

Normal Total Leukocyte Count in Patients Despite Acute Appendicitis Clinically and Preoperatively

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ABSTRACT

Background: The main objective of this study was to ascertain the proportion of individuals diagnosed with acute appendicitis who exhibited clinically and preoperatively normal levels of total leukocyte count.

Methodology: During the months of June 2021 and March 2022, researchers from the Department of Surgery at Jinnah Postgraduate Medical Center in Karachi, Pakistan, conducted a prospective observational study. All the patients presented with an impression of acute appendicitis above the age of twelve were included. Complete history, clinical examination, emergency investigations including CBC, UCEs, Ultrasound, X-Rays, Alvarado score were recorded in a predefined pro forma. Patients with low ALVARADO score and normal TLC with signs and symptoms of acute appendicitis were compared with CRP levels which directed the decision of appendectomy rather than conservative management. Per operative findings of stages of acute appendicitis such as acute inflamed, suppurative, gangrenous and perforated appendix were also noted. Appendix was sent to the laboratory and histopathological reports of the specimen were assessed.

Results: Patients diagnosed with acute appendicitis and subsequently operated on totaled 270 in the study, 156 (57.78%) were having and ALVARADO score of less than 7 mostly due to normal TLC, while 114 patients (42.22%) were having ≥ 7 ALVARADO score. Preoperatively and histopathological reports of 270 patients of appendicitis 25% patients were acutely inflamed/catarrhal stage, 15.5% gangrenous, 20.59% perforated, while higher number of patients i.e. 38.91 were suppurative appendicitis.

Conclusion: Most patients presenting with symptoms of acute appendicitis have normal TLC, meaning low TLC. This needs to be confirmed by caring out by proper examinations and getting inflammatory markers or in cases confirmatory CT if diagnosis can not be made clinically or by lab investigations.

Keywords: Appendicitis, ALVARADO score, C-reactive protein, total leukocyte count

INTRODUCTION

The most common operation on the abdomen is removal of the appendix owing to appendicitis. In patients under the age of 40, it constitutes a surgical urgency as the leading cause of acute abdomen. The male prevalence rate was consistently greater across all age groups. The lifetime risk of AA in men is 8.6%, whereas in women it is 6.7%.¹ In the diagnosis of acute appendicitis TLC has an important role as it has 2 scores in the ALVARADO SCORE; a clinical signs and symptoms along with laboratory investigation. WBC count is elevated in almost 70% of the cases with right lower abdomen pain.²

Acute appendicitis is often diagnosed using a combination of clinical factors such as a patient's medical history, a physical exam, an assessment of abdominal symptoms, and laboratory testing. However a low ALVARADO SCORE does not entirely exclude acute appendicitis specially in the developing world as patients mostly present either late or have already got antibiotics prescribed by GP or self medication which is quite common among developing world.³

Pakistan is one of the developing countries with a population of estimated 22 crores, out of which a majority of population lies under the poverty line.⁴ Karachi city has the largest population in the country estimating more than three crores. This study was conducted in one of the largest public hospitals in Karachi (Jinnah postgraduate medical center). Here the patients presenting are mostly the ones who lie way beyond the poverty line; hence the patient mostly presents late to the hospital after getting failed from home remedies and local practitioners therapies.

In this study, the aimed to find out the patients with impression of acute appendicitis clinically but low tlc which will be compared to inflammatory markers i.e. CRP levels, then the histopathological reports. Misdiagnosis or conservative treatment mostly lead to complications like perforation of lump formation.⁵⁻⁷

CRP is an inflammatory marker quietly increased or raised in inflammatory conditions like acute appendicitis.⁸ Normal CRP ranges 3.5 to 5. A CRP level of 40 or higher may indicate a suppurative or inflammatory condition. Perforated or gangrenous appendicitis may be present if the C-reactive protein level is above

hundred but below one hundred and fifty—very high risk for necrotizing appendicitis.⁹⁻¹⁰

Patients presenting late to a tertiary care public hospital with the impression of acute appendicitis are prone to developing complications of the disease. They mostly have taken some previous medications which also interfere with the misdiagnosis. Low ALVARADO score due to decreased TLC can lead to misdiagnosis. This research aims to determine the frequency of acute appendicitis characterized by normal TLC and a low ALVARADO score, notwithstanding patients' and doctors' pre- and post-operative perceptions of the severity of the condition. This study aimed to examine the total leukocyte count, ALVARADO score, and CRP levels of individuals experiencing severe abdominal pain that was thought to be caused by acute appendicitis.

MATERIAL AND METHOD

A cross-sectional observational study was carried out in the hospital's surgical wards by the surgical residents at Jinnah Postgraduate Medical Center during the months of June 2021 and March 2022. The residents were responsible for both the study's conduct and its performance. Before they started collecting data, the institutional review board at Jinnah Postgraduate Medical Center gave them permission to do so. Participants were invited to take part in the study if they were over the age of 12 and had received a diagnosis of acute appendicitis within the parameters of the study's time range. The investigation did not include patients who were above the age of 50 or who were pregnant at the time of the study. The participants in this study were selected at random using a sample method known as convenience sampling, which does not rely on probability.

Demographic parameters including age, gender, marital status, addictions, presenting complaints, and important findings from the clinical examinations were all recorded in a predefined pro forma. General physical examination was conducted by an experienced consultant. ALVARADO Score was assessed for each patient. Complete blood count, urea creatinine, electrolyte, and coagulation profile tests were performed on all patients. The

surgeon who made the incision also recorded notes about the progression of the procedure and any per-operative findings, such as the severity of the patient's appendicitis, while he or she was there. Before any data was gathered, a request for the informed verbal and written consent of all patients who were eligible to participate was made.

The analysis of the data was done with the help of the Statistical Package for the Social Sciences. Continuous data was presented as mean ± SD such as age, mean bloo. The data was analyzed using Graph-Pad prism 5. Types of appendicitis evaluated in patients were simply presented as percentile. Results of age group, control and patients, and male, female were analyzed using unpaired t-test at the level of 95% C.I. Values were considered as significant if P <0.05.

RESULTS

In the current study of appendicitis n=270 patients with impression if acute appendicitis were included. Initially the patients were categorized as low ALVARADO and high ALVARADO score and preoperatively and histologically as acutely inflamed, suppurative gangrenous and perforated. The research discovered that out of 270 individuals who were diagnosed with appendicitis, 25% of them had acute inflammation, 15% had gangrene, and 20% had perforations. Nevertheless, the most common type of appendicitis was suppurative appendicitis, which accounted for 38.91 percent of the cases as illustrated in **Figure 1**.

Types of appendicitis diagnosed in patients



Figure 1: Percentage of cases of appendicitis according to complications.

The different characteristics of appendicitis patients were calculated as mean±SD. The results were statistically analyzed by comparing with the different characteristics of healthy individuals using unpaired t-test. The results showed that respiratory, pulse rate, temperature, sodium and potassium levels of appendicitis patients were significantly (< 0.0001, < 0.01, <0.05, <0.001) higher than the control group as presented in Table 1.

Table 1: General characteristics of control and inflamed appendix patients.

Characteristics	Mean± SD		p < value
	Control	Appendicitis	
Age (years)	23.5±2.1	22.2±3.1	0.001
Respiratory Rate	13.5±1.5	20.7±3.8	0.0001
Pulse rate (beats/mint)	87.5±7.0	105.2±10.0	0.0001
Temp (°F)	97.8±9.5	100.6±10.4	0.01
Hb (%)	14.2±0.6	13.5±1.4	0.05
Plt (x10 ⁹ /L)	195.5±10.5	165.3±12.6	0.004
Na (mEq/L)	135.8±7.5	129.8±8.6	0.05
K (mEq/L)	4.2±0.4	3.8±0.6	0.001
Cr (mg/dL)	1.1±0.08	1.2±0.1	0.05

t-test was applied at 95% confidence interval P<0.05* , p<0.001**, p<0.0001***

CRP, TLC and neutrophils percentage are considered as the standard biomarkers in appendicitis. In the current study the results of CRP, TLC and neutrophils percentage in appendicitis patients were significantly <0.0001, <0.001elevated as compared to the normal healthy individuals as indicated in **Table 2**.

Table 2: Comparison of inflammatory markers between control and confirmed appendicitis group

Characteristics	Mean± SD		p < value
	Control	Appendicitis	
CRP (mg/dL)	3.4±0.5	55±4.5	0.0001
TLC (x10 ⁹ /L)	9.2±1.5	12.3±3.6	0.001
Neutrophils (%)	69.4±4.8	75.7±8.9	0.001

t-test was applied at 95% confidence interval P<0.05* , p<0.001**, p<0.0001***

In appendicitis ALVARADO score is considered the gold standard parameter for confirmation and making diagnosis of appendicitis. In current study ALVARADO score suggest that out of 270 patients n=114 individuals achieve mean ALVRADO score about 7.17±0.9 with TLC ≥ 11000 while 156 patients were identified with mean ALVARADO score of 5.6±0.9 with TLC≤ 11000 at p< 0.0001 as mentioned in table 3

Table 3: Alvarado score of age groups

S.No	Alvarado score Mean±SD		P-value
	(n=114) TLC ≥ 11000	(n=156) TLC ≤ 11000	
1.	7.17±0.9	5.6±0.9	< 0.0001

t-test was applied at 95% confidence interval P<0.05* , p<0.001**, p<0.0001***

According to the ALVARADO analysis the important signs and symptoms that were considered for this study were migratory pain, loss of appetite, vomiting, rebound tenderness, high temperature, signs of infection (leukocytosis) and shifting dullness. According to the ALVARADO score, patients with score 7.17±0.9 were majorly with migratory pain, nausea /vomiting, tenderness and leukocytosis. These parameters were also found in the majority of patents with ALVARADO score 5.6±0.9. Anorexia was the symptom reported in a low number of patients as presented in **Figure 2**.

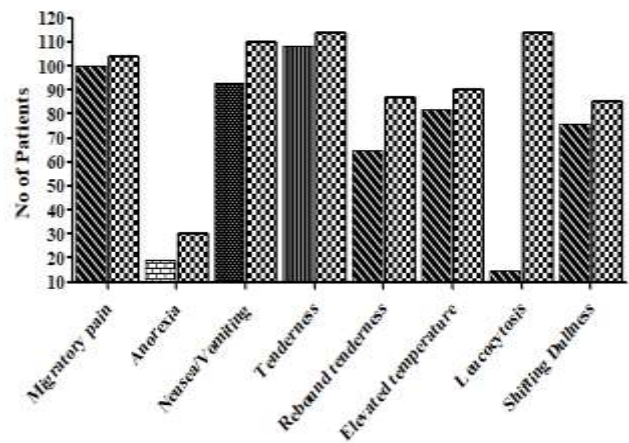


Figure 2: Number of patients according to the ALVARADO score.

In this study according to the ALVARADO score, patients were divided into low ALVARADO and higher ALVARADO scores. The total leucocytes count (TLC) in higher ALVARADO was significantly (p<0.0235) higher than the low ALVARADO score patients. Similarly, the CRP level of high ALVARADO was also significantly (p < 0.0001) higher than low ALVARADO score

patients. The neutrophils percentage was also significantly higher ($p < 0.003$) in high ALVARADO score patients **Table 4**.

Table 4: Comparison of inflammatory markers between high and low ALVARADO score.

Characteristics	Mean \pm SD75 \pm 4.5		p-value
	Low ALVARADO	High ALVARADO	
TLC ($\times 10^9/L$)	9.2 \pm 1.8	12.8 \pm 3.4	0.0235
CRP (mg/dL)	35 \pm 10	75 \pm 4.5	0.0001
Neutrophils (%)	62.7 \pm 3.9	75.7 \pm 4.5	0.003

t-test was applied at 95% confidence interval $P < 0.05^*$, $p < 0.001^{**}$, $p < 0.0001^{***}$

DISCUSSION

We carried out a study regarding the symptoms of acute appendicitis, its diagnosis based on clinically evaluated ALVARADO score, high scores confirming the diagnosis and surgical intervention is required without any delay. The base of our study is to correctly diagnose and to plan for intervention in the one who had lower scores.

Lower ALVARADO score mostly was based upon the lower count of total leukocyte count (TLC). In the present study 156 (57.78%) out of 270 patients included in the study were having a normal TLC while 114 (42.22%) were having higher TLC hence high ALVARADO score.

Our study findings are in line with recent literature.¹¹⁻¹⁴ The research looked at two hundred thirty-eight people who had symptoms of acute appendicitis based on a physical exam and ultrasound imaging but had normal TLC (4,500-11,000 WBCs/mL). According to the findings of the study, the vast majority of patients were equal or younger than 25 years old. Pain was felt in the right iliac fossa (RIF) by all study participants; however, only 83.6%, 79.0%, 73.9%, 63.1%, and 15.1% of patients had rebound tenderness, anorexia, nausea/vomiting, fever, and dysuria, respectively. Patients with normal TLC who had a suspicion of acute appendicitis were diagnosed with acute appendicitis based on the findings of physical examination and ultrasonography in 198 (83.2%) of those patients. There were no differences in the prevalence of acute appendicitis based on age or gender ($p = 0.988$ and $p = 0.913$, respectively). Individuals who had clinical and ultrasound suspicion of acute appendicitis despite having normal TLC were found to have acute appendicitis, which runs counter to the common belief that TLC eliminates acute appendicitis from the differential diagnosis. This raises concerns since a case that was ignored could potentially develop problems at a later time. Evaluating clinically worrisome cases that have normal TLC levels requires extreme attention so that appendicitis is not missed and surgical outcomes are improved.¹¹

In 2009, Shafi SM et al. conducted a study published in Saudi J Gastroenterol that assessed the diagnostic utility of total leukocyte count, C-reactive protein, and neutrophil count in cases of acute appendicitis. **The study revealed that** Histopathological analysis confirmed appendicitis in 92% of individuals. Ninety patients with acute appendicitis showed significantly raised TLC levels, while only 88 had elevated CRP levels, 91 had an elevated neutrophil percentage, and 4 had normal CRP values. As a result, the TLC had a positive predictive value of 91.8%, a sensitivity of 97.82%, and a specificity of 55.55%. CRP had a sensitivity of 95.6%, a specificity of 77.7%, and a positive predictive value of 95.6%. A percentage of neutrophil count showed 98.9% sensitivity, 38.88% specificity, and 89.21% positive predictive value.¹⁵

While comparing 357 patients hospitalized with right lower quadrant abdominal pain who were not operated on, Lau WY and colleagues discovered that substantially more patients with appendicitis than patients with normal appendices had higher TLC or NP ($P < 0.001$). (P less than 0.001). In patients who had an appendectomy, a rise in TLC had a sensitivity of 81.4% and a specificity of 77.3% for diagnosing appendicitis. Increasing either TLC or NP led to a rise in sensitivity but a decline in specificity. However, when high TLC and NP were administered

simultaneously, sensitivity dropped while specificity improved. In the case of acute appendicitis, a high TLC is a helpful diagnostic indication, especially when combined with an elevated NP. Since these blood tests can give both false positive and negative results, the TLC and NP should only be interpreted in the context of the patient's physical symptoms if they are present.¹⁶

Two hundred sixteen patients who were being evaluated for acute appendicitis at Al Fateh Teaching Hospital for Children in Benghazi, Libya, between the months of October 2001 and May 2002 had blood samples taken in order to determine their levels of C-reactive protein (CRP), total white blood cell count (WBC), and neutrophil percentage. Among those who were diagnosed with appendicitis, one hundred and fourteen people had CRP levels that were greater than eight micrograms per milliliter, one hundred and nine had total WBC counts that were greater than 11,000/microl, and one hundred and eleven had a neutrophil proportion that was greater than 75%.¹⁷

From June 20th, 2013, to June 19th, 2014, researchers in Abbottabad, Pakistan's Surgical "C" unit at Ayub Teaching Hospital, conducted a cross-sectional study. A total of 130 people with appendicitis sought care in OPDs and ERs. Non-physicians accounted for 30.77 percent of complex appendicitis presentations, followed by surgeons' conservative therapy at DHQ facilities (23.08 percent) and home therapy (23.08 percent).¹⁸

One of the most prevalent reasons for a visit to a tertiary care hospital emergency room is appendicitis. Low socioeconomic position, home cures or local practitioners delivering early pain management, and in many cases, blind prescribing of antibiotics all contribute to patients presenting late to public sector hospitals in Pakistan. The treatments may interfere with the clinical diagnosis, causing a false negative reading of any of the MANTRELS of the ALVARADO score, leading to acute appendicitis complications.

A low ALVARADO due to normal TLC should not always exclude the diagnosis of acute appendicitis and possible complications could be avoided. Additional investigations like the inflammatory markers should be considered in normal TLC in patients with signs and symptoms of acute appendicitis. Confirmatory CT abdomen can be carried out if facility available in the hospital setup.

CONCLUSION

The TLC is normal or low in most people with acute appendicitis symptoms. If a diagnosis cannot be determined clinically or via laboratory testing, it is necessary to carry out the appropriate diagnostic procedures, such as a thorough physical examination, the collection of inflammatory markers, and, in certain instances, a confirmatory CT scan.

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