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ORIGINAL ARTICLE

Diagnostic Value of TLC, CRP and Serum Bilirubin in Suspected Cases of Acute Appendicitis

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ABSTRACT

Background: Acute appendicitis is the most common surgical emergency and appendectomy remains the most frequently performed emergency operations worldwide. So, we aimed to minimize negative appendectomy in the General Surgery department in Zagazig University hospitals and to put a protocol to deal with suspected cases in the future.

Methods: This study was carried out in the emergency unit of General Surgery department of Zagazig University Hospitals between the period from January 2018 to January 2019, the study included 112 patients suspected to have acute appendicitis. Complete blood count (CBC), C-reactive protein (CRP), Serum bilirubin (S. Bilirubin) were estimated for all patients preoperatively.

Results: From the results we found that from 39 complicated cases total leucocyte count (TLC) was negative in 2 cases only and regarding to CRP it was negative in 4 cases, also we found that Bilirubin was positive in 38 cases. From these cases 26 were complicated. Bilirubin was positive in only 1 case of negative appendectomy cases.

Conclusions: white cell count, C-reactive protein and Serum bilirubin measurements are useful in the assessment of acute appendicitis. If used judiciously, they may spare a group of patients not only an unnecessary surgical procedure, but also unnecessary admission to hospital for observation.

Keywords: acute appendicitis; CRP; TLC; bilirubin.



INTRODUCTION

Acute appendicitis is the most common surgical emergency and appendectomy remains the most frequently performed emergency operations worldwide [1]. The diagnosis of appendicitis requires a mixture of observation, clinical acumen and surgical science. Despite appendicitis being a common disease, its presentation is not always typical and misdiagnosis is therefore not uncommon [2]. Diagnostic difficulties may lead to negative appendectomy or cases of missed appendicitis resulting in complications such as appendicular perforation or abscess formation [3]. Diagnostic scoring systems have been developed in an attempt to improve the diagnostic accuracy of acute appendicitis. The most prominent of these scores, developed by Alvarado, gives points for symptoms (migration of pain, anorexia, and nausea), physical signs (right lower quadrant tenderness, rebound tenderness, and pyrexia), and laboratory values (leukocytosis and left shift). Although these scores can help guide clinical thinking, they do not markedly improve diagnostic

accuracy [4]. Other diagnostic aids including ultrasound (US), computed tomography (CT) or even magnetic resonance imaging [MRI], do exist in order to help confirm the diagnosis or to guide the surgeon's decision on operative management or a period of observation when appendicitis is suspected. However, these diagnostic tools may be expensive, may involve high radiation exposure, and may not always have accurate and reproducible results [5]. The diagnostic and discriminatory role of white cell count (WCC), C-reactive protein (CRP) and serum bilirubin in acute appendicitis has been studied expansively but still remains contentious. Literatures point that a rise in serum bilirubin level in patients with clinically suspected appendicitis may be a predictor for perforation of appendix. It is well established that when microbes invade the body, leukocytes defend it. This leads to increase in the leukocyte count. Bacterial invasion in the appendix leads to transmigration of bacteria and the release of pro-inflammatory cytokines such as TNF-alpha, IL6 and cytokines. These reach the liver via portal circulation and may

produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow [6]. We performed our study in order to minimize negative appendectomy in the General Surgery department in Zagazig University hospitals, not to miss positive cases of appendicitis and to put a protocol to deal with suspected cases in the future. For this aim we selected patients with acute appendicitis presented to Zagazig University Hospitals, evaluated the diagnostic value of serum biomarkers (TLC, S. Bilirubin, CRP) in suspected appendicitis and compared the outcome after performed investigations.

METHODS

This study was carried out in the emergency unit of General Surgery department of Zagazig University Hospitals and included 112 patients suspected to have acute appendicitis, their age ranged from 16-60 years old. We excluded Patients with past history of jaundice or liver disease, Pregnant women, Patients on analgesics, Patients with Hemolytic disease, Patients with cholelithiasis, Patients with cancer of hepatobiliary system, Patients known to be on treatment for any collagen or vascular disease and Patients with any current infection (upper or lower respiratory or urinary tract infection). Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. All patients were subjected to the following: History taking, including: a) Personal History: name, age, sex, residency. b) Present history: we asked about a complaint. We analyzed complaint to know onset, course, duration, what increase, what decrease and associations. c) Past history. d) Family history. Clinical Examination, including General examination for vital signs (Temperature, pulse, blood pressure and respiratory rate) and local examination (abdominal examination): by inspection, palpation, to know if there were any organomegaly, lymphadenopathy or palpable mass in the abdomen and auscultation of abdomen to assess bowel movement. Pre-interventional investigations were done and included: Complete blood count (CBC). liver function tests including: Serum bilirubin (direct – total), Kidney function test, CRP, Coagulation profile (PT, PTT, INR) and pregnancy test for female patients. Abdominal ultrasound: to confirm the diagnosis and search for the complication (appendicular abscess – appendicular mass – peritoneal collection . . . etc). ECG and cardiac consultation were done for patients above 40 years

and IV fluids, antibiotic (ceftriaxone 1gm/24) were given as Preparation.

Procedure Anesthesia used was general or spinal according to evaluation of anesthesiologist and Antibiotic was given with induction of anesthesia. Then, sterilization of abdomen and the incision used was McBurney's incision, followed by Opening of various layers of the abdominal wall (skin –subcutaneous tissue –external oblique aponeurosis –internal oblique and tranversus abdominis muscles- peritoneum). In order to preserve the integrity of abdominal wall, incision of external oblique aponeurosis and the internal oblique muscle was done along the line of its fibers to reduce the risk of later incisional hernia. On entering the peritoneum, the cecum was identified and delivered then the appendix was mobilized. The mesoappendix was ligated and then the appendix was ligated and divided at its base. Finally, Closure of each layer of the abdominal wall in turn was done.

Post-Operative care: The patients received medical treatment including antibiotic (1gm Ceftriaxone /12h), anti-stress ulcer measures (Zantac amp/12h) and IV fluids which were stopped when intestinal sounds became audible. Then patients started oral fluids. The patients were discharged when oral fluid was tolerated with instructions for follow up every 3days at outpatient clinic for open appendectomy for observation of wound.

Statistical analysis: All results will be revised for completeness, and logical consistency. Preceded data will be entered on the computer using a database developed for data entry on Microsoft Office Excel program 2007. Data will then be transferred to the Statistical Package of Social Science, version 16 (SPSS-v16) for quantitative data analysis. Simple frequencies will be used for data checking. Descriptive statistics will be used for data summarization. Graphs will be used to illustrate simple information. Bi-variety relationships will be displayed in cross tabulations. Suitable statistical tests of significance will be used where appropriate.

RESULTS

From total 112 patients, were included 54 (48. 2% %) males and 58 (51. 8%) females. male to female ratio is (1: 1. 07) with slight increase in number of females more than male, as in (Table 1 and figure 1). The overall number of acute appendicitis cases is 106 while negative appendectomy cases are 6 cases. 39 cases of 106 are complicated cases (gangrenous, perforated appendix or appendicular abscess), as in (Table2 and figure 2). We found that from 39 complicated cases TLC was negative in 2 cases only and regarding to CRP it was negative in 4 cases. In addition, S. Bilirubin was positive in 38

cases from these cases 26 were complicated. S. bilirubin was positive in only 1 case of negative appendectomy cases, as shown in (Table 3). TLC was found to have high sensitivity to complicated cases but low specificity to both acute and complicated cases, as in (Table 4). Furthermore, S. Bilirubin has high specificity for both acute and complicated cases, as shown in (Table 5). Combination of TLC and bilirubin

markedly increase the specificity to both acute and complicated cases, as in (Table 6). Combination of CRP and bilirubin markedly increases the specificity to both acute and complicated cases, as in (Table 7). Combination of the three biomarkers not obviously improve the sensitivity but markedly improve the specificity, as shown in (Table 8).

Table 1: Number of males and females

Sex	Count	Percentage
Male	54	48.2%
Female	58	51.8%

Table 2: Distribution of patients according to pathological finding

Acute appendicitis 106 (94.6%)		
Complicated appendix	Non complicated appendix	Negative appendectomy
39 (34.9%)	67(59.8%)	6 (5.3%)

Table 3: Distribution of TLC, CRP and s. bilirubin according postoperative pathological findings

	Negative appendectomy	Non complicated appendicitis	Complicated appendicitis
TLC positive (TLC >10000/UL)	3(2.6%)	42(37.5%)	37(33%)
TLC negative	3(2.6%)	25 (22.3%)	2(1.7%)
CRP positive (CRP>5 mg/L)	2(1.7%)	56(50%)	35(31%)
CRP negative	4(3.4%)	11(9.8%)	4(3.4%)
Bilirubin positive (bilirubin>1.2 mg/L)	1(0.9 %)	3(2.7%)	26(23.2%)
Bilirubin negative	5(4.4%)	64(57%)	13(11.6%)

Table 4: The sensitivity, specificity, accuracy and positive predictive value of TLC

	Sensitivity	Specificity	Accuracy	Positive predictive value
TLC to acute appendicitis	74.53%	50.00 %	73.21%	96.34%
TLC to complicated appendicitis	94.87%	37.31 %	58.49%	46.84%

Table 5: The sensitivity, specificity, accuracy and Positive predictive value of Serum bilirubin

	Sensitivity	Specificity	Accuracy	Positive predictive value
Serum bilirubin to acute appendicitis	26.42%	83.33 %	29.46%	96.55%
Serum bilirubin to complicated appendicitis	66.67%	97.01 %	85.85%	92.86%

Table 6: The sensitivity, specificity, accuracy and Positive predictive value of combination of TLC and bilirubin

	Sensitivity	Specificity	Accuracy	Positive predictive value
TLC& bilirubin to acute appendicitis	24.53%	100.00 %	28.57%	100.00 %
TLC & bilirubin to complicated appendicitis	64.10%	98.51 %	85.85%	96.15%

Table 7: The sensitivity, specificity, accuracy and Positive predictive value of combination of CRP and bilirubin.

	Sensitivity	Specificity	Accuracy	Positive predictive value
CPR& bilirubin to acute appendicitis	23.58%	100.00 %	27.68%	100.00%
CPR& bilirubin to complicated	61.54%	98.51 %	84.91%	96.00%

Table 8: The sensitivity, specificity, accuracy and Positive predictive value of combination of TLC, CRP and bilirubin.

	Sensitivity	Specificity	Accuracy	Positive predictive value
TLC& CRP &bilirubin to acute appendicitis	23.58%	100.00 %	27.68%	100.00%
TLC& CRP &bilirubin to complicated appendicitis	61.54%	98.5%	84.91%	98.00%

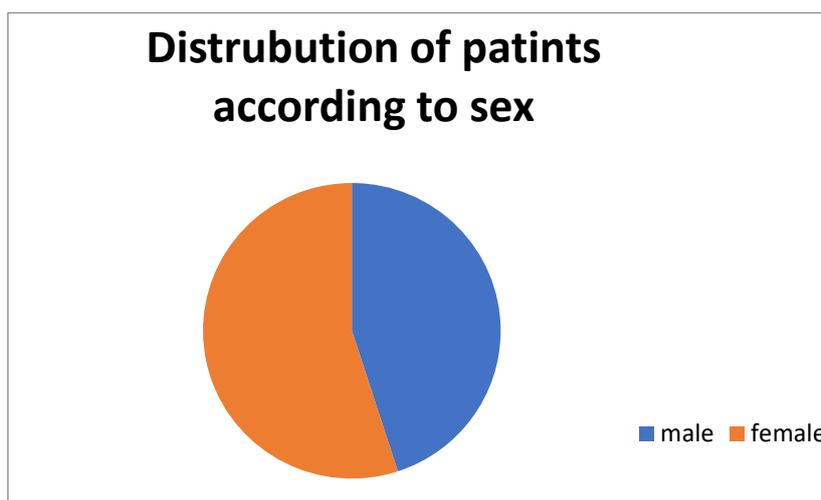


Figure (1): A pie chart shows the distribution of patient according to sex in this study

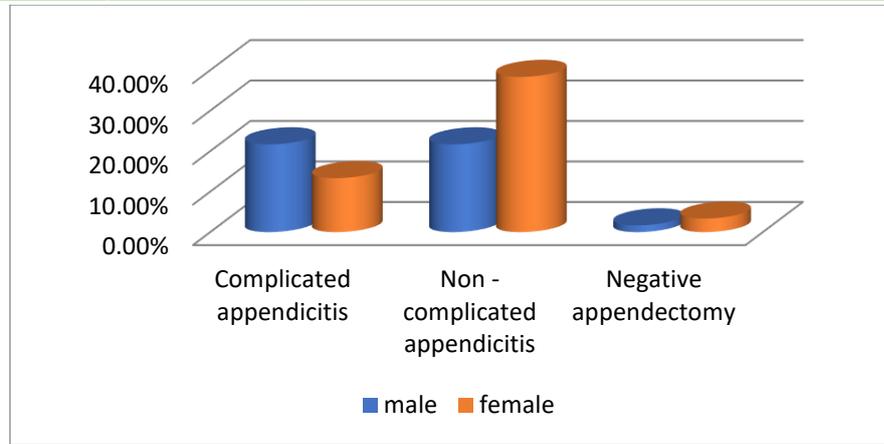


Figure (2): A graph shows The distribution of patients according to post-operative pathological findings in this study.

DISCUSSION

Although acute appendicitis is the most common abdominal surgical emergency, the diagnosis can be extremely difficult at sometimes [7].

This is due to absence of a pathognomonic sign or symptom, the poor predictive value of associated laboratory testing and its varied presentation at diagnosis [8]. The rate of negative appendectomy still imposes a burden on health service resources and despite the extraordinary advances in modern radiography imaging and diagnostic laboratory investigations. The accurate diagnosis of acute appendicitis remains a challenge. Although there are various diagnostic aids for appendicitis, no single test can reduce the rate of negative appendectomy to zero [9]. In our study, the number of female patients (58) is more than the number of male patients (54). However, the complications in male are more common than the complications in female, (in male, 25 patients had a complicated appendicitis in comparison to 14 cases in females).

By history taken from patients we noticed delay in seeking medical advice and taking analgesic in males more than females. In our study, the overall negative appendectomy rate was 5.3 %, which is slightly lower than the value of most of our references. This is explained by the delay in presentation of patients and a large number of patients who had a diagnostic quandary were subjected to diagnostic laparoscopy and another causes other than appendicitis were found.

In our study we investigated the value of TLC, CRP and total bilirubin in patients with suspicion of appendicitis and correlated the values with the intra-operative findings and histopathological examination of the specimens. TLC >10000/UL was found to have high sensitivity (74. 5%), (94. 5%), but less specificity (50%), (37. 3%)to both cases of acute and complicated appendicitis respectively. CRP >5 mg/L was found to have high sensitivity (89.7%)for diagnosis of complicated appendicitis, but had a very low specificity (16. 4

%). Normal levels of both TLC and CRP rule out a diagnosis of complicated appendix but do not necessarily rule out acute appendicitis (AA). This is in contrast to the findings of Khan et al. [10] who have suggested that normal TLC with normal CRP levels decrease the possibility of AA and that the patient can be discharged without more reviews. But Sengupta et al. [11] reports that the possibility of negative appendectomy in patients with both positive tests has been less than 10. 0%. A combination of TLC (>10000/mm³) and CRP (>5mg/L) had high sensitivity (87. 1%) detect complicated appendicitis. this is confirmed by Mir et al. [12]in their study. In our study, bilirubin level was highest among patients with complicated appendicitis. Specificity of bilirubin to acute and complicated cases was (83.3%) and (97%) respectively. This observation is supported by Estrada et al. [13] who found that the mean bilirubin levels in patients diagnosed with complicated appendicitis were higher as compared to that in patients with acute uncomplicated appendicitis. In a study done by Panagiotopouet al. [14] the sensitivity of CRP and bilirubin in cases of acute appendicitis was 68% and 50% respectively. The specificity of CRP and bilirubin was 66% and 68% respectively. While in cases of complicated appendicitis, sensitivity of CRP and bilirubin was 100% and 65% respectively. Specificity of CRP and serum bilirubin was 66% and 68% respectively. In the study that was done by Chaudhary et al. [15] on cases of complicated appendicitis only, the sensitivity of CRP and bilirubin was 100% while the specificity was 95. 2% and 92. 5% respectively. High results of this study is due to including patients with any pyogenic intraperitoneal reaction eve if appendix was not perforated or gangrenous. But in our study these cases were included as non-complicated appendicitis. In comparison to our study, there is a study done by Emmanuel et al [6]. The sensitivity of CRP and bilirubin in a case of acute appendicitis

was 90% and 30% respectively. The specificity of CRP and bilirubin was 71% and 88% respectively. While in cases of complicated appendicitis, sensitivity of CRP and bilirubin was 91% and 70% respectively. Specificity of CRP and serum bilirubin was 36% and 98% respectively. Higher results in this study can be explained by absence of exclusion criteria. So high levels of bilirubin and CRP can be found hepatic patients and patients with inflammatory diseases.

We noticed that the specificity of TLC to detect acute appendicitis increased from 50% to 100% by combination with bilirubin. Also it increased from 37% to 98.5% for complicated appendix when combined with bilirubin. Dramatic increase in specificity of CRP for both acute (100%) and complicated appendicitis (96%) when combined with S. Bilirubin. When the three markers were combined no significant increase in sensitivity occurred, but we obtain highest specificity for acute appendicitis (100%) and also complicated cases (98%).

CONCLUSIONS

We assume that this results can give a high suspicion to the development of complication in acute appendicitis when all markers are raised. This study sends two important messages in the management of AA. The first message is that if all the three markers (WBCC, CRP & S. Bilirubin) levels were normal in a patient with suspicion of AA; the presence of inflamed appendix is unlikely and re-evaluation of the patient over a period of time is perhaps a better option than proceeding to operation. The second message is that the measurement of CRP & S. Bilirubin in cases of suspected AA is important and it's better not to depend on the evaluation with WBC alone, the combination of all inflammatory markers will reduce the incidence of negative appendectomy.

Conflicts of interest: None.

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