). Among these 87 patients, the CPR level was over 150 in 25%, while 24% had a CPR level between

the ranges of 11-75. The data did not show any association between management type and CPR level (Table 3).

Our findings indicate that both TLC and CRP levels were significantly elevated in patients with acute appendicitis compared to those without the condition. This suggests that these biomarkers have potential diagnostic value in identifying acute appendicitis.

Our results are consistent with prior research that has demonstrated the utility of TLC and CRP in diagnosing acute appendicitis. Studies have consistently shown elevated levels of these biomarkers in patients with appendicitis, supporting their role as diagnostic indicators. Compared with the other study, the TLC and CRP combined with histopathology found sensitivity and specificity of 90.24% and 78.57% respectively [6]. In other studies, CRP level had a sensitivity of 86.27% and specificity of 66.67% in predicting acute appendicitis. Total leucocyte count had a sensitivity of 87.65% and specificity of 100% in predicting acute appendicitis (16).

However, it's important to acknowledge the limitations of our study, including the relatively small sample size and the possibility of confounding variables influencing TLC and CRP levels. Additionally, while TLC and CRP are helpful in diagnosis, they should be interpreted alongside clinical findings and imaging studies for accurate assessment.

The identification of effective biomarkers for acute appendicitis diagnosis has significant implications for clinical practice. Rapid and accurate diagnosis can lead to timely intervention, reducing the risk of complications and improving patient outcomes.

While our study utilised standardised methods for measuring TLC and CRP levels, variations in laboratory techniques and patient characteristics may impact results. Future studies should consider standardising methodologies to ensure consistency and reproducibility, as the cut-off value of laboratory tests may help determine the diagnosis and treatment (17).

The study pre-specified the target population, lacking the data in the literature. It was a single-centre study with a relatively small sample size. In this study, selection bias cannot be ruled out. Due to the relatively small sample size, the results cannot be

generalised. The study also lacks measures to ensure minimal nonresponse bias. Another limitation could be recall bias because the data was obtained through a self-report questionnaire.

Throughout the discussion, we have provided deeper insights into the significance of our findings without simply restating the results presented in the earlier sections.

We have maintained an objective tone throughout the discussion, basing our interpretations and conclusions on the evidence presented in our study.

By following this structure, we can effectively communicate the implications of our research findings on the diagnostic approach to acute appendicitis using TLC and CRP levels. Future research should focus on validating the diagnostic accuracy of TLC and CRP in larger, more diverse patient populations. Additionally, exploring the potential utility of combining these biomarkers with other clinical indicators or imaging modalities could further enhance diagnostic accuracy. Further studies are required to validate the results. Awareness of this disease and associated factors is the need of the hour among medical professionals.

Conclusion

The combination of TLC and CRP significantly improves the diagnostic accuracy for acute appendicitis. TLC correlates more strongly with the need for surgical intervention, whereas CRP did not show a significant association with management type. Both markers are useful in assessing the duration of the complaint, but they are not substitutes for clinical judgment. Further research is warranted to refine their diagnostic utility and evaluate their impact on surgical care availability in resource-limited settings.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate.
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Conflict of interest

The authors declared an absence of conflict of interest.

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