Original Article

Role of White Blood Cell Count in Diagnostic Accuracy of Acute Appendicitis

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ABSTRACT

Objective: To assess the role of white blood cell count (WBC) in the diagnosis of acute appendicitis and its relation to histopathological findings.

Methodology: A descriptive cross sectional study was conducted at Aziz Fatimah Hospital Faisalabad. One hundred patients with acute appendicitis were encompassed in our work. Diagnosis was confirmed after careful clinical assessment aided with classical sign and symptoms. White Blood cell count of every patient was done from laboratory of our hospital. Specimen of appendix of every patient was sent for histopathology. In addition, pre-operative white blood cell count (WBC) was compared with postoperative histopathology reports to assess WBC count's significance in the identification of acute appendicitis.

Results: Out of 100 cases, 63 were male, and 37 were females. Age of the patients was between 12 to 55 years, mean age being 20.9 years. Commonest age group was 17 to 30 years (n=73). The sensitivity and specificity of WBC count were calculated 27% and 43.75% respectively, while positive and negative predictive value was 71.87 and 10.1%, respectively. Mean ± SD of TLC of patients with normal and inflamed appendix was 10781±291.0 and 95908 ± 329.43respectively, this difference was not statistically different (p value=0.16). Neutrophils count was 66. 86% in patients with inflamed appendix and nearly equal to this 65.18% was noticed with normal appendix on histopathology (p value=0.15). Odd Ratio were insignificant showing WBCs are nor independent predictors of acute appendicitis (p value 0.30)

Conclusion: White blood cell count is not a very good and reliable investigation for diagnosis of acute appendicitis. Patient can be having acute appendicitis with normal white blood cell count.

KEYWORDS: White Blood Cells, Acute Appendicitis,

INTRODUCTION

Acute appendicitis is one of the frequently seen surgical conditions that present as acute abdomen and needs surgery on emergency basis. It is true that it is a very frequent disease presenting in every surgical Emergency, even then its diagnosis becomes a challenge for the surgeons. It is reported that acute appendicitis is wrongly diagnosed in 20-40 % of patients. And a delay in diagnosis can result in many complications like perforated appendix, appendicular abscess, and appendicular mass, localized or generalized peritonitis leading to septicemia and adhesions in abdomen.[1] it is commonly seen between 7-15 years of age but it can affect the patients of any age. Acute appendicitis is largely diagnosed on basis of clinical evaluation. This include history of usual symptoms (migratory pain, nausea/vomiting and anorexia) and performance of clinical signs in abdomen such as tenderness in right lower quadrant (McBurney's point), rebound tenderness, elevated temperature. The laboratory tests are not persistent and their value in diagnosis of disease is a question mark, chiefly the leukocyte count and C-reactive protein (CRP), which are though sensitive but are not very specific for acute appendicitis. However, a combination of both tests in addition to signs and symptoms seems to improve their specificity significantly.[2,3] Though biomarkers and radiological

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investigations are important adjuncts to history and clinical examination, their limitations show that clinical evaluation of patient is still the mainstay of diagnosis.[4] A clinical classification is used to decide management based upon simply inflamed appendix and complicated (gangrenous or perforated) appendicitis. Still many patients present with equivocal signs and symptoms, which is one of the most challenging dilemma for surgeons.[5] An appendectomy performed on the basis of clinical diagnosis for a suspected appendicitis and it turns out to be normal appendix on the histo-pathological examination, is labeled as negative appendectomy. A negative appendectomy has a risk of postoperative complication rate of around 10%, so it is very important to correctly diagnose it in time.[6] Patients in whom diagnosis of acute appendicitis is established are largely treated depending upon clinical history and clinical findings of patients on examination; the significance of laboratory tests is still a controversy. Different studies have evaluated the role of certain inflammatory markers like total leukocyte count, granulocytes, C reactive proteins, interleukin 6, D lactate, leukocyte elastase activity and phospholipase activity that can help to confirm the diagnosis of acute appendicitis.[7] Without the help of laboratory and radiological investigations, sometimes it gets very difficult to make a definite diagnosis of acute appendicitis. White blood cell count is one of the laboratory investigation that may help in diagnosis. That's why it is being assessed in the studies.[8] Leukocytes are the main cells responsible for the host defense in the presence of various pathogens in the body. They are further divided into phagocytic cells and non-phagocytic cells. Phagocytic cells include neutrophils, eosinophils and monocytes. Non phagocytic cells include lymphocytes and basophils. These cells release certain immunoregulatory cytokines that play an important role in humeral and cellular immunity. [9] Younger age (≤15 years), normal total leukocyte count, Computed tomography grade of less than 3 and appendix diameter of less than 6 mm on computed tomography are found to be independent predictive factors for negative appendectomy.[10] We conducted the study to evaluate significance of white blood cell count if it can help in aiding the clinical diagnosis of acute appendicitis.

METHODOLOGY

It was descriptive, cross sectional study conducted at surgical department of Aziz Fatima trust hospital in a period of 15 months ranging from 18^{tht} Jan 2020- 31st Mar 2021. We included 100 consecutive patients who has clinical diagnosis of acute appendicitis as a part of our study. Prior to study ethical approval was taken from institutional ethical committee (IEC-886-20). Patients above 12 years of age of both gender, and were clinically diagnosed as acute appendicitis based upon signs and symptoms and afterward underwent appendectomy were included in the study. Patients with acute appendicitis typically had complains of persistent pain in paraumblical or epigastric region that shifted to right iliac fossa and confined at Mcburney' s point (at junction of medial 2/3 and lateral 1/3 of a line joining umbilicus and anterior superior iliac spine. Associated symptoms were nausea, anorexia and vomiting. On deep palpation, there was tenderness and rebound tenderness. Selected patients had positive Obturator and Psoas tests but abdominal signs were minimal indicating position of the appendix in pelvis. Patients who had appendicitis in pregnancy, immunocompromised and those with other acute inflammatory diseases or preexisting infections were excluded from our study. Interval appendicectomy was also excluded from the study. Informed written consent was taken from each patient for open appendectomy. Blood samples were taken before surgery and sent to laboratory of Aziz Fatima Hospital for leukocyte count. Reference range for TLC was taken as 4,500-11,000 WBCs/µL.[11] TLC > 11,000 WBCs/µL considered Leukocytosis Neutrophil count >75% considered neutrophilia. Specimen of appendix was sent to laboratory of Aziz Fatimah Hospital for histopathological examination. Microscopic findings of remarkable penetration of mucosa and muscular layer with polymorphonuclear neutrophils, ulceration of epithelium and crypt abscess formation were considered as confirmation of acute appendicitis. Pre-operative white blood cell count (WBC) was compared with postoperative histopathology report of Specimen.

Statistical Analysis: Data was analyzed by SPSS22. Quantitative data is presented as mean and standard deviation. Intergroup comparison of normally distributed quantitative parameters was done by the Student's t-test .Qualitative data is expressed as frequencies and percentages and compared using the Chi-square test.

Binomial logistic regression model was used to investigate whether WBCs are independent risk factor for Acute appendicitis or not. Results of binomial logistic regression are presented as odd ratio (OR) and 95% CI. Sensitivity and Specificity of WBC count test was estimated. p level ≤0.05 was considered statistically significant**.**

RESULTS

Of the 100 patients included in study, 63 (63%) were females while 37 (37%) were male patients. Age range was 12 to 55 years.

Table 1: Pre -Operative Physical Findings of Patients on Clinical Examination (N=100)

Physical findings	Percentage
Pain in right iliac fossa	100%
anorexia	92%
Nausea/ vomiting	89%
Fever	42%
Tenderness	97%
Rebound tenderness	74%

Physical findings of patients on examination were presented in table1. Out of total 100 patients Total leukocyte count was raised just in 32% and it was normal in 68 % of the patients. Neutrophilia was noticed in only 35% of the all patients (Table 2). Mean ± SD of TLC of patients with normal and inflamed appendix was 10781±291.0 and 95908 ± 329.43 respectively, this difference was not statistically different (p value = 0.16). Neutrophils count was 66. 86% in patients with inflamed appendix and nearly equal to this 65.18% was noticed with normal appendix on histopathology (p value = 0.15)

Table 2: Frequency of Acute Appendicitis based on Postoperative Histopathological Findings in Patients With Normal And Raised WBC Count.(N=100)

White blood cell count	Acute appendicitis on histopathology N (%)	Normal appendix on histopathology N (%)	P value
leukocytosis (n=32)	23(71.9)	9(28.1)	0.02*
Normal TLC (n = 68)	61 (89.7)	7(10.3)	
Neutrophilia (n=35)	30 (85)	5(14.3)	0.73
Normal neutrophil count N= 65	54(83.1)	11(16.9)	

Cut off point of for total leukocyte count (TLC): 11,000 WBCs/µL, Neutrophil count cut Off: 75%,
p value < 0.05 considered significant

On histopathological findings, Seventy four percent of the specimens divulged neutrophil infiltration of the mucosal and muscularis layer extending into the lumen and there was ulceration in mucosa. Ten percent the specimens had hyperplasia of lymphoid follicles that suggested early pathological changes. Per operative, appendiceal luminal obstruction was seen in 36% of patients.

Table 3: Sensitivity and Specificity of WBC for diagnosis of appendicitis.

Sensitivity	27.38%
Specificity	43.75%
Positive predictive value	71.87%
Negative predictive value	10.1%

Acute appendicitis on the basis of on histopathology was found in 61 (89.7%) in patients with normal TLC and only 23 (71.9%) in patient with raised TLC, however appendix was found normal in 9(28.1%) of patients even with raised TLC (Table 2).

Table 4:Binomial Logistic Regression Analysis: Predicting Acute Appendicitis by WBC Count (N=100)

White Blood Cells	Odd Ratio	95% confidence interval	P value
Total Leukocyte Count	0.297	0.99 -0.89	0.30
Neutrophil count	1.23	0.309 - 4.932	0.76

WBC = White Blood Cells, p value< 0.05 considered significant

Sensitivity and specificity of WBC count is presented in table 3. Table 4 shows insignificant Odd Ratios indicating that TLC and neutrophil count was not independent predictors of acute appendicitis.

DISCUSSION

Acute appendicitis is still a diagnostic challenge. Some of the patients may have atypical symptoms of the disease. Though ultrasound and CT Scan is being used on a large scale but there is no significant change in reducing the rate of negative appendectomy or misdiagnosis of acute appendicitis and subsequent complication like perforated appendix.[12] Different inflammatory markers are being assessed that may help in diagnosis of the disease. Differential leukocyte count is globally used to diagnose acute appendicitis for many past decades, however now in this recent era many of the researchers has reported conflicting results and found acute appendicitis even with normal WBC count. We conducted the study to know if TLC count

is helpful in finally establishing the diagnosis but we have concluded that we cannot rely wholly on WBC for operative decision. Clinical judgment is still on the top of list for the diagnosis and operative decision of acute appendicitis.[13] In the current study, contrary to the routine impression that normal TLC rules out the differential diagnosis of acute appendicitis, a substantial proportion of patients found to have acute appendicitis on histopathology report even with the normal WBC count .The results of our study have shown that total leukocyte count is not a diagnostic criteria for acute appendicitis since it was found normal in 89.7% of patients who were having histopathological evidence of acute appendicitis. Similarly 28.1% patients with raised TLC had normal appendix on histopathology. Our results showed the sensitivity, specificity, positive predictive value and negative predictive value of WBC count was 27%, 43.75%, 71.87% and 10.1% that is contrary to Joshi A et al.[14] Yokoyama et al study favors result of our study that WBC count and neutrophil count are not helpful for surgical indications. [15] Recent studies suggest that a significant number of patients of acute appendicitis have normal TLC and neutrophil count. So they should be observed carefully before discharging them.[16] previous study of Bilal M, et al strongly favors results of our study who found that TLC count was normal in 83.2% of patients.[11] our findings are in accordance with study by Er S et al also reported that 81% of the patients with a normal WBC Count had Acute Appendicitis while 19% had a normal appendix.[17]Alam et al also concluded normal TLC count in 83.9% of patients with diagnosis of acute appendicitis based upon clinical findings.[18] Apart from the TLC , we also noticed that the 83.1% patients with normal neutrophil count had inflamed appendix and 14.3% of the patients with raised neutrophil had the normal appendix. Contrary to our findings In Al-gaithy et al study documented that TLC with predominance of neutrophil counts were significantly higher in patients with inflamed and complicated than normal appendix.[19]In current study we found insignificant OR ratios reflecting WBCs count are not useful for predicting diagnosis of acute appendicitis. Our results are supported by Er S etal, who also reported insignificant OR.[17]A complete clinical examination of patient is more important than laboratory evaluation of WBC count. Normal WBC count does not rule out acute appendicitisIn our study, pain in right iliac fossa was present in 100% of patients, anorexia in 92% of patients, nausea and vomiting in 89%, fever in 42% of patients, tenderness in 97% and rebound tenderness in 74% of patients. Nepal, Rabindra et al established a near similar percentage of RIF pain (100.0%), rebound tenderness (82.1%), anorexia (80.2%) and nausea/vomiting (74.5%) in patients with clinical diagnosis of acute appendicitis.[20] Similarly The generalized pain was also reported in 100% of patients of Al-Gaithy et al study.[19] Estimation TLC and neutrophil count is not sufficient for the diagnosis of acute appendicitis, and normal TLC values cannot exclude acute appendicitis. The clinical evaluation of the surgeon should continue to be a priority in diagnosing acute appendicitis to prevent undesirable complications such as perforation and peritonitis represents a very serious dilemma for surgeons.

CONCLUSION

White blood cell count is not a very good and reliable investigation for diagnosis of acute appendicitis. One must rely upon clinical findings to make final decision for appendectomy. It also does not indicate severity of disease, here again clinical findings are more reliable. Also the sensitivity of this test is not sufficient to rule out the disease.

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Author's Contribution:

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Dr. Khurram Saqib	Literature search, data collection, results, second draft write up.
Dr. M. Saleem	Study concept and design, analysis, final review, overall supervision.
Dr. Aalia Farhan	Data Collection Statistical analysis proved the manuscript.
Dr. Humaira Ahmad	Concept, Data analysis & approved the manuscript.
Dr. Hamza Rana	Concept, result write up & approved manuscript.
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