

HIGH TOTAL LEUKOCYTE COUNT IN THE DIAGNOSIS OF ACUTE APPENDICITIS

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ABSTRACT

Objectives: To establish the sensitivity and specificity of the white cell count using auto analyzer in patients presenting with acute appendicitis.

Material and Methods: This cross sectional study was conducted in the Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad; from March 2010 to February 2011. All adult patients with acute appendicitis undergoing emergency appendectomy were included, while conservatively managed cases were not included. Informed consent was obtained from all the patients prior to inclusion in the study as a part of ethical practice. Patients were admitted through emergency. The data was collected regarding personal profile of the patient, detailed history, and thorough clinical examination; and relevant investigations were performed. TLC was calculated by auto analyser (SYSMEX® model SF-3000). Decision of operation was based purely on clinical grounds. Findings of histopathology (degree of inflammation of appendix as observed by the pathologist) were noted for final diagnosis (taken as gold standard). Data was analyzed on SPSS version 13.0. Chi square test was used to find any association of TLC (high, normal) with acute appendicitis (normal, mild, moderate and severe) at 5% level of significance. P value of <0.05 was considered statistically significant.

Results: Results are based on data from 147 patients that underwent appendectomy, including 82 males and 65 females. TLC was raised (above 11000/mm³) in 89 patients while 58 had TLC within normal range (below 11000/mm³). Depending on operative findings, majority of the patients (68%, n=100) had markedly inflamed appendix while 45 (30.6%) had mildly inflamed and only two (1.4%) had normal looking appendix. On histopathological examination appendix was found to be acutely inflamed in 128 (87%) patients while 19 (13%) patients had negative appendectomy. The raised TLC had a sensitivity of 64.8%, specificity 89.4%, positive predictive value 97.6%, negative predictive value 27.5%, and accuracy 68%.

Conclusions: Raised total leukocyte count is found to be a useful diagnostic tool for the diagnosis of the acute appendicitis. It can be safely opted as a marker for the grading and status of appendicitis.

Key Words: Acute, abdomen, Abdominal pain, Appendicitis, Appendectomy, Leukocyte count.

INTRODUCTION

Acute appendicitis is still one of the commonest surgical emergencies. Although majority of the cases present with typical clinical features; at times it may be difficult to confirm or exclude presence of appendicitis on account of clinical findings alone, primarily because of variable position of the appendix. Despite advances in imaging modalities the negative appendectomy rate is still high even in developed world; and the definite diagnosis of appendicitis still remains a clinical decision, augmented by appropriate tests. One of them is estimation of total leukocyte count (TLC) that is given much importance. However, it has been observed that at times TLC value does not correspond to the condition of appendix found on exploration. Acute appendicitis is

still one of the commonest surgical emergencies¹. The diagnosis is primarily clinical. A typical patient is one presenting with right lower abdominal pain, nausea and vomiting; and has got tenderness and guarding in right iliac fossa on examination.² However these sign and symptoms are not very specific for appendicitis and can mimic any other acute abdominal condition³. The picture is more confused by the variable position of the appendix⁴. Despite the indisputable progress of technology (laboratory analyses, scintigraphy, ultrasonography, computed tomography), the diagnosis of acute appendicitis often remains uncertain; with a rate of useless appendectomies amounting to almost 20% of cases⁵, or even higher⁶. Diagnosis is particularly difficult in young females¹; therefore, majority of patients with negative appendectomies is female⁷.

Acute appendicitis used to be called as the disease of developed countries with an association of high protein intake, but the incidence is also increasing in developing countries⁸. It is a disease of young adults⁹. The incidence of acute appendicitis shows seasonal

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variation; more cases are reported in summer season from March to October⁹, especially from May to July¹¹. No age is immune, but the people at the extremes of their age show a higher complication rate; partly because classic symptoms of acute appendicitis are seldom seen in the elderly¹².

Although all clinical and laboratory variables are weak discriminators individually, they achieve a high discriminatory power when combined¹³. However, they can be very non-specific at times¹⁴. The total leukocyte count (TLC) is one of these investigations that has been given much significance.

In past, the TLC used to be calculated by using microscope and 'Neubar' scale, but now most of the centres are using 'auto analyzer' that calculates the count by the technique of 'flow cytometry'. This analysis may be affected by a number of factors. Therefore, it has been observed that at times TLC value (performed by auto analyzer) does not correspond to the condition of appendix found on exploration. The current study was an attempt to establish the sensitivity and specificity of the white cell count using auto analyzer in patients presenting with acute appendicitis, and to determine its correlation with the pathological condition of appendix, keeping histopathology as the 'gold standard'.

MATERIAL AND METHODS

This cross sectional study was conducted in the Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad; from March 2010 to February 2011. Study was conducted after getting formal permission from the hospital ethical committee. All adult patients with the clinical diagnosis of acute appendicitis, later undergoing emergency appendectomy, were included in the study, while those managed conservatively were not included. Informed consent for inclusion in the study was obtained from all the patients prior to inclusion in the study as a part of ethical practice. Patients were admitted through surgical outdoor clinics and emergency. The data was collected regarding personal profile of the patient, detailed history of the present illness, and thorough clinical examination. Routine investigations included blood complete picture, urine analysis, chest X-ray, and abdominal ultrasound. TLC was calculated by auto analyser (SYSMEX® model SF-3000). Decision of operation was based purely on clinical grounds. During surgery, position and condition of appendix were noted, including state of surrounding tissues. Findings of histopathology (degree of inflammation of appendix as observed by the pathologist) were taken as the 'gold standard' and used as the base for the final diagnosis. All the information was entered into well structured proforma designed for this study.

Data was stored and analyzed on SPSS version 13.0. Mean and standard deviation were calculated for TLC and neutrophil percentage. Frequencies and

percentages were calculated for age and gender, position and condition of the appendix, and presence of any reactionary fluid. Chi square test was used to find the association of TLC (high, normal) with the pathological status of appendix (normal, mild, moderate and severe appendicitis) at 5% level of significance. P value of <0.05 was considered statistically significant.

RESULTS

The study enrolled a total of 147 cases of acute appendicitis including 82 males and 65 females. The mean age of patients was 23.2 ± 8.8 years, ranging from 14 to 65 years. Majority of the patients was young as 45% were in their 2nd decade of life and 42% in the 3rd decade, while only 2% patients were more than 50 years of age (Table 1).

History revealed that in 134 (90.7%) cases pain started in the right lower quadrant of abdomen, 12 (7.9%) had onset of pain in epigastrium, and one (1.4%) had it around the umbilicus. All the study patients had tenderness and rebound tenderness in the right iliac fossa. The TLC was raised above 11,000/mm³ in 85 cases (58%) while it was below that level in 62 cases (42%). The mean TLC was 11676/mm³ (SD \pm 4357.5). The average neutrophil count was 77% (SD \pm 13.7).

Surgical exploration revealed 139 appendices (94.6%) in the retrocecal position. In 100 (68%) cases appendix appeared markedly inflamed; while in 45 (30.6%) patients it appeared mildly inflamed. Twelve cases of the markedly inflamed group had gangrenous condition of appendix while four had perforated appendix. Fifty (34%) patients had serous fluid in peri-appendiceal region; while 29 (20%) had purulent reactionary fluid (Table 2).

The histopathological findings were taken as gold standard. It revealed acutely inflamed appendix in 128 cases (87.0%) and normal appendix in 19 (13.0%). In the first group, 14 had gangrenous appendix, and 43 had mucosal ulcers. In the second (normal) group, 13 had lymphoid hyperplasia and six had no findings at all; one of them was only fibrosed. One appendix had a worm in the lumen.

It was found out that acute suppurative appendicitis, and gangrene/perforation of the appendix, all were significantly associated with raised TLC values (>11000/mm³). This comparison is shown in Table 3.

Chi square test was used to determine various outcome values for TLC in diagnosing appendicitis on the basis of histopathology. The number of true positive, false positive, true negative, and false negative cases is shown in Table 4. On the basis of these calculations, it was found that TLC showed 64.8% sensitivity, 89.4% specificity, 97.6% positive predictive value, 27.5% negative predictive value, and 68% accuracy.

DISCUSSION

Although it is more common in males as compared to females¹, a study has shown that about

Table 1: Demographic features of the study patients (n=147)

Age groups	No. of patients and percentage
11-20 years	66(45.0%)
21-30 years	62(42.0%)
31-40 years	13(09.0%)
41-50 years	03(02.0%)
Above 50 years	03(02.0%)
Gender distribution	
Male	82(56.0%)
Female	65(44.0%)
Mean age (SD)	23.2 years (± 8.8)
Median age	21.5 years
Age range	14-65 years

Table 2: Operative findings of the study patients (n=147)

	No. of patients & percentage
Position of appendix	
Retrocecal	139(94.6%)
Pelvic	03(02.0%)
Para-cecal	03(02.0%)
Sub-cecal	02(01.4%)
Physical condition of appendix	
Markedly inflamed	100(68.0%)
Mildly inflamed	45(30.6%)
Normal looking	02(01.4%)
Reactionary fluid in peri-appendiceal region	
No reactionary fluid	68(46.0%)
Serous fluid	50(34.0%)
Purulent fluid	29(20.0%)

50% of the women of reproductive age group may have risk of getting acute appendicitis¹⁰. Yang HR reported that leukocyte count, neutrophil percentage, and C-reactive proteins are shown to give valuable information in the diagnosis of acute appendicitis¹⁵. Patients with normal results in all three tests are highly unlikely to have acute appendicitis and should be evaluated with extra

caution before surgery. Khan MN believed that both the inflammatory markers i.e. TLC and C-reactive protein can be helpful in the diagnosis, when measured together as this increases their positive predictive value¹⁶. Wu HP observed that total neutrophil count and C-reactive protein may serve as predictive parameters for early diagnosis of acute appendicitis¹⁷. Lee PWR concluded that although a white-cell count below 10,000/mm³ does not exclude the diagnosis of acute appendicitis, such a result should prompt further review and consideration of the diagnosis¹⁸. Miskowiak J and Burcharth F had the opinion that a single white cell count is neither sensitive nor specific in the diagnosis of acute appendicitis¹⁹.

Despite advances in the diagnostic modalities the diagnosis of acute appendicitis remains uncertain in 30 to 40% of the cases²⁰. Although the diagnosis is primarily made on clinical grounds because of typical clinical features, these signs and symptoms are not very specific and can mimic any other acute abdominal condition²¹. The variable position of appendix further complicates the picture. Timely decision of operation is not only very important, but also difficult, as unnecessary surgical intervention carries a definite risk of morbidity and mortality²².

In spite of the development of various diagnostic scores and diagnostic aids²³, the ideal diagnostic test has yet to be discovered⁵. The TLC is very helpful in the diagnosis of acute appendicitis. It is a convenient and easily available test in almost all laboratories, plus it is not very expensive. Mild leukocytosis, ranging from 10000 to 18000 is usually present in patients with acute uncomplicated appendicitis and is often accompanied by a moderate polymorphonuclear predominance²⁴. In the current study we evaluated the role of raised TLC in the diagnosis of acute appendicitis. The cut off value for positive TLC was 11000/mm³. The results showed that TLC was moderately sensitive (64.8%) and specific (89.4%) for the diagnosis of acute appendicitis; and with high positive predictive value of 97.6% it is a good choice for emergency investigations to cater with suspected cases of appendicitis. However, the accuracy of TLC was not high in the current study with only 55% chances of diagnosing appendicitis. It was also observed that the pathological parameters of appendicitis such as acute suppurative appendicitis, early acute appendicitis and gangrene/perforation appendicitis all were significantly associated with the raised TLC.

Table 3: Comparison of TLC values with different types of appendicitis (n=147)

Condition of appendix on histopathology	TLC value		P-value
	Above 11,000/mm ³ (n=85)	Below 11,000/mm ³ (n=62)	
Acute suppurative appendicitis	83 (97.6%)	45 (33.3%)	0.001
Gangrenous appendix	12 (14.0%)	—	
Perforated appendix	04 (4.7%)	—	
Normal appendix	02 (2.4%)	17 (28.9%)	0.001

Table 4: Chi square comparison of TLC value and condition of appendix

TLC value	Histopathology of appendix	
	Inflamed	Not inflamed
Raised above 11,000/mm ³	True positive (TP) 83	False positive (FP) 02
Below 11,000/mm ³	False negative (FN) 45	True negative (TN) 17
Outcome values for TLC		
Sensitivity	64.8%	
Specificity	89.4%	
Positive predictive value	97.6%	
Negative predictive value	27.5%	
Accuracy	68.0%	

In a similar setting Kamran H and colleagues revealed that TLC is 76.5% sensitive and 73.5% specific, with a positive predictive value of 92.5%¹⁴. These figures are comparable to our findings. Another study from UK on the role of white cell count and C-reactive proteins in the diagnosis of acute appendicitis reported a high sensitivity and moderate specificity of 83% and 62.1% respectively. The positive predictive value and negative predictive value for white cell count were 92% and 96% respectively¹⁶.

The demographic features of the patient population in Kamran et al study were similar to those of our study. They had higher male population (58%); while the average age was 21years, with majority of the patients in their second and third decade of life. However, in the UK based study by Khan MN and colleagues, majority of the patients were females.

In our study we had histopathologically proven normal appendix in 13% of the patients. Studies from different centers have shown that all the investigations including simple white cell counts, computerized tomography, ultrasonography, peritoneal aspirations, barium enema, and laparoscopy, have their own limitations when it comes to diagnosing acute appendicitis^{25,26}. They are time consuming, operator dependent, usually not easily available everywhere; and some are invasive as well.

Acute abdominal pain is a non-specific symptom of many diseases. An efficient diagnosis evaluation, including physical examination and blood tests are performed in most cases. Compared to other invasive and inconvenient sophisticated investigations, the search of such a tool that can be easily available, and be cost effective and hassle free, could be an ideal choice for surgeons worldwide especially in the settings of developing world. Exadaktylos AK and colleagues report that abdominal ultrasonography of patients with acute abdominal pain is very helpful in confirming or excluding the clinically suspected cases of appendicitis, and thus is an important diagnostic tool, albeit in minority of the patients²⁷.

The implications of negative appendicectomy can be two fold. First, although appendicectomy is considered a safe operation, it still has got associated complications namely wound infection, intra abdominal abscess formation, development of adhesions, bowel obstruction, and those related to induction of general anesthesia. Secondly, the patients with persistent symptoms after operation are unsatisfied with the health care they received, and pose to be a burden on the hospital resources.

To improve the diagnostic accuracy surgeons have relied on a good history and sound clinical examination along with laboratory investigations. For achieving improved sensitivity and specificity rates different attempts have been made. Many investigators have tried sequential leukocyte counts and 'neutrophil: leukocytic ratio'. Attention has been focused on other inflammatory markers which can be raised in appendicitis, like C-reactive protein (an acute phase protein marker). There has been scientific evidence that CRP level increases in appendicitis and this increase is related to the severity of appendiceal inflammation²². However, CRP levels can elevate from other complications as well like pneumonia, pelvic inflammatory disease and urinary tract infections.

CONCLUSION

TLC is moderately sensitive and specific in diagnosing acute appendicitis with high positive predictive value. This test is easily available in our local settings even at primary health care level and is very cost effective.

RECOMMENDATIONS

However, before generalization of these observations we recommend that further evidence may be generated on the topic with strong research methodology and larger population sample.

REFERENCES

1. Qureshi WI, Khalid MD. Surgical audit of acute appendicitis: Proceeding of Shaikh Zayed Postgrad Med Inst Jun 2000; 14(1): 7-12.
2. Bilal M Khan, Asim I, Khalid S. Frequency of acute appendicitis in patients presenting with acute abdomen in Emergency department: One year experience. *J Rawal Med Coll* 1999; 3(1-2): 35-36.
3. Cook K. Evaluating acute abdominal pain in adults. *JAAPA* 2005; 18: 22-29.
4. Delic J, Savkovic A, Isakovic E. Variations in the position and point of origin of vermiform appendix. *Med Arch* 2002; 56: 5-8.
5. D'Abbicco D, Amoruso M, Notarnicola A, Casagrande B, Epifania B, Margari A. [Acute appendicitis: is this common pathology still of interest?]. *Chir Ital.* 2007; 59(2): 155-70.
6. Hallfeldt K, Puhlmann M, Waldner H, Schweiberer L. [Diagnostic problems in acute appendicitis and indications for laparoscopic appendectomy]. *Langenbecks Arch Chir Suppl Kongressbd.* 1996; 113: 553-55.
7. Nazir A, Khalid JA, Aamir ZK, Tahir AS. Acute appendicitis: Incidence of negative appendectomies. *Ann King Edward Med Uni* 2002; 8(1): 32-34.
8. Khan IUR, Siddiqui AI. A comparative investigation into Appendicitis. *Ann King Edward Med Coll* 2004; 10: 263-64.
9. Nadeem MA, Asim K, Gondal KM, Andrabi I, Tariq M, Majeed Ch. Appendectomy: A contemporary appraisal. *Ann King Edward Med Uni* 1999; 5(2): 184-87.
10. Chloptsios C, Stamatiou K, Kavouras N, Moustakis E, Ilias G, Lebrun F. Appendicitis in pregnancy: a case report and a review of the current literature. *Clin Exp Obstet Gynecol* 2007; 34: 115-16.
11. Wei PL, Chen CS, Keller JJ, Lin HC. Monthly variation in acute appendicitis incidence: a 10-year nationwide population-based study. *J Surg Res.* 2012; 178(2): 670-76.
12. Pokharel N, Sapkota P, Kc B, Rimal S, Thapa S, Shakya R. Acute appendicitis in elderly patients: a challenge for surgeons. *Nepal Med Coll J.* 2011; 13(4): 285-88.
13. Sezer TO, Gulece B, Zalluhoglu N, Gorgun M, Dogan S. Diagnostic value of ultrasonography in appendicitis. *Adv Clin Exp Med.* 2012; 21(5): 633-36.
14. Latif T, Riaz M. The white blood cell count is not a criterion for the diagnosis of Acute Appendicitis. *Proceeding Sheikh Zayed Postgrad Med Inst* 2002; 16: 37-39.
15. Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Role of leukocyte count, neutrophil percentage and C-reactive protein in the diagnosis of acute appendicitis in the elderly. *Am Surg.* 2005; 71: 344-47.
16. Khan MN, Devi E, Irshad K. The role of white cell count and C-reactive protein in the diagnosis of acute appendicitis. *J Ayub Med Coll.* 2004; 16: 17-19.
17. Wu HP, Chang CF, Lin CY. Predictive inflammatory parameters in the diagnosis of acute appendicitis in children. *Acta Paediatr Taiwan.* 2003; 44: 227-31.
18. Lee WPR. The leukocyte count in acute appendicitis. *Br J Surg* 2005; 60(8): 618-19.
19. Miskowiak J, Burcharth F. The white cell count in acute appendicitis. A prospective blind study. *Dan Med Bull* 2008; 29(4): 210-11.
20. Anderson R, Hgander A, Ghazi S, Ravan H, Offenbartl S, Nystron P. Diagnostic value of disease history, clinical presentation and inflammatory parameters of appendicitis. *World J Surg* 1999; 23(2): 133-40.
21. Khan I, Rehman A. Application of Alvarado scoring system in diagnosis of acute appendicitis. *J Ayub Med Coll Abbottabad* 2005; 21(2): 125-32.
22. Shoshatari MHS, Askarpour S, Alamshah M, Elahi A. Diagnostic value of quantitative CRP measurement in patients with acute appendicitis. *Pak J Med Sci* 2006; 22(3): 300-3.
23. Erikson S, Granstorm L, Caristrom A. The diagnostic value of repetitive pre-operative analysis of C-reactive protein and TLC in patients with suspected acute appendicitis. *Scan J Gastroenterol* 1994; 29: 1145-49.
24. Kamran H, Naveed D, Nazir A, Hameed M, Ahmad M, Khan U. Role of total leukocyte count in diagnosis of acute appendicitis. *J Ayub Med Coll Abbottabad* 2008; 20(3): 70-71.
25. Exadaktyls AK, Sadowski-Cron C, Mader P, Wissemann M, Dinkel HP, Negri M. Decision making in patients with acute abdominal pain at a university and a rural hospital: does the value of abdominal sonography differ? *World J Emerg Surg* 2008; 3: 29-31.
26. Coleman C, Thompson J, Bennioin R, Schmit P. White blood cell count is a poor predictor of severity of disease in diagnosis of appendicitis. *Am Surg* 1998; 64(10): 983-85.
27. Malik K, Khan A, Waheed A. Evaluation of Alvarado score in the diagnosis of acute appendicitis. *J Coll Phys Surg Pak* 2000; 10: 392-94.