ABSTRACT

Objective: Early diagnosis and prompt surgical intervention can reduce the rate of complications in acute appendicitis. However, accurate diagnosis remains a common surgical problem. We aimed to determine the value of preoperative serum bilirubin level and white blood cells count in simple and complicated acute appendicitis.

Methods: This was a prospective observational study carried out from January 2017 to December 2018 at Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Southwestern Nigeria. Preoperative samples for total serum bilirubin (TSB), direct bilirubin (DB) and WBC were taken for all patients diagnosed of appendicitis. Data were analyzed using SPSS version 21. A p-value <0.05 was considered statistically significant.

Results: Eighty-one patients were seen during the study period. Their ages ranged between 8 and 77 years (mean: 28.6±13.6). There were 48 (59.3%) males and 33 (40.7%) females (M:F=1.5:1). Sixty-two (76.5%) patients had simple appendicitis while 19 (23.5%) had perforated appendicitis. The mean TSB were 0.8±0.5 and 1.4±0.4 mmol/L (P=0.01), mean DB were 0.37±0.23 and 0.64 ±0.38 mmol/L (P=0.01) while the mean WBC were 9.7±4.3 and 11.4±3.0 x10⁹/L (P=0.12), for simple and complicated appendicitis respectively. TSB had a sensitivity of 84%, specificity 81%, positive predictive value (PPV) 57% and negative predictive value (NPV) of 94%. Total WBC had a sensitivity of 68%, specificity 60%, PPV 34% and NPV of 86%.

Conclusion: High TSB is a useful adjunct to improving the diagnostic yield in perforated appendicitis. Hyperbilirubinemia and clinical features consistent with complicated appendicitis should warrant early surgery.

Key words: Acute appendicitis, complicated appendicitis, serum bilirubin, white blood cells, predictive value.

INTRODUCTION

Acute appendicitis is the most common cause of acute abdomen and also the most frequent indication for abdominal surgical emergencies worldwide (1). It accounts for about 40% of all surgical emergencies in the western world. The incidence is increasing in Nigeria like other developing countries, where acute appendicitis was initially considered to be rare, and this probably has been due to increasing adoption of western diet (2,3).

The importance of early diagnosis and prompt surgical intervention cannot be over emphasised in the successful treatment of acute appendicitis. Delay in diagnosis and treatment usually results in increased rate of complications, longer hospital stays and high mortality (4). The diagnosis of acute appendicitis is mainly clinical. However, in atypical presentations accurate diagnosis could be a major challenge. Several haematological and biochemical parameters, including white blood cell count (WBC), C-reactive protein, interleukin-6, and procalcitonin have been employed to further improve the clinical diagnosis (5). Imaging studies like ultrasonography, computerised tomography, and magnetic resonance imaging as well as scintigraphy and laparoscopy have all been used for more accurate diagnosis where these facilities are available (6-9). Apart from the ultrasonography, all these other investigations are not available in our hospital, and most patients cannot afford the cost where the facilities could be accessed. In spite of all these diagnostic aids for acute appendicitis, no single test has been found to reduce the rate of negative appendicectomy to zero (10).

The occurrence of jaundice in sepsis is a common phenomenon and is well recognised. This has been found to be associated with a variety of causative bacteria of which Gram-negative bacteria are the most commonly implicated organisms (11). Studies have shown that jaundice can be associated with acute appendicitis and recently hyperbilirubinemia has been found to have a correlation with appendiceal perforation suggesting that it could be a useful predictor of complicated appendicitis (12-14). It was on this background that this study was carried out to determine the diagnostic value of preoperative serum bilirubin levels and WBC in selected patients with simple and complicated appendicitis, and also to determine their predictive values in complicated cases.

MATERIALS AND METHODS

Study design

The study was carried out in Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Southwestern Nigeria. This is a tertiary health institution that serves as a referral center for the primary and secondary health facilities in Ekiti State and neighbouring states. This was a prospective observational study carried out over two years from January 2017 to December 2018. Approval for the study was obtained from the Ethics and Research Committee of the Ekiti State University Teaching Hospital.

Study population and sampling technique

All patients with features of acute appendicitis, including those complicated by abscess, gangrene, or perforation, that required emergency operation were included in the study. Patients with appendiceal mass and those with atypical presentations that did not require operation were excluded. Other patients excluded were those with haemoglobinopathies, haemolytic anaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency, recent...
history of jaundice, hepatitis, or other liver diseases. Patients who were not willing to participate and those whose blood samples were not completed were also excluded.

Data collection
The following data were collected using a proforma designed for the study: patient’s biodata, symptoms and signs of appendicitis, investigation results which included ultrasound scan, full blood count, and preoperative serum bilirubin estimation (total and direct). The blood samples were collected while securing intravenous access and before administration of antibiotics. Samples for serum bilirubin (total and direct) were collected inside lithium heparin specimen bottle which was covered immediately with a black polythene bag to prevent exposure to visible light. The samples were analysed within one hour of collection.

Both total and direct bilirubin were analysed using commercial kits (Randox, United Kingdom). White blood cell count (WBC) was analysed on a 3-part haematology analyser (Swelab, Sweden). Hyperbilirubinaemia was defined as a total serum bilirubin (TSB) level greater than 1.0 mmol/L and normal reference range for total WBC was 2.5–10.0 x10⁹/L.

Data on the intraoperative findings were documented and histopathology of the resected appendix specimen was considered as the final diagnosis. Thereafter, patients were categorised into those with simple appendicitis in one group and those with complications like abscesses, gangrene, and perforation in another group.

Statistical analysis
Data was analysed using the statistical package for social sciences (SPSS), version 21. Independent sample t-tests were used to compare means across the two groups of patients (simple acute appendicitis and complicated appendicitis). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios for TSB and WBC were calculated to determine the validity of the tests as a diagnostic tool in preoperative identification of complicated appendicitis. A p-value <0.05 was considered statistically significant.

RESULTS
A total number of 81 patients were seen during the study period. Their ages ranged between 8 and 77 years and the median age was 26 years (mean:28.6±13.6). There were 48 (59.3%) males and 33 (40.7%) females with a male to female ratio of approximately 1.5:1. The age distribution of patients are shown in Table 1. About two-thirds of patients were seen in the second and third decades.

All patients presented with abdominal pain with the duration of pain ranging from 2 hours to 9 days (mean: 59.8±48.0 hours). Thirty (37.0%) patients presented within 24 hours, 48 (59.3%) in 48 hours, while the rest came after 72 hours. Anorexia was present in 75 (92.6%), nausea and vomiting in 66 (81.5%), fever in 55 (67.9%), and dysuria in 6 (7.4%). Intra-operatively, the locations of the appendix were retrocaecal in 67 (82.7%), pelvic 9 (11.1%), paraocaecal 3 (3.7%), subhepatic 1 (1.2%), and subcaecal 1 (1.2%).

Histopathology revealed that 62 (76.5%) patients had simple appendicitis while 19 (23.5%) had complicated appendicitis. One patient, who had a normal uninflamed appendix, was not included in the analysis.

The mean values for WBC, TSB, and direct bilirubin (DB) were shown in Table 2. The mean WBC, TSB and direct bilirubin in complicated appendicitis were greater than that of simple appendicitis, but only those of TSB and DB were statistically significant (p-value= 0.01). Table 3 shows test results and their validity.

<table>
<thead>
<tr>
<th>Tests</th>
<th>Total bilirubin vs. histology</th>
<th>WBC vs. histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>True negative</td>
<td>50</td>
<td>37</td>
</tr>
<tr>
<td>False positive</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>False negative</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.84</td>
<td>0.68</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.81</td>
<td>0.60</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.57</td>
<td>0.34</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.94</td>
<td>0.86</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>4.42</td>
<td>1.72</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.20</td>
<td>0.52</td>
</tr>
<tr>
<td>Inference</td>
<td>Sometimes useful test</td>
<td>Rarely useful test</td>
</tr>
</tbody>
</table>

DISCUSSION
Most patients in our study were seen in their second and third decades of life with a mean age of 28 years. Nineteen (23.5%) patients had perforations. Complications are still common as a result of delayed presentation and/or delayed diagnosis. In this study, 33 (40.7%) patients presented after 72hrs with the longest duration being 9 days. Studies have shown that perforation usually occurs after 48 hours of onset of symptoms (15).

Accurate diagnosis in patients with acute appendicitis is still a common problem for the clinician (16). The diagnostic uncertainty either leads to negative appendectomies in some cases or at the other extreme an increase in complications like
abscess formation, gangrene, perforation, and generalized peritonitis, with attendant high morbidity and mortality. Despite the fact that the diagnosis of appendicitis is mainly clinical, laboratory investigations, imaging techniques, and other diagnostic armamentaria can aid accurate diagnosis and help strike a balance between the two extremes of removing an uninflamed appendix and increased complications.

In our study the mean TSB was statistically significantly higher in complicated appendicitis than in simple appendicitis. This finding is similar to those reported in previous studies (13,14,17). Therefore, a normal plasma bilirubin level combined with clinical features of acute appendicitis largely supports the presence of an uncomplicated appendicitis but does not rule out perforation in few cases.

Different mechanisms have been adduced to hyperbilirubinaemia in systemic infections. Sepsis in the portal system can disrupt the excretion of bilirubin into biliary canaliculi while pro-inflammatory cytokines and nitric oxide can also trigger intrahepatic cholestasis (11,13,18). The more the severity of infection, the higher the level of serum bilirubin (18,19). Also, the mean value of WBC was higher in complicated appendicitis although this was not statistically significant like those reported by other authors (14,15,20). This disparity may be due to the sample size in our study. Furthermore, our study did not consider the antibiotics use prior to presentation which may affect the haematological features of an infected appendix.

In our study, the sensitivity, specificity, PPV and NPV of TSB in perforated appendicitis were 84%, 81%, 57%, and 94% respectively. Ahmed et al. (20) and McGowan et al. (14) reported a lower sensitivity of 60% and 63% respectively, but the specificity of 80% and 88% in both were comparable to our findings. The positive likelihood ratio and negative likelihood ratio were 4.42 and 0.20 respectively in our study. A positive likelihood ratio of >5 or a negative likelihood ratio <0.2 is indicative of strong diagnostic evidence (21). With our values very close to this standard, we can infer that serum bilirubin could be a useful diagnostic marker of complicated acute appendicitis among our patients.

The sensitivity, specificity, PPV and NPV obtained for WBC in perforated appendicitis were 68%, 60%, 34% and 86% respectively. These results were generally lower than those obtained for TSB. However, Wu et al. (22) and Xharra et al. (23) reported higher sensitivities of 80% and 85% and specificities of 71% and 68% respectively.

While it might be true that the WBC also has a place in diagnosis, TSB could be a more useful test in accurately diagnosing a complicated appendicitis in our setting. However, McGowan et al. had reported WBC as a biochemical marker of perforation in acute appendicitis (14). The initial inflammatory response in acute appendicitis is more of an increase in neutrophil count without necessarily affecting the total WBC, but the latter number increases with time as inflammation progresses (24). The WBC can also be elevated in many inflammatory conditions thereby making it a non-specific test in the diagnosis of acute appendicitis (25, 26).

A combination of full clinical evaluation, laboratory tests, and radiological investigations are still needed to improve the diagnostic yield in appendicitis and plan for appropriate management. Even with the recent advances in the diagnostic field, there is no single clinical or laboratory test that can accurately predict acute appendicitis or perforated appendicitis (27).

In conclusion, hyperbilirubinaemia could serve as a biochemical marker for complicated appendicitis. In resource-constrained settings where CT or other imaging techniques are not readily available or too expensive to afford by patients, TSB and DB could be a useful adjunct to improving the diagnostic accuracy in complicated appendicitis and should be included in the assessment of patients. Elevated TSB in a patient with suspected acute appendicitis should warrant urgent surgical intervention.

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