Journal of Surgery and Trauma 2020; 8(4):151-155.
jsurgery.bums.ac.ir

ORIGINAL ARTICLE

Diagnostic value of clinical and laboratory symptoms in the diagnosis of acute appendicitis in patients with suspected acute appendicitis referring to Imam Reza Hospital in Birjand

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Received: November 24, 2020 ***Revised: January 11, 2021*** ***Accepted: January 16, 2021***

Abstract

Introduction: Appendicitis is a challenging condition for emergency specialists and surgeons to diagnose. If it is not treated in time, the inflamed tissue of the appendix ruptures, causing peritonitis and shock. This study evaluated the diagnostic value of clinical and laboratory symptoms in the diagnosis of acute appendicitis.

Methods: This descriptive cross-sectional study was carried out on a total of 134 patients with suspected appendicitis referring to the Emergency Department of Imam Reza Hospital in Birjand, Iran, within 2013 and 2015 using convenience sampling. The data collection tool was a questionnaire covering patients' demographics, clinical signs, and laboratory and pathology test results. Sensitivity and specificity, positive predictive value, negative predictive value, likelihood ratio, area under the receiver operating characteristic (ROC) curve (AUC), and cut-off point of each test (i.e., white blood cell, aspartate transaminase, alanine transaminase, C-reactive protein, polymorphonuclear leukocytes, lymphocytes, total and direct bilirubin, iron, and total iron-binding capacity) were analyzed using SPSS software (version 18) and MedCalc software (version 19). A p-value of 0.05 was considered statistically significant.

Results: In this study, 68 and 66 participants were male and female, respectively. The mean age of the patients was 24.44±11.26 years. Pathological examination showed that six patients underwent a negative appendectomy. A positive appendectomy was noted in 128 subjects. Histopathological results confirmed the perforation of the appendix in 78 patients. Among the laboratory tests, only the accuracy of serum iron was fair in the diagnosis of acute appendicitis (AUC numerical value in the ROC curve=0.787). The accuracy of other tests based on the AUC numerical value in the ROC curve was poor or failed.

Conclusions: Although the accuracy of serum iron based on the numerical value of AUC in the ROC curve was diagnostically fair for acute appendicitis, it is suggested to carry out further studies with larger sample sizes in order to draw definitive conclusions given the small sample size in this study.

Key words: Appendicitis, Diagnosis, Signs and symptoms

Introduction

Acute appendicitis is one of the most common surgical emergencies with a prevalence rate of 9.38 per 100,000 individuals in the United States (1, 2). There is rarely a day when appendicitis cannot be

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[DOI: 10.32592/jsurgery.2020.8.4.104]

observed in a given emergency department across the world (3). The incidence of acute appendicitis is reported at 7%, being more likely within the age range of 10-30 years. This probability is 6.7% for men and 8.6% for women, and it is more prevalent in the second decade of life (4). Appendectomy (due to appendicitis) is the most common emergency surgery globally performed and stands as one of the greatest advances in public health in the past 150 years (5). This condition is more prevalent in men; however, appendectomy is more common among women (3). Nearly, 300,000 appendectomies are annually conducted in the United States, most of which are carried out in an emergency for the prevention of complications, including perforated appendicitis (6).

Despite numerous studies carried out on patients with acute appendicitis, the disease remains a clinical challenge for surgeons. Moreover, despite over 100 years of study, the perception of the underlying causes of appendicitis is still incomplete (7) and the disease continues to be difficult to diagnose (8). It is a sensitive and difficult task to diagnose acute appendicitis (5), which is based on history taking, clinical examination, and laboratory findings. In fact, a definitive clinical diagnosis of the disease is also often difficult for experienced surgeons (2). Clinical symptoms include periumbilical pain shifting to the right lower quadrant, nausea, and vomiting. However, a vivid clinical image is obtained in only 50-60% of patients (9). If appendicitis is not treated in time, the inflamed tissue of the appendix ruptures, causing peritonitis and shock. This can be the mechanism of mortality in this group of patients (5). Therefore, specialists use various paraclinical methods to increase diagnostic power (2). However, imaging methods and paraclinical tests have been able to increase the accuracy of appendicitis diagnosis only to a limited extent.

Imaging methods used in the diagnosis of appendicitis include ultrasound and computed tomography scan, the role of which in increasing the sensitivity and accuracy of acute appendicitis diagnosis has not been significant, despite technical advances in recent years (10). Given the abnormal forms of acute appendicitis and presence of the classic pattern in approximately half of the patients, 15-30% of cases are normal and healthy appendices that are operated on by mistake (11). For many years, the test of choice for appendicitis has been white blood cell (WBC) count and polymorphonuclear percentage. Nevertheless, other laboratory methods have also been studied due to the low sensitivity of this technique (12). The role of preoperative laboratory tests in increasing diagnostic accuracy is still debated. There is hardly a consensus on the significance of blood tests, including WBC counts, increased inflammatory markers, and even liver function tests, such as bilirubin, in the diagnosis of appendicitis (13). Many experts have used C-reactive protein (CRP) to diagnose disease severity and assess the quality of treatment. However, it produces varying and uncertain results (14). Therefore, the current study was performed to determine the diagnostic value of clinical and laboratory symptoms in acute appendicitis.

Methods

This descriptive-analytical study was carried out on a total of 134 patients with suspected acute appendicitis referring to the Emergency Department of Imam Reza Hospital in Birjand within 2013 and 2015 using convenience sampling. The patients who were candidates for appendectomy were included in the study after a thorough examination by a surgeon. A complete explanation about the project and objectives were given to the participants, and they agreed to participate in the study. Subsequently, a demographics form was completed for each participant. Given the exclusion criteria, history taking and initial examination were carried out and necessary tests were requested for the diagnosis of acute appendicitis. Peripheral blood samples were taken from the patients suspected of having acute appendicitis and sent to the laboratory in citrate test tubes. After the centrifugation of the blood samples, the sera were prepared and stored in capped Eppendorf tubes at -60°C until testing.

The tests, including complete blood count, aspartate transaminase, alanine transaminase, total and direct bilirubin, iron, and total iron-binding capacity, were measured by standard methods, and high-sensitivity CRP was measured through the immunoturbidometric method using Pars Azmoon kits (Pars Azmoon commercial kits, Tehran, Iran). The patients were prepared and transferred to the operating room for an appendectomy. After the surgery, all the appendix specimens were transferred to the pathology laboratory. Only one individual performed serum tests with a spectrophotometer for the minimization of technician error. The examination of histopathology of appendix specimens was also confirmed by a pathology faculty member from Birjand University of Medical Sciences. Finally, the results of serum tests were compared with pathological findings.

Given the similarity of symptoms and multiple

[DOI: 10.32592/jsurgery.2020.8.4.104]

Table 1: Interpretation of the numerical values of the area under the curve in the receiver operating characteristic curve

Numerical value of AUC in the ROC curve	Accuracy of a diagnostic test (correctness of test results)
0.9 to 1	Excellent
0.8 to 0.9	Good
0.7 to 0.8	Fairly good
0.6 to 0.7	Weak
0.5 to 0.6	Useless
<0.5	Not reliable

AUC: Area under the curve; ROC: Receiver operating characteristic

abdominal differential diagnoses, the patients undergoing other surgeries, such as ovarian cysts, for any reason were excluded from the study. If the patient did not macroscopically have acute appendicitis, the surgeon would perform a complete intra-abdominal exploration for other causes. In case another disease was noted, a biopsy would be performed if necessary and all of the above-mentioned procedures were reported in the surgery description. The obtained information was analyzed in SPSS statistical software (version 18). Sensitivity and specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio, area under the receiver operating characteristic (ROC) curve (AUC), and cut-off point of each test were computed. The numerical value of the AUC is on a scale between 0 and 1, indicating the power of detection or accuracy of a test result. The AUC values close to 0.5 demonstrate parity between true-positive rate and false-positive rate; nonetheless, the values smaller than 0.5 show a higher false-positive rate. An accurate guide to classifying the accuracy of a diagnostic test is the conventional academic scoring system (Table 1) (15).

Results

Out of 134 subjects, 68 (50.7%) and 66 (49.2%) cases were male and female, respectively. The obtained results showed that the mean age of the patients was 24.44±11.26 years with a minimum age of 6 years and maximum age of 70 years. A total of 110 subjects (88%) did not have a history of appendicitis in their siblings/parents; however, 15 (12%) subjects had a familial history of appendicitis. The pathology examination reported appendicitis in only 128 patients (95.5%). The highest and lowest frequency of appendicitis were related to perforated appendicitis (n=78) and purulent appendicitis (n=17), respectively. The prevalence of chronic appendicitis was reported as 24.6% (n=33).

The results showed nausea in 66% and 72% of the patients with simple and complex appendicitis, respectively. Furthermore, vomiting was observed in 50.9% and 60% of the subjects with simple and complex appendicitis, respectively. In addition, anorexia was reported in 52.8% and 52% of the patients with simple and complex appendicitis, respectively. Only 3.7% of the patients reported the aggravation of pain after food intake. The onset of pain was sudden in 79.2% and 64% of patients with simple and complex appendicitis, respectively. Moreover, the quality of pain was constant in 70.8% and 76% of the cases with simple and complex appendicitis, respectively. Pain shifting was also observed in 53.8% and 48% of the patients with simple and complex appendicitis, respectively.

Among the patients with appendicitis, lymphocytes, WBC, and iron levels were abnormal (89.8%, 51.6%, and 30.5%, respectively). Table 2 tabulates the frequency of laboratory parameters among the study cases with appendicitis. In addition, Table 3 summarizes the sensitivity, specificity, PPV, NPV, likelihood ratio, and area under the ROC curve of laboratory parameters in the study subjects.

Table 2: Frequency of laboratory parameters among patients with appendicitis

Laboratory parameters	Normal n (%)	Abnormal n (%)
BIL T	126 (98.4)	2 (1.6)
BIL D	128 (100.0)	0 (0.0)
AST	127 (99.2)	1 (0.8)
ALT	128 (100.0)	0 (0.0)
TIBS	116 (90.6)	12 (9.4)

BIL T: Bilirubin total; BIL D: Bilirubin direct; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TIBS: Total iron-binding capacity

[DOI: 10.32592/jsurgery.2020.8.4.104]

Table 3: Sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio, and area under the receiver operating characteristic curve of laboratory parameters among patients with appendicitis

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio	Area under the ROC curve	Cut-off point
LYMPH	72.6	83.3	93.9	12.5	0.93	0.07	0.613 (0.419-0.807)	15.55
WBC	46.8	83.3	98.3	6.8	0.60	0.136	0.636 (0.442-0.831)	12
PMN	50	66.6	96.9	5.8	0.32	0.24	0.237 (0.102-0.372)	82
BIL T	34.3	83.3	97.7	5.6	0.44	0.168	0.600 (0.362-0.837)	0.15
ALT	47.6	83.3	98.3	6.9	0.61	0.134	0.695 (0.526-0.864)	6.5
AST	41.4	66.6	96.3	5.06	0.265	0.375	0.620 (0.422-0.818)	5.5
CRP	93.3	83.3	93.3	4.2	0.14	0.228	0.407 (0.185-0.629)	109.5
Serum iron	64.8	83.3	98.8	10	0.83	0.09	0.787 (0.662-0.912)	48.5
TIBS	28.1	83.3	98.8	5.1	0.36	0.184	0.451 (0.205-0.698)	406.5

ROC: Receiver operating characteristic; LYMPH: Lymphocytes; WBC: White blood cells; PMN: Polymorphonuclear leukocytes; BIL T: Bilirubin total; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive protein; TIBS: Total iron-binding capacity

Among the laboratory tests, only the accuracy of the serum iron parameter was fair in the diagnosis of acute appendicitis (the numerical value of the AUC in the ROC curve=0.787). The accuracy of other tests was poor or failed based on the numerical value of AUC in the ROC curve.

Discussion

A parameter that can diagnose acute appendicitis has always been a concern of physicians. Many different parameters have been studied or are being investigated for this purpose. In the present study, among the laboratory tests, only the serum iron had fair accuracy. The accuracy of other tests based on the numerical value of the AUC in the ROC curve was poor or failed. It seems that there has been no study carried out on the relationship between serum iron levels and acute appendicitis; therefore, studies with a closer relationship are reported in the current study.

The results of a study carried out by Ertekin et al. (2017) showed that the red cell distribution width (RDW) level was significantly higher in patients with acute appendicitis, compared to that reported for the control group. The commonly used low-cost RDW test may be an important hematologic parameter in the diagnosis of acute appendicitis. The low sensitivity and specificity of RDW decrease the chances of its use as a marker for the definitive diagnosis of acute appendicitis. Ertekin et al. believed that further studies are required to investigate the association between acute appendicitis and hematologic markers. Furthermore, in order to confirm or reject such a correlation, it is needed to incorporate pathophysiological findings (16).

However, in another study conducted by Narci et al. (2013), the level of RDW was lower in patients with acute appendicitis. The difference in the RDW between acute appendicitis and control groups was very small and nonconducive to diagnosis. According to the aforementioned study, it is required to carry out prospective and multicenter studies with large sample sizes in this field (17).

In this regard, the results of a study performed by Ulukent et al. (2016) showed that the neutrophil to lymphocyte ratio and number of leukocytes are better inflammatory markers for acute appendicitis. A higher level of platelet lymphocyte ratio is an important parameter in the diagnosis of acute appendicitis. However, the ROC analysis indicated that mean platelet volume and RDW levels are not useful markers in terms of sensitivity and specificity as other markers. According to the results of the present study, it is believed that further prospective and large-scale studies are required to identify more specific and reliable biomarkers for the diagnosis of acute appendicitis (18).

It is important to note that the diagnosis of acute appendicitis is based on history taking, clinical examination, and laboratory findings and the fact that serum markers are best helpful when used in conjunction with comprehensive history taking and clinical examination (19). One of the limitations of the present study was the limited sample size and one-centeredness of the study setting.

Conclusions

Although the accuracy of the serum iron level based on the AUC numerical value in the ROC curve was fair in the diagnosis of acute appendicitis, it is

[DOI: 10.32592/jsurgery.2020.8.4.104]

required to carry out multicenter studies with large sample sizes to draw definitive conclusions.

Acknowledgments

This article was extracted from a research project entitled "Evaluation of some biochemical parameters in the diagnosis of acute preoperative appendicitis" (code#420) guided by Surgery and Trauma Research Center and supported by the Research Vice-Chancellor of Birjand University of Medical Sciences. The authors would like to express their gratitude to all the physicians and nurses of Imam Reza Hospital in Birjand and participants who helped during the research project. The authors would also like to show appreciation to Clinical Research Development Unit of Razi Hospital affiliated with Birjand University of Medical Sciences for their support and cooperation during the study.

Funding

The current study was not financially supported by any institution.

Conflict of Interest

The authors declare that there is no conflict of interest.

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[DOI: 10.32592/jsurgery.2020.8.4.104]