***Original Research Article***

**THE SENSITIVITY AND SPECIFICITY OF** **WHITE BLOOD CELL COUNT AS A BIOMARKER FOR THE DIAGNOSIS OF ACUTE APPENDICITIS.**

**Abstract**

**Introduction**

The diagnosis of acute appendicitis is largely clinical. However, diagnostic difficulties may arise with many cases resulting in significant morbidity and mortality. The diagnostic and discriminatory values of white blood cell (WBC) count in acute appendicitis have been studied extensively, but the results remain controversial. This study aimed to assess the sensitivity and specificity of WBC count as a biomarker for the diagnosis of acute appendicitis

**Materials and methods**

This was a one-year prospective hospital-based study carried out on sixty-six (66) consecutive patients presenting to the accident and emergency ward, who had appendicectomy following a clinical diagnosis of acute appendicitis. Before surgery, samples for WBC count were collected from all recruited patients. Intraoperative macroscopic assessment and histopathological examination were done for all appendixes.A proforma was used to collect data. All the statistical analyses were performed using statistical package for social sciences (IBM SPSS) version 21. Calculations of mean, standard deviations, and associations between the variables were tested for statistical significance using appropriate statistical tools. p-values less than 0.05 were considered significant.

**Results:** The median age was 25 years and male: female ratio was 1:1.8. Thirteen of the appendixes removed had normal histopathologic examination. The diagnostic accuracy, sensitivity, specificity and positive predictive value for preoperative WBC count were 73%, 72%, 77% and 93% respectively.

**Conclusion**: The diagnosis of appendicitis should be made primarily based on clinical findings. All patients with suspected acute appendicitis should have WBC count done. If the WBC count is normal, acute appendicitis is very unlikely.

**Key words**: appendix, acute appendicitis, appendicectomy, negative appendicectomy, white blood cell count, WBC

**Introduction**

Acute appendicitis remains one of the most common diseases treated by the general surgeon, with appendicectomy being the most commonly performed emergency surgery.[[1]](#endnote-1) The clinical diagnosis of acute appendicitis relies upon a detailed history, and thorough physical examination.[[2]](#endnote-2) The diagnosis is largely clinical and once established, operative management is advised.[[3]](#endnote-3) Despite appendicitis being a common disease, its presentation is not always typical and misdiagnosis is not uncommon.2,[[4]](#endnote-4) Misdiagnoses have a major impact on healthcare systems, as well as important legal consequences.[[5]](#endnote-5) Moreover, diagnostic difficulties may lead to negative appendicectomies or cases of missed appendicitis which might result in complications such as appendiceal perforation or abscess formation. [[6]](#endnote-6) The rate of negative appendicectomy has been reported to be 15-30%,8 with the reported postoperative morbidity associated with these negative explorations being 5-15%.8 To this end, diagnostic aids such as scoring systems,9,10 ultrasonography, computed tomography(CT)11 or even magnetic resonance imaging(MRI)12 have been devised. These seek to help confirm the diagnosis and guide the surgeon’s decision on operative management.13 However, these diagnostic adjuncts may either be too expensive, not readily available, involve exposure to high dose radiations, or may not always have accurate and reproducible results.13-19

The diagnostic and discriminatory values of WBC count in acute appendicitis have been extensively studied, but results remain controversial. Therefore, the aim of this study was to analyze the role of WBC count in improving the accuracy of diagnosis of acute appendicitis.

**Materials and methods**

 This study was a cross-sectional, prospective hospital-based study carried out in a tertiary health institution over a period of 12 calendar months. All patients with acute right iliac fossa pain, aged eighteen years and above, with clinical examination features suggestive of acute appendicitis were recruited into this study. Patients who had inflammatory conditions that could lead to WBC elevation, and those who declined to participate in the research were excluded from the study.

 Consecutive patients who fulfilled the inclusion criteria were enrolled into the study as they presented to the accident and emergency room. The objectives of the study were explained to each patient at the time of enrolment. A detailed clinical history was taken from all patients who met the inclusion criteria, and full physical examination performed on them. Once a diagnosis of acute appendicitis was made, an informed consent form was given to the patient and the details of the research fully explained to them. Once written consent was given, the patients were recruited into the study, taking into consideration the conditions for inclusion and exclusion.

About 3mls of blood was then collected into an EDTA bottle for the WBC count. Laboratory reports of WBC were categorized into normal and high using cut-off values used by the laboratory. The reference cut off value for WBC was 8000cells/mm3. Predictive values for both tests were calculated using the appropriate formulas.

All the 66 patients recruited into the study had appendicectomy. All the procedures were performed as emergencies under general anaesthesia with muscle relaxation. Appendicectomy and a histopathology examination were done for all patients. The intra-operative findings were compared with histopathology results and then correlated with WBC values.Patients were followed up until eventual discharge from clinic.

Data collection was done using a proforma designed for this study. All relevant information including biodata, clinical, laboratory, intraoperative, and histological findings were entered into the proforma sheet at the time of presentation, and when subsequent data became available. Data were entered in a spread sheet and analyzed using IBM® SPSS (Statistical Package for Social Sciences) version 21. The sensitivity, specificity, and predictive values for WBC count were calculated using the appropriate formulas.

**Results**

A total of 66 patients who met the inclusion criteria were recruited into the study. The age range of the participants was 18 – 90 years, with median age of 25 years and and mean age of 30 ± 8.4 years. The largest proportion of patients was in the age group 18 – 25 years, representing 50% (n= 33) of the participants. There were 24 males and 42 females in this study, giving a male-female ratio of 1:1.8. Most of the participants were students (51.5%). Those with secondary (24.2%) and tertiary (60.6%) levels of education constituted the majority in terms of levels of education. The clinical presentations of the study participants are as shown in table 1.

**Table 1: Clinical Presentations of Study Participants.**

|  |  |  |
| --- | --- | --- |
| **Variables** | **Frequency (n =66)** | **Percent (100%)** |
| **Fever**Yes No | 3333 | 50.050.0 |
| **Anorexia**Yes No | 5412 | 81.818.2 |
| **Nausea and Vomiting**Yes No | 4917 | 74.225.8 |
| **Right Iliac Fossa Pain**Yes | 66 | 100.0 |

On examination, fever (temperature of ≥ 37.50C) was present in 50.0% of patients. All the patients had right iliac fossa tenderness with 93.9% of the patients also having rebound tenderness. Pointing was present in 98.5% of the study participants, positive Rovsing sign, Psoas sign and Obturator sign were present in 43.9%, in 45.5%, in 19.7% of the patients respectively. Rectal wall tenderness on digital rectal examination was found in 18.2% of the patients.

Table 2 shows the preoperative WBC status of the study participants.

**Table 2: Preoperative WBC results of the study participants**

|  |  |  |
| --- | --- | --- |
| **Variables** | **Frequency (n=66)** | **Percent (100%)** |
| **PREOPERATIVE LABORATORY FINDINGS** |  |  |
| **White Cell Count (Cells/mm3)**Normal High | 2541 | 37.962.1 |

WBC, Mean ± SD = 9746 ± 4531

1. [↑](#endnote-ref-1)
2. [↑](#endnote-ref-2)
3. [↑](#endnote-ref-3)
4. [↑](#endnote-ref-4)
5. [↑](#endnote-ref-5)
6. All 66 patients had appendicectomies based on clinical diagnosis of acute appendicitis. Of these 66 patients, retrocaecal appendix was seen in 72.7%, pelvic 22.7%, pre-ileal 3.0% and post-ileal 1.5%.Of these 66 patients, one (1.5%) had intraoperative macroscopic staging of normal appendix, 49 (74.2%) had inflamed appendix, 5 (7.6%) had gangrenous appendix and 11 (16.7%) had ruptured/perforated appendix.

Of the 11 (16.7%) patients with ruptured/perforated appendix, five (7.6%) had rupture at the tip, three (4.5%) at the body, and three (4.5%) at the base. In 13 of these 66 patients who had appendicectomies, normal appendix was found on histology, representing a negative appendicectomy rate of 19.7%. There was no significant difference between the presence of acute appendicitis and gender, (p=0.072) although 25.6% (n= 17) of females had negative appendicitis on histology compared to 9.1% (n=6) of males.

The preoperative WBCs were analyzed to see their relationship to histology (Table 3). Out of 53 confirmed cases on histology, 38 positive cases of WBC were true positives yielding a sensitivity of 72.8%. Out of 13 confirmed negative cases on histopathology, 10 negative cases of WBC were true negatives, giving a specificity of 77%. Out of 41 positive cases of WBC, 38 were true positives, thus giving a positive predictive value of 93%. There were 25 negative cases of WBC with 10 being true negatives. This gave a negative predictive value of 40%. Thus, overall accuracy of WBC in the diagnosis of acute appendicitis was 73%.

**Table 3:** **Comparing White Blood Cell Count Values and Histology (True Disease Status) of Study Participants**

|  |  |  |
| --- | --- | --- |
| **Test Results** | **Histology (Gold Standard)** |  |
| **Appendicitis**  | **No Appendicitis** | **Total** |
| White blood cell (high) | 38 (True Positive) | 3 (False Positive) | 41 |
| White blood cell (normal) | 15 (False Negative) | 10 (True Negative) | 25 |
| Total | 53 | 13 | 66 |

Table 4 shows a summary of the indices of diagnostic values for White Blood Cell count. The sensitivity, specificity, and accuracy of WBC in predicting acute appendicitis were: 72%, 77% and 73% respectively.

**Table 4: Summary of Diagnostic Accuracy, Sensitivity, Specificity, Positive Predictive Values of the White Blood Cell counts**

|  |  |
| --- | --- |
|  | **Indices of Diagnostic Values** |
| **Diagnostic Method**  | **Accuracy (%)** | **Sensitivity (%)** | **Specificity (%)** | **Positive Predictive Value (%)** |
| White blood cell count (WBC) | 73 | 72 | 77 | 93 |

Attempts were also made to find out how this inflammatory marker predicted severity of acute appendicitis. Table 5 shows a comparison of the mean values of WBC count with all stages of acute appendicitis. It was observed that there was a progressive rise in the mean values of this biomarker from normal appendix to uncomplicated appendicitis, and to complicated appendicitis. There was statistically significant difference in the WBC count between those with normal appendix and those with uncomplicated appendicitis (p value = 0.049). There was also statistically significant difference in the WBC count between those with uncomplicated appendicitis and those with complicated appendicitis (p value = 0.0001).

**Table 5: Mean white blood cell count with all stages of acute appendicitis**.

|  |  |  |
| --- | --- | --- |
| **Variables** | **Patients** | **White blood cell count (cells/mm3)** |
| Normal Appendix | 13 | 6623.08±2217.01 |
| Acute appendicitis | 37 | 8423.28±2925.40 |
| Complicated appendicitis | 16 | 15343.75±4279.40 |
| Normal Appendix vs Acute appendicitis | p= 0.049 |
| Acute appendix (uncomplicated) vs Complicated appendicitis | p= 0.0001 |

**Discussion**

The diagnosis of acute appendicitis is largely clinical. This entails a detailed history and thorough physical examination.20 The most important step in the management of patients with suspected acute appendicitis is reaching the decision about operative intervention and its timing so that complications of appendicitis are kept to a minimum.14 The burden of negative appendicectomies cannot be overemphasised. It is associated with appreciable degree of morbidity and mortality, including a significant increase in length of hospital stay, complications due to postoperative infection and death.21

The use of various diagnostic tools has been suggested as a means of improving the accuracy of diagnosis of acute appendicitis, hence reducing the rate of negative appendicectomy. Thus, this study examined the role of WBC count in improving the accuracy of diagnosing acute appendicitis. The overall accuracy of WBC count in diagnosing acute appendicitis, in this study, was found to be 73%. Also, the sensitivity, specificity, and positive predictive values were high These values are consistent with those of Nasir *et al*, who in their work found diagnostic accuracy, sensitivity, specificity and positive predictive values for WBC count to be 74%, 74.4%, 72.7% and 90.6% respectively.22 But in the work done by Agrawal *et al* 23in Nepal, the positive predictive value was 81%129, which is much lower than that obtained in the present study. The reason for this difference may be due to the high cut-off for WBC count of > 11,000 cells/mm3 used in their study as against > 8,000 cells/mm3 used in the present study.

 Reliance on WBC count as an adjunct to clinical findings in the diagnosis of acute appendicitis will prove helpful in a low resource setting like ours, where the cost of CT scan might not be affordable by most of the patients. Moreover, performance of this test will not cause any delay in the management of these patients as test results can be available within 2 hours of presentation.

Distinguishing between uncomplicated and complicated appendicitis is very important in determining whether to operate. Some authors even suggest that medical treatment could be suitable in uncomplicated appendicitis, although this is not a standard of care.5 In the present study, it was observed that WBC count was able to distinguish normal appendix from acute appendicitis. This was in keeping with previous studies.14,16Also, regarding predicting severity, i.e. distinguishing between uncomplicated and complicated appendicitis, WBC count performed very well.

A thorough clinical history and detailed examination is more important than laboratory assessment of white blood cell count in the diagnosis of acute appendicitis as a normal white blood cell count does not rule out acute appendicitis. In this study, right iliac fossa pain was present in all patients, nausea and vomiting in 74.2% of patients, and fever in 50% of patients. All the study participants had tenderness with 93.9% of the patients having rebound tenderness. Rabindra and Lohani24 in a study done in Nepal reported a comparable percentage of right iliac fossa pain (100.0%), anorexia (80.2%), nausea and vomiting (74.5%) and rebound tenderness (82.1%), in subjects with acute appendicitis. Similarly, Humes and Simpson25 in their study noted abdominal pain in 99% of patients, nausea in 81.7%, anorexia in 72.4%, and emesis in 67.7%.

**CONCLUSION**

 All patients presenting with right sided lower abdominal pain, in whom acute appendicitis is suspected, should have WBC count done preoperatively. If the WBC count is normal, acute appendicitis is very unlikely. These patients should be investigated further for other causes of right sided lower abdominal pain, especially in females who may require radiological investigations like ultrasound scan.

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