The Uncertainty of Total Leukocyte Count in Diagnosing Acute Appendicitis

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ABSTRACT:
Background: Acute appendicitis is a frequently encountered surgical disease. Detection is difficult even with imaging and blood investigations. Total leukocyte count is a promising investigation. Its role in the confirmation of acute appendicitis is investigated and analysed in the present study. **Aim and Objective:** To determine the accuracy of leukocyte count in diagnosing acute appendicitis. **Methods:** Patients having suspicion of acute appendicitis treated by surgical intervention (appendicectomy) were included in the study. The leukocyte count measured before surgery, was compared with histopathology findings of the appendix. Parameters of diagnostic accuracy of leukocytosis were measured by standard formulae. **Results:** There were total 180 suspected cases of acute appendicitis which underwent surgery. Among the cases, 132 were having raised total leukocyte count (TLC) and 48 with normal leukocyte count. The histopathology revealed inflamed appendix in 121 (true positive) out of 132 patients of raised TLC group while 41 (false negative) out of 48 patients of normal TLC group. The sensitivity of the test was calculated to be 74.69%, while the specificity was 38.89%. The positive predictive value (PPV) was found to be 91.67%, indicating that among the cases with high TLC and inflamed appendix, 91.67% of them actually had acute appendicitis. However, the negative predictive value (NPV) was only 14.58%, indicating that among cases with normal TLC and normal appendix, only 14.58% of them actually had no acute appendicitis. **Conclusions:** Leukocyte count is a great criteria for ruling in acute appendicitis, but a poor criteria to rule out acute appendicitis because of its low negative predictive value and specificity. Clinical diagnosis still holds more importance over biochemical and radiological diagnosis.
Key Words: Leukocytosis, Negative Appendictomy, ALVORADO score.

INTRODUCTION:

Acute appendicitis is the most common abdominal surgical emergency. The diagnosis is based on clinical assessment, laboratory and radiological investigations and emergency appendicectomy is the treatment of choice. However, a missed or delayed detected case of acute appendicitis is a disaster as it later presents with life-threatening complications and may result in medicolegal issues.

Raised total leukocyte count (TLC) is a frequent finding in patients with acute appendicitis. It holds the major weightage in the ALVORADO score over other symptomatic, signs and biochemical parameters, used to diagnose appendicitis. As a convention, a normal leukocyte count usually rules out the differential diagnosis of acute

appendicitis. The term "Leukocytosis or raised leukocyte count" is usually used when the total leukocyte count is more than 11,000 per microlitre of blood, depicting infection and inflammation in the body.

Recent studies claimed that a substantial proportion of patients with normal TLC also had acute appendicitis and warranted a careful evaluation of such cases before sending them home as reported by Vaidya VP et al in 2020 in Nagpur, Singh et al in 2016 and Bilal et el in 2021 in Pakistan.[1,10,3]

However, the reported frequency of acute appendicitis among normal TLC patients, varied greatly among studies which necessitated the present study. Sometimes it was depicted in a few studies that even perforated appendix has normal TLC and differential leukocyte count.[2]

AIM AND OBJECTIVE:

To determine the presence of acute appendicitis in patients of normal TLC and raised TLC using histopathology as gold standard with the objective to determine the accuracy of leucocyte count in the diagnosis of acute appendicitis.

MATERIALS AND METHODS:

This was a cross-sectional observational study conducted in the Department of Surgery, Assam Medical College, Dibrugarh from 1st March 2021 to 28th February 2022. The study included 180 patients aged above 18 years with clinical features suggestive of acute appendicitis. Patients with previously treated appendicitis, appendicular lump/peritonitis, urinary tract infections (UTI) with ureteric/renal calculi, pregnancy, hematological diseases, malignancies, and immunocompromised patients were excluded from the study. After getting the permission from the ethical committee, written informed consent was obtained from all patients. Physical findings of pain in the right iliac fossa (RIF) presenting within three days, nausea/vomiting, anorexia, and fever were included in the study. Blood complete picture of the patients presenting with clinical findings showing suspicion of acute appendicitis was sent. Ultrasonography was done. Open appendectomies were done by consultant/senior residents or by junior residents under direct supervision. Intraoperative findings were noted and recorded. The specimen was sent for histopathology examination. Patients were called for follow-up after one week with histopathology report.

Acute appendicitis was diagnosed on basis of histopathology of excised tissue (mucosal inflammation, neutrophil infiltrates, wall necrosis).

The frequency of acute appendicitis compared across normal TLC and raised TLC patient group, various age and gender groups.

Qualitative variables like gender, pain RIF at presentation, nausea/vomiting, anorexia, fever, rebound tenderness, confirmed diagnosis of acute appendicitis on histopathology have been presented as frequency and percentage.

2 x 2 table was employed to determine sensitivity, specificity, positive predictive value and negative predictive value. Chi-square test was used to compare percentages and a p-value of less than 0.05 was considered statistically significant.

RESULTS:

Table 1: Baseline characteristics of the study population.

Age In Years	**Number**	**Percentage**
<25	126	70.00
26-45	23	12.78
>46	31	17.22
Sex		

MALE	102	56.67
FEMALE	78	43.33
Physical Finding		
Pain In RIF	180	100.00
Rebound tenderness	151	83.89
Anorexia	142	78.89
Nausea/vomiting	133	73.89
Fever	115	63.89

Based on the analysis, the majority of patients with acute appendicitis are below 25 years old, comprising 70% (n=126) of the total patients. The 26-45 age range had 12.78% (n=23) of the patients, while those over 46 years old had 17.22% (31). In terms of gender, males had a higher incidence of acute appendicitis at 56.67% (n=102) compared to females at 43.33% (n=78). (Table 1)

Physical findings revealed that pain in the right iliac fossa was present in all patients (100%), while rebound tenderness and anorexia were present in 83.89% and 78.89% of the patients, respectively. Nausea/vomiting was seen in 73.89% of the patients, while fever was present in 63.89% of the cases. These findings suggest that pain in the right iliac fossa, rebound tenderness, anorexia, nausea/vomiting, and fever are common physical findings in patients with acute appendicitis. (Table 1)

Table 2: Leukocyte count and histopathology among the patients (n=180)

	HPE OF APPENDIX		**Total**
	Inflamed appendix	**Normal appendix**	
High TLC	121	11	132
Normal TLC	41	7	48

There were 132 patients with elevated leukocyte counts (>11000) and there were 48 patients with leukocyte counts in normal range (<11000). The diagnosis of acute appendicitis was made in 41 out of 48 (85.4%) patients with normal TLC and in 121 out of 132 (91.8%) patients with raised TLC. (Table 2)

Table 3: Comparison of acute appendicitis across various subgroups of patients

Age In Years	**Total cases**	**Acute appendicitis**		**p-value**
		N	**%**	
<25	126	105	83.33	0.99
26-45	23	19	82.60	
>46	31	26	83.87	
SEX				
MALE	102	84	82.35	0.862
FEMALE	78	65	83.33	

When stratified, there was no statistically significant difference in the frequency of acute appendicitis across various age (p-value = 0.99) and gender (p-value = 0.862) groups.

Table 4: Leukocyte count and histopathological examination among the patients.

	HPE OF APPENDIX		**TOTAL**
	Inflamed appendix	**Normal appendix**	
High TLC	121[TP]	11[FP]	132
Normal TLC	41[FN]	7[TN]	48

The overall sensitivity, specificity, positive predictive value and negative predictive value of elevated leukocyte counts for inflamed appendix were 74.69%, 38.89%, 91.67%, and 14.58% respectively.

Sensitivity = 121/162 x 100 **= 74.69%**

Specificity = 7/18 x 100 = 38.89%

Positive predictive value (PPV) = 121/132 x 100 = **91.67%**

Negative predictive value (NPV) = 7/48 x 100 = **14.58%**

Based on the histopathological examination (HPE) of the appendix, there were a total of 180 cases, out of which 162 were inflamed and 18 were normal. In addition, the HPE results were compared with the total leukocyte count (TLC) of the patients. Out of 132 cases with a high TLC, 121 were identified as inflamed appendix (true positive), while 11 were identified as normal appendix (false positive). Out of 48 cases with normal TLC, 7 were identified as normal appendix (true negative), while 41 were identified as inflamed appendix (false negative).

The sensitivity of the TLC in identifying inflamed appendix was calculated as 121/162 x 100 = 74.69%, which indicates that the test correctly identified 74.69% of the cases with inflamed appendix. The specificity was calculated as 7/18 x 100 = 38.89%, which indicates that the test correctly identified 38.89% of the cases with normal appendix. The positive predictive value (PPV) was calculated as 121/132 x 100 = 91.67%, which indicates that the test correctly predicted 91.67% of the cases with inflamed appendix among all the cases identified as inflamed appendix by the test. The negative predictive value (NPV) was calculated as 7/48 x 100 = 14.58%, which indicates that the test correctly predicted 14.58% of the cases with normal appendix among all the cases identified as normal appendix by the test.

In summary, TLC was found to have moderate sensitivity and low specificity in identifying cases of inflamed appendix. The PPV of the test was high, indicating that if the test identifies a case as inflamed appendix, there is a high likelihood that the case is truly inflamed. However, the NPV of the test was low, indicating that if the test identifies a case as normal appendix, there is a low likelihood that the case is truly normal. These findings suggest that while the HPE of the appendix is a useful tool in diagnosing inflamed appendix, it should not be relied upon as the sole diagnostic method and should be used in conjunction with other clinical and diagnostic tools.

DISCUSSION

Acute appendicitis is the most common cause of the acute abdomen requiring surgery with a lifetime risk of 7%, which is maximal in childhood and declines steadily with age as the lymphoid tissue and vascularity atrophy as stated in study Dynamote et al.[4]

Although only a few patients progress to the potentially lethal complications, early surgery for all patients with suspected appendicitis has become the definitive method of preventing severe peritoneal sepsis.[5]

However, a missed case of acute appendicitis is a catastrophe as it later presents with life-threatening complications and results in medicolegal issues.[4,5]

Raised total leukocyte count is a frequent finding in patients with acute appendicitis. As a convention, a normal leukocyte count usually rules out the differential diagnosis of acute appendicitis.[6]

Recent studies claimed that a substantial proportion of patients with normal TLC had acute appendicitis and warranted a careful evaluation of such cases before sending them home.[7,8,9,10.] However, the reported frequency of acute appendicitis among TLC normal patients varied greatly among studies which necessitated the present study.

The diagnosis of acute appendicitis was made in 41 (85.4%) patients with normal TLC and suspicion of acute appendicitis on physical findings and ultrasound. When stratified, there was no statistically significant difference in the frequency of acute appendicitis across various age (p-value = 0.988) and gender (p-value = 0.913) groups.

Our observation matches with that of Alam et al[9] (2014) who reported a similar frequency of 83.9% for acute appendicitis in patients with clinical suspicion but normal TLC count at Pakistan Institute of Medical Sciences, Islamabad.

In another local study, Jamaluddin et al[11] (2013) reported this frequency to be 82.0% among patients presenting at Dow University of Health Sciences with clinical suspicion of acute appendicitis but with normal total leukocyte count. Sadettin Er et al[7] (2018) reported a similar frequency of acute appendicitis (80.9%) among TLC normal patients in Turkey.

Singh et al[10] (2016) reported a slightly higher frequency of 88.5% in India.

Elevated leukocyte count was highly sensitive (81.77%) for diagnosing acute appendicitis. This finding is in conformity with De Carvalho et al., Gulzar et al. and Kamran et al. who have reported sensitivity of elevated leukocyte count for acute appendicitis as 88.7%, 80% and 76.5% respectively.[12,13,14]

The specificity of leukocyte count for acute appendicitis was found to be disappointingly low comparable with De Carvalho et al. have reported an even lower specificity of only 20%.[12]

Because of the inherent problem of low specificity, leukocyte count may mislead the diagnosis at times. Several of our patients with acutely inflamed complicated appendix had a normal leukocyte count. Similar observations have been reported by other published studies also.[13,14]

The sensitivity and specificity of leukocytosis were found to be 74.6 percent and 38.89 percent respectively. The positive predictive value and negative predictive value of leukocytosis was 91.67 percent and 15.58 percent respectively.

A study conducted by Al-Gaithy et al[6] shows sensitivity and specificity were 76% and 65% respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 97% and 16% respectively

The present study adds to the already published local and international research evidence on the topic. In the present study, contrary to the routine impression that normal TLC rules out the differential diagnosis of acute appendicitis, a substantial proportion of patients with clinical and ultrasound suspicion of acute appendicitis but normal TLC actually had the disease.

LIMITATION OF STUDY

One major limitation of the current study is that the inflammatory response that leads to an elevation of the total leukocyte count may take time to develop, which could explain cases of acute appendicitis with a normal TLC count. This implies that some patients with acute appendicitis may be missed by relying solely on TLC counts and emphasizes the importance of clinical judgment in making a proper diagnosis.

CONCLUSION

Clinical judgment is still the most important factor in the management of patients with suspected acute appendicitis. Routine use of CT scan or diagnostic laparoscopy for all patients who are suspected to have acute appendicitis is neither cost-effective nor safe.

In the present study, contrary to the routine impression that normal TLC rules out the differential diagnosis of acute appendicitis, a substantial proportion of patients with clinical and ultrasound suspicion of acute appendicitis but normal TLC had acute appendicitis which is worrisome as a missed case may later present with complications like perforation peritonitis. The present study thus warrants cautious evaluation of clinically suspected cases with normal TLC count, to avoid a missed appendicitis and improve the outcome in future surgical practice.

In an attempt, to reduce the removal of normal appendices (negative appendicectomies), one should not lead to an increase in the number of perforations.[15]

Leukocytic count is a great criteria for ruling in acute appendicitis, but a poor criteria to rule out acute appendicitis because of its low negative predictive value and specificity. It is still a useful investigation in decision making in doubtful cases. Clinical diagnosis still holds more importance over biochemical and radiological diagnosis. But clinical correlation is mandatory.

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