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Accuracy of C-reactive protein and leukocyte count in the diagnosis of acute appendicitis compared to histopathological examination

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ABSTRACT

Background. One of the most common causes of acute surgical abdomen is acute appendicitis. The aim of this study was to compare the accuracy of C-reactive protein (CRP) and the total leukocyte count (TLC) with the postoperative histopathological examination in the diagnosis of acute appendicitis. *Methods*. It is a prospective observational study over a period of 18 months, on patients who underwent emergency appendectomy. Purposive sampling method and Chi square test were used for the study to find significant association between the variables. *Results*. The mean age of the participants was 24.06 ± 8.61 years (74.7% men and 25.3% women). All cases had abdominal pain, and 86.7% anorexia, 57.3% migraine, 49.3% vomiting, 38.7% fever. In the case of the normal appendix, TLC was positive in 31% of cases; in cases with inflamed appendix 65% of cases were positive for TLC, while in cases with gangrenous and/or perforated appendix all cases were positive for TLC. CRP had a sensitivity of 88.7%, 69.23% specificity, 93.22% PPV and 56.25% NPV for diagnosis. When both TLC and CRP were used, they have a high sensitivity (90.32%) compared to single use and reported to histopathological findings, and a high PPV value (93.33%). *Conclusions*. The combined sensitivity and specificity values of TLC and CRP were higher in the diagnosis of acute appendicitis, thus reducing the number of negative appendicectomies and the need for a CT scan, which is generally expensive and associated with the risk of radiation.

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Introduction

One of the most common causes of acute surgical abdomen is acute appendicitis. Acute appendicitis affects about 7% of the population at some point in their lives; the peak occurrence occurs between the ages of 10 and 30 [1]. In 70% of cases, the clinical presentation is typical and there is no difficulty in diagnosis. The other 30% have an unusual clinical appearance, which is a diagnostic challenge for surgeons, especially in the elderly, in women of reproductive age and in cases where the appendix is in an aberrant location. This uncertainty in preoperative diagnosis leads to unnecessary laparotomy and appendicectomy [2].

Acute appendicitis is diagnosed based on a history and physical examination, as well as a high WBC count and, if necessary, an imaging investigation [3,4]. About 70% of patients with acute appendicitis have an increased WBC count. However, a high WBC count can be caused by a wide variety of abdominal and pelvic diseases. For this reason, WBC count alone is not considered an appropriate marker of acute appendicitis due to its limited sensitivity and specificity [5,6].

Ultrasound (USG) and doppler sonography are useful for detecting acute appendicitis, especially in children. In some cases (approximately 5%) USG does not show any abnormality despite the presence of acute appendicitis. This false negative finding is especially common in early appendicitis (before the appendix has been significantly distended, the retrocecal appendix being the most common position), and when a large amount of fat and intestinal gas is present, which makes the view of appendix to be technically difficult [7]. A large population study, published in 2001, showed that the accuracy of diagnosing acute appendicitis has not increased in the last 15 years, despite advances in imaging technology [8]. The aim of this study is to see how accurate CRP and TLC are in association when diagnosing acute appendicitis.

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Materials and Methods

This is a prospective observational study conducted at Pesimsr, Kuppam over a period of 18 months (Jan 2020 - June 2021). Patients who presented for acute appendicitis and underwent emergency appendicectomy were considered for the study. The purposive sampling method was used as the sampling technique, and the total sample size was found to be 75.

Associated inclusion criteria:

- patients aged 18 to 64 years,
- clinically diagnosed with acute appendicitis,
- and patients who have undergone appendicectomy

Exclusion criteria:

- population with a history of recurrent pain in the right iliac fossa
- patients with appendicular mass or peritonitis
- patients managed conservatively

Diagnosis and treatment used in this study

- patients presenting to the outpatient surgery or emergency room with a clinical diagnosis of acute appendicitis
- patients who have undergone routine and special investigations (TLC, CPR, etc.)
- histopathological examination was performed for patients who underwent appendectomy

Procedure for data collection

- Data were collected from patients undergoing appendectomy at the PESIMSR Department of General Surgery.
- Histopathological reports of post appendicectomy cases were also collected.
- Data related to CPR and TLC were collected from all patients who underwent appendectomy.

Statistical analysis of data

Data entry was performed using Microsoft Excel 2013 and analysis was performed using SPSS V 16. Qualitative data was expressed in frequencies and percentages and quantitative data in mean and standard deviation. Nonparametric statistics i.e., the Chi square test was used to find the significant association between the two qualitative variables. The diagnostic evaluation included the sensitivity and specificity that were calculated. Bar diagram and pie chart were used to represent the data; p value <0.05 was considered statistically significant.

Results

According to Table 1, the mean age of the participants was 24.06 ± 8.61 years; 41.3% belonged to the 14-20 age group, 41.3% belonged to the 21-30 age group, 12% belonged to the 31-40 age group, 2.7% belonged to the 41-50 age group, and 2.7% belonged to the age 51-60 group. 74.7% were men and 25.3% were women, with predominantly men in the study.

Table 1. Age and gender distribution of study participants

Age limits	Frequency	Percentage
14 – 20	31	41.3%
21 – 30	31	41.3%
31 – 40	9	12%
41 – 50	2	2.7%
51 – 60	2	2.7%
Total	75	100%
Mean ± SD	24.06 ± 8.61	

According to Figure 1, all cases had abdominal pain, 86.7% had anorexia, 57.3% had migraines, 49.3% had vomiting, 38.7% had fever, 56% had rebound tenderness and all patients had RIF tenderness. In the present study it was observed that 49.3% had abdominal guarding, 57.3% had increases pulse rate, 48% had raised temperature, 8% had Rovsing's sign.

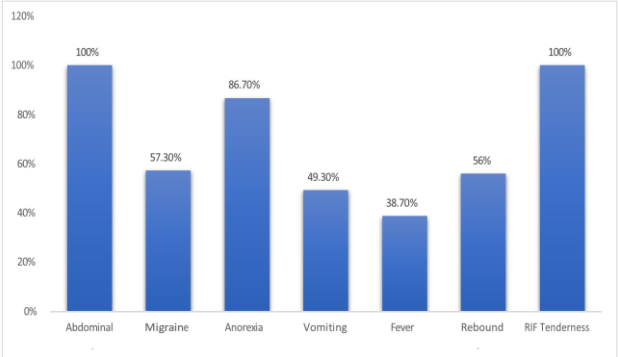

Figure 1. Distribution of signs and symptoms

Figure 2 shows that in the present study 74.7% had acute appendicitis and 25.3% had normal appendix.

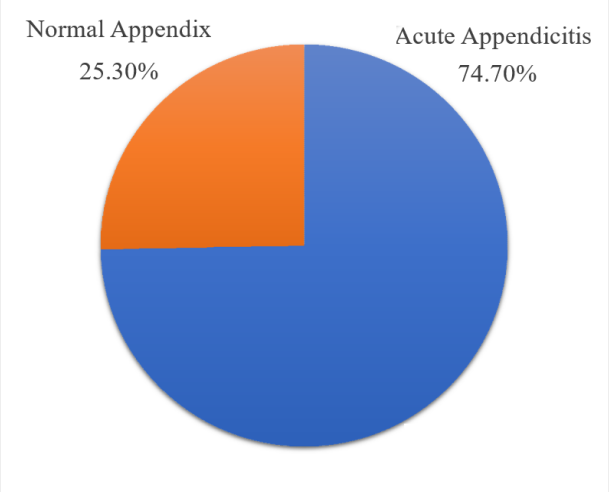

Figure 2. Ultrasonography evaluation

As shown in Table 2, 17.3% had a normal appendix, 53.3% had an inflamed appendix, 2.7% had a perforated appendix, and 26.6% had a gangrenous appendix.

Table 2. Histopathological diagnosis

Diagnosis	Frequency	Percentage
Normal appendix	13	17.3%
Inflamed appendix	40	53.3%
Perforated appendix	2	2.7%
Gangrenous appendix	20	26.6%
Total	75	100%

Table 3 shows that for normal appendix TLC was positive among 31% of the cases, in cases with inflamed appendix 65% of the cases had positive for TLC, in cases with perforated appendix and gangrenous appendix all the cases were positive for total count. The association was statistically significant.

Table 3 – Association between Total Leucocyte Count and histopathological findings

	Positive	Negative
Normal appendix	4	9
Inflamed appendix	26	14
Perforated appendix	2	0
Gangrenous appendix	20	0
Total	52	23
Chi square test = 19.17, p=0.0001*, Statistically significant		

Table 4 shows that for normal appendix CRP was positive in 31% of cases, when the appendix was inflamed 85% of cases were positive for CRP, in cases with perforated appendix in 50% of cases CRP was increased, and in the gangrenous appendix all cases were positive for CRP. CRP levels were elevated significantly in cases with appendicitis. The association was significant ($p<0.05$).

Table 4. Association between CRP and histopathological findings

	Positive	Negative
Normal appendix	4	9
Inflamed appendix	34	6
Perforated appendix	1	1
Gangrenous appendix	20	0
Total	59	16
Chi square test = 25.13, p=0.0001*, statistically significant		

Table 5 presents that in cases with acute appendicitis 88.7 % were positive for CRP, while in cases with normal histopathological findings 30.7% of the cases had a positive CRP. Thus, it was observed that there was a statistically significant difference in the histopathological findings and the values of CRP. CRP has a diagnostic accuracy consisting of 88.7% sensitivity, 69.23% specificity, 93.22% PPV, and 56.25% NPV.

Table 5. Diagnostic accuracy of CRP compared to histopathological findings

	Diagnostic accuracy
Sensitivity	88.71%
Specificity	69.23%
Positive predictive value	93.22%
Negative predictive value	56.25%
Accuracy	85.33%

Table 6 shows a significant association between TLC values and the histopathological findings. Sensitivity was 77.41%, specificity was 69.23%, PPV was 92.3%, NPV was 39.1%, and the diagnostic accuracy was 76%.

Table 6. Diagnostic accuracy of TLC compared to histopathological findings

	Diagnostic accuracy
Sensitivity	77.41%
Specificity	69.23%
Positive predictive value	92.30%
Negative predictive value	39.13%
Accuracy	76%

In Table 7 it can be seen that when both TLC and CRP were used, they have a higher sensitivity (90.32%) compared to single use and reported to histopathological findings, and a high PPV value (93.33%).

Table 7. Diagnostic Accuracy of CRP and TLC compared to histopathological findings

	Diagnostic accuracy
Sensitivity	90.32%
Specificity	69.23%
Positive predictive value	93.33%
Negative predictive value	60%
Accuracy	86.67%

Discussion

Acute appendicitis is sometimes a difficult diagnosis to establish and is probably the most common diagnostic challenge facing clinicians. Atypical manifestations, especially in the elderly, are not uncommon. The most commonly used methods for diagnosing acute appendicitis are symptoms, clinical evaluation, and biochemical testing. When acute appendicitis is diagnosed, the leukocyte count

is commonly used. Due to its low specificity, some authors consider that an increased leukocyte count is a sensitive test, but not a diagnosis for acute appendicitis. C-reactive protein (CRP) and total leukocyte count (TLC) are used to diagnose acute appendicitis. Hepatocytes produce CRP in response to infection or tissue inflammation [9-11].

In the study by Nazir et al. [12] the mean age was 32±7 years in the laparoscopic appendectomy group and 34±7 years in the open appendectomy group. Twenty-nine patients were in the 15 to 30 age group (44.62%) in the laparoscopic surgery group, and 27 patients were in the 15 to 30 age group in the open surgery group (41.54%). The laparoscopic surgery group had 36 patients aged 31 to 50 years (55.38%), and the open surgery group had 38 patients (58.46%) aged 31 to 50 years. The observations made in this research were almost in line with the present study. In the study by Kathare et al. the average age similar to that observed in current research has also been observed [13]. In the present study, it was observed that open laparotomy was closely related to cases with preoperative morbidity, and this was in accordance with the existing literature. Similar findings were made in the study by Nazir et al., Kathare et al. and Mohamed et al. [12-14]. Subedi et al. concluded that the detection of acute appendicitis is determined primarily by the surgeon's assessment based on clinical features and physical examination [15].

But the cause and evolution of acute appendicitis varies depending on several factors. Wade et al. observed in their analysis that the ultrasonographic investigation, although useful and safer, showed normal findings among 24% of patients who had acute appendicitis [16]. Therefore, it has been concluded that ultrasonography alone cannot be used to evaluate/ exclude a patient with acute appendicitis. Neutrophilia > 75% will occur in 78% of cases, according to most research. When TLC and neutrophil count are combined, only about 4% of cases with acute appendicitis get a normal result. According to Doraiswamy et al., NC is particularly useful in the diagnosis of acute appendicitis in children. The sensitivity, specificity and predictive value of positive and negative tests are improved when WBC, NC and CRP are combined [17]. According to Al-Gaithy, physicians should not rely on high TLC or a high number of neutrophils as indicators of appendicitis, as clinical data are superior in making decisions about appendicectomy [18]. When simple acute appendicitis was detected, WBC was the test of choice according to research by Grönroos et al., but it is a poor predictor of persistent inflammation [19]. Dueholm et al. found that WBC had the best sensitivity (83%) and predictive value of negative tests (88%) when combined with NC, and that combining these tests with CRP increased sensitivity to 100% [20]. Similarly, Thimsen et al. noted in their study that if symptoms persist for more than 12 hours and CRP is negative, acute appendicitis can be safety ruled out [21]. In our research, 74% of complex appendicitis had a very high CRP score, but only 20% of uncomplicated appendicitis had elevated CRP. The relevance of CRP as a predictor of disease severity needs to be further analyzed. In the research of Shrive et al, which was performed on a total of 98 individuals, acute appendicitis was verified histopathologically in 89 (91%) of them, while 9 normal appendixes (9%) were excised. CRP values were consistent (positive or negative) in 93 people, false positive in one (11%) and false negative in four patients with acute appendicitis (4%). The clinical diagnosis, on the other hand, was adequate in 89 cases (91%) and erroneous in 9 cases (9%), the difference being statistically significant (p value= 0.009) [22].

Conclusions

The diagnostic accuracy of CRP and TLC was studied individually and in combination. The sensitivity and specificity of TLC and CRP were higher if taken in combination (accurately predicting acute appendicitis in such cases), reducing the number of negative appendicectomies and the need for a CT scan, which is usually more expensive and associated with radiation risk.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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