Original Article

Journal of Iranian Medical Council, Volume 5, Issue no. 1
http://dx.doi.org/10.18502/jimc.v5i1.9585

Evaluating Efficacy, Specificity, and Sensitivity of Liver Enzymes Levels for Early Diagnosis of Acute Appendicitis and its Complications

Hassan Motamed* and Maryam Fatahian Nejad

Department of Emergency Medicine , Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

*** Corresponding author**

Hassan Motamed, MD

Department of Emergency Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
Email: hasan_motamed@yahoo.com

Received: Jun 7 2021
Accepted: Sept 8 2021

Citation to this article:
Motamed H and Fatahian Nejad M. Evaluating Efficacy, Specificity, and Sensitivity of Liver Enzymes Levels for Early Diagnosis of Acute Appendicitis and Its Complications. *J Iran Med Counc*. 2022;5(1):168-77.

Abstract

Background: The most common etiology for patients with acute abdominal pain presenting in emergency departments is acute appendicitis. This study aimed to evaluate the effectiveness of liver enzymes in early diagnosis of acute appendicitis and prediction of its complications.

Methods: 176 patients with the chief complaint of abdominal pain presented in the emergency departments were enrolled in this study. All included patients underwent standard approach for acute abdomen with target focus for appendicitis. Samples for serum levels of ALT and AST on arrival have been arranged for all included. Patients were evaluated for appendicitis and diagnosis confirmed by histopathology. AST, ALT variables and confirmed diagnosis of acute appendicitis, and related complications have been evaluated for any correlations using Kruskal-Wallis test.

Results: Based on the results, 67 simple, 24 complicated appendicitis, and 85 cases of normal appendix were evaluated. The mean AST was significantly different in normal, simple appendicitis, and complicated groups ($p=0.019$), but the mean ALT failed to show a significant difference. The differential test showed that there was a significant difference between the two appendicitis groups and the normal group in AST ($p<0.05$), but not between the two appendicitis groups. The p-values of AST and ALT were 0.17 and 0.2, respectively.

Conclusion: According to the results of this study, it seems that increased AST may be increased in simple/complicated appendicitis in contrast to normal group, but regarding AUC curve data, AST and ALT fail to have the necessary diagnostic accuracy and efficiency to diagnose acute appendicitis and predict its complications.

Keywords: Acute appendicitis, Early diagnosis, Liver enzymes

Introduction

Acute appendicitis is considered the most common etiology for patients with acute abdominal pain presenting in the emergency departments (1). The disease most often occurs following obstruction due to fecality or lymph node hyperplasia, but cases of non-obstruction can be observed in viral infections such as cytomegalovirus, AIDS, and bacterial infections including campylobacteriosis and Yersiniosis (2). It has been reported that about 7% of people experience acute appendicitis during their lifetime, most often occurring between the ages of 10 and 30 years (3). Considering that the negative appendectomy rate is 5-40%, the acute appendicitis diagnosis is a surgical challenge, and perforation leads to surgical intervention in 5-30% of the cases (4).

Acute appendicitis is usually detected in reference to findings from the history of patients, clinical signs, and also laboratory information. The clinical diagnosis accuracy in acute appendicitis varies between 76 and 92% (3). The misdiagnosis of acute appendicitis is more common in women due to the wide variety of differential diagnoses in the field of gynecology such as ectopic pregnancy, ovarian torsion, Mittelschmerz, *etc* (5). Among the imaging techniques, ultrasound is a non-invasive method, which is safe, cheap, and available in most medical centers in the country and is used as a selective imaging approach in diagnosing appendicitis and also maintain relatively satisfactory accuracy (87-96%) (6). Although Computed Tomography (CT) scan is considered a reliable diagnostic technique, it shows weaknesses such as enhanced radiation and charge (4). The misdiagnosis rate of acute appendicitis remains constant although the two mentioned imaging techniques are used to diagnose appendicitis (6). One of the main questions in the evaluation of patients with suspected acute appendicitis is whether laboratory tests in the initial evaluation of patients for disease rejection have high power or not. The most requested tests for inflammatory markers are Polymorphonuclear cells (PMNs), White Blood Cells (WBCs), and C-Reactive Protein (CRP) (7). In recent years, D-dimer and Procalcitonin (PCT) have also been investigated as new biomarkers for diagnosing acute abdomen (8,9). Given the low negative predictive value of ESR and CRP, the normality of each of these tests may not be sufficient to rule out acute appendicitis (10,11). Also, as a sequence of low diagnostic and sensitivity value of D-dimer and PCT, they cannot be suitable markers for the diagnosis of appendicitis (8). To reduce the ruptured appendix complications, early and rapid detection of appendicitis is essential. Negative appendectomy also has surgical and anesthesia complications similar to positive appendectomy, which include postoperative infections, intestinal obstruction due to adhesions, and the possibility of infertility in young women (3). None of the above clinical and laboratory tests can diagnose appendicitis with a high rate of confidence, and imaging techniques (ultrasound and CT scan) have several limitations such as cost, radiation, and operator dependence. Thus, the use of an affordable, cheap and sensitive paraclinical method can reduce the rate of negative appendectomy to some extent. There are many benefits for the patient avoiding unnecessary surgery, and incurring costs and complications are among the most common ones. This study aimed to evaluate the efficiency, specificity, and sensitivity of alanine transaminase (SGPT/ALT) and aspartate transaminase (SGOT/AST) for diagnosis of acute appendicitis and its complications.

Materials and Methods

This study was aimed at determining the efficacy, specificity, and sensitivity of serum ALT and AST levels in diagnosing acute appendicitis and its complications. 176 patients over 18 years of age with the chief complaint of abdominal pain with initiation of pain in 2-6 recent hours, presented in the emergency departments of two university hospitals in Ahvaz, Iran, were enrolled in this cross-sectional study for further evaluation regarding acute abdomen. Patients with cirrhosis, inflammatory bowel disease, malignancies, previous abdominal surgery, pregnant women, and patients with a history of the previous appendectomy were excluded from the study. All included patients underwent standard approach for acute abdomen with target focus for appendicitis. 1.8 *ml* of venous blood sample was collected from all the included patients to determine the serum levels of ALT and AST on arrival. Patients ruled out for acute appendicitis by clinical and paraclinical routine standards for acute appendicitis and acute abdomen

were discharged home. Other patients with suggestion of acute appendicitis diagnosis based on clinical and paraclinical standard, underwent appendectomy, and all these patients were evaluated for macroscopic report of surgeon and histopathologic evaluation for appendix tissue samples.

Statitical analysis

Data were analyzed using SPSS version 22 (IBM SPSS STATISTICS 22, IBM Inc., New York, USA). Descriptive results are presented as: number, percent, mean, and standard deviation. AST, ALT variables, and confirmed diagnosis of acute appendicitis and related complications were evaluated for any correlations using Kruskal-Wallis test. The relationship between two qualitative variables was evaluated by chi-square test, and quantitative variables were compared by one-way analysis of variance. At multiple levels of qualitative variables, the ROC test was used to obtain the ROC curve and the value below the AUC diagram and diagnostic and accuracy indicators including sensitivity and specificity. Also, the relationship between the quantitative variables was examined by the Pearson correlation test. According to the Yadav and Chandra study in which the sensitivity and specificity of ALT were 34.67 and 100%, respectively, and the sensitivity and specificity of AST were 30.67 and 100%, respectively, and the prevalence of appendicitis was 0.937, the sample size was calculated. Since there was no presumption about the desired value of d, d was considered and calculated equal to p=0.1 (4).

The Ethic code for this research was granted by Ethics committee of Ahvaz Jundishapur University of Medical Sciences: IR.AJUMS.REC.1398.101.

Results

102 out of 176 included patients underwent appendectomy as a part of their clinical evaluation and treatment. Also, 74 out of 176 included patients with abdominal pain excluded for acute abdomen and acute appendicitis were discharged for diagnosing nonspecific abdominal pain and non-acute abdomen diagnosis. 11 out of 102 patients who underwent

Table 1. Comparison of mean AST and ALT between various types of complicated appendicitis

Complication type	n	AST Mean ± SD	ALT Mean ± SD
Abscess - Phlegmon	4	12.25 ± 6.70	25.50 ± 8.58
Perforation	2	26.50 ± 12.02	22.50 ± 9.19
Gangrene	12	24.08 ± 9.83	23.83 ± 13.25
Gangrene -Perforation	6	27.50 ± 20.87	34.00 ± 7.37
Total	24	23.17 ± 13.42	26.04±11.46
p-value (Kruskal-Wallis test)		0.176	0.202

Liver enzymes in *IU/ml*

Table 2. Comparison of mean AST and ALT between simple and complicated appendicitis groups and normal group

Group	AST Mean ± SD	ALT Mean ± SD
Normal (n = 85)	18.79 ± 10.32	25.59 ± 9.46
Simple appendicitis (n = 67)	22.60 ± 11.00	23.63 ± 11.09
Complicated appendicitis (n = 24)	23.17 ± 13.42	26.04 ± 11.46
Total (n = 176)	20.84 ± 11.15	24.90 ± 10.37
p-value (Kruskal-Wallis test)	0.019	0.116

Liver enzymes in *IU/ml*

Table 3. The association of WBC distribution based on ALT and AST values

Leukocytosis	ALT		AST	
	Normal frequency	Normal frequency	Normal frequency	Abnormal frequency
Normal	43 (95.6%)	2 (4.4%)	43 (95.6%)	2 (4.4%)
High	55 (100%)	0 (0%)	52 (94.5%)	3 (5.5%)
Total	97 (98%)	2 (2%)	95 (95%)	5 (5%)
p-value	0.2		0.99	

appendectomy were reported for normal appendix and were ruled out for acute abdomen after surgery. Based on the results, we categorized the patients in two appendicitis groups: simple appendicitis (67 patients) and complicated appendicitis (24 patients, including 4 cases of abscess-phlegmon, 2 cases of perforation, 12 cases of gangrene, and 6 cases of gangrene-perforation). The chi-square test showed that the age ratio was not the same in the three groups ($p<0.05$), in a way that in the normal group, 34% of the cases were over 40 years old, while in the simple appendicitis group 14.9% were over 40 years old, exhibiting a significant difference compared to the normal group. The sex ratio was the same in the three groups, and no significant difference was shown ($p>0.05$).

Out of 24 patients with complications of appendicitis, 4(16.7%) were abscess-phlegmon type, 2(8.3%) were perforated, 12(5%) were gangrenous, and 6(5%) were gangrenous-perforated. The Kruskal-Wallis test showed that there was no significant difference considering ALT and AST values in different types of appendicitis complications (Table 1). The mean serum glutamic-oxaloacetic transaminase (AST) was significantly different in the three groups (normal, simple appendicitis, and complicated) ($p=0.019$), but no significant difference was observed in the mean serum glutamic pyruvic transaminase (ALT) (Table 2). The differential test showed that there was a significant difference between the two appendicitis groups and the normal group in AST ($p<0.05$), but not between the two appendicitis groups and normal group in ALT. The p-values of AST and ALT were 0.17 and 0.2, respectively. Therefore, the means of SPGT and AST in different types of complicated appendicitis were not significantly different. The frequency of abnormal ALT and AST values was not significantly different based on the pain duration, pain site, and leukocytosis. Using the Receiver Operating Characteristic (ROC) curve to determine the diagnostic accuracy of AST and ALT (with lower normal values < 31 in women, < 41 in men for ALT, < 31 in women, and <37 in men for AST), it was found that AST with area under the ROC = 0.623, $p=0.005$, sensitivity of 0.61%, and specificity of 0.53% lacked the necessary diagnostic accuracy (considering very low sensitivity and specificity and the area under the curve was less than 0.7). On the other hand, ALT with area under the ROC = 0.43 and $p=0.16$, lacked efficiency in diagnosing appendicitis due to sensitivity and specificity close to zero and area under the curve of less than 0.5 and specificity and sensitivity of close to zero (Figures 1 and 2).

Two (4.8%) patients with pain duration of 1 day and less and 9 (4.3%) patients with a pain duration of more than 1 day had abnormal ALT. The Fisher's exact test with $p=0.99$ failed to show a significant relationship between abnormal ALT and pain duration. The Fisher's exact test with $p=0.2$ failed to indicate a significant relationship between ALT and WBC count (Table 3). It should be noted that only 2 (4.4%) patients with abnormal ALT had normal WBC count. Of 45 patients with normal WBC, 2 (4.4%) had abnormal AST, and of 55 patients with high WBC, 3 (5.5%) had abnormal AST. The Fisher's exact test with $p=0.99$ failed to show a significant relationship between these two variables (Table 3).

Discussion

Acute abdominal pain is a common complaint of patients of emergency departments (12), and 8% of referrals to the emergency departments with acute abdominal pain are caused by appendicitis (13). In the case of appendicitis, it is often difficult to make

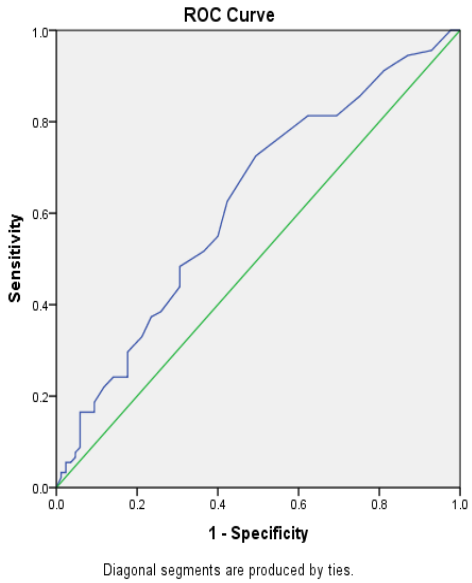

Figure 1. ROC curve for AST efficiency in appendicitis diagnosis.

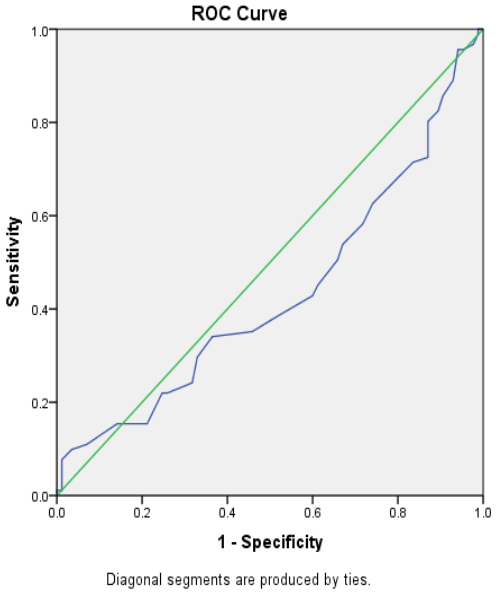

Figure 2. ROC curve for ALT efficiency in appendicitis diagnosis.

an accurate diagnosis, since classic symptoms and signs are not always present, and different symptoms can make it difficult to diagnose acute appendicitis (14). Despite advances in diagnostic methods, the detection of acute appendicitis is even now a surgical challenge, and the negative appendectomy rate varies between 8% and 12% in men and between 25% and 45% in women (15,16). Then again, in order to reduce the ruptured appendix complications such as peritonitis, phlegmon, and abscess, timely and accurate detection of appendicitis may be necessary. Negative appendectomy also has surgical and anesthesia complications similar to positive appendectomy, which include postoperative infections, intestinal obstruction due to adhesions, and the possibility of infertility in young women. For this reason, diagnostic methods that reduce negative appendectomy, as well as reduction of complications and mortality due to appendicitis, are widely addressed by the scientific community (17).

In practice, the diagnosis of acute appendicitis is supported by high levels of inflammatory markers such as WBC, CRP, and ESR; however, none of these markers have the diagnostic accuracy required to diagnose appendicitis (18). Recent studies have shown the positive predictive value of direct and indirect bilirubin and liver enzymes in the diagnosis of appendicitis (4). Although some others stated that the parameters of liver function in appendicitis are increased, their diagnostic accuracy is not adequate (19). Thus, due to the inconsistencies, studies are still being undertaken in this direction.

In our experiment, 176 individuals were evaluated for their complaint regarding abdominal pain, and after standard evaluation and treatment, correlation of their final diagnosis was analyzed in contrast to their liver enzyme levels.

The age range observed in appendicitis is 1 to 89 years, but it most often occurs between the ages of 5 and 45 years with an average age of 28 years (20). In a study conducted by Farrokh *et al*, the mean age of 77 patients undergoing appendectomy was 26.6 ± 0.9 years with a range of 12 to 44 years (21). In the Nyuwi *et al* study, among 82 patients, the mean age of patients was 37.26±1.6 years. In that study, the majority of patients were in the age range of 30 years (22).

In the study conducted by Menteş *et al*, the mean age of patients with acute appendicitis was 27.8± 7.7 years (age range 20-57 years) (23). Studies by Farrokh, Nyuwi, and Menteş on the appendicitis prevalence in 40-year patients were similar to the present study. In the present study, out of 91 patients with appendicitis, based on pathology, 67 had simple appendicitis (73.62%), 4(4.39%) had an abscess-phlegmon type, 2 (2.19) had a perforated type, 12 (13.18%) had a gangrenous type, and 6 (6.59%) had

a gangrenous-perforated type. In the study conducted by Farooqi *et al* on 1008 patients having symptoms of appendicitis, according to the pathological findings, 700 patients were detected with acute appendicitis, which was perforated in 27% of patients (9). In the study carried out by Farooqi *et al*, the prevalence of perforated appendicitis has been shown to be higher than that in the present study, which is probably due to the differences between the studied populations and diagnostic processes in different centers. In Saadati *et al*'s study of 1090 patients, 712 (68.6%) cases had acute simple appendicitis, 87 (8.3%) cases had gangrenous appendicitis, 120 (11.5%) cases had perforated appendicitis leading to erythonitis, 35 (3.3%) had appendicitis leading to phlegmon, and 83 (8%) had an appendicular abscess (25).

In our study, the acute appendicitis prevalence was similar to the study conducted by Saadati, but the other prevalence rates were slightly different, probably due to differences in the populations studied and the classification. In the current study, the prevalence rates of lower abdomen tenderness, pain over 1 day, and leukocytosis were 50.3, 58, and 55%, respectively. In the study conducted by Alhamdani *et al*, 70% of patients suffering from acute appendicitis had lower abdominal tenderness symptoms, which was more common in pathology than patients without appendicitis (16). The higher rate of lower abdominal quadrant tenderness in the last study compared to the present study is probably due to the fact that in the present study, the prevalence of lower abdominal quadrant tenderness in all patients suffering from acute abdominal pain (with or without a diagnosis) was reported appendicitis, but in the study conducted by Alhamdani, it was reported in patients with a final diagnosis of appendicitis.

In this study, in the three groups of simple appendicitis (22.6011.00±) and complicated appendicitis (23.1713.42±), the mean AST was significantly higher compared to the normal group (18.7910.32± *units per milliliter*). However, ALT showed no significant difference between them. Furthermore, the SPGT and AST levels in the two groups of simple and complicated appendicitis were not significantly different from each other, and there was no significant difference in various types of complicated appendicitis. Using the ROC curve to determine the diagnostic accuracy of AST and ALT, it was determined that AST with AUC=0.623 and p=0.005 lacked the necessary diagnostic accuracy. On the other hand, ALT with AUC=0.43 and p=0.16 had no efficiency for diagnosing appendicitis.

In the study of 100 patients presenting to emergency departments with appendicitis symptoms, conducted by Nevler *et al*, the areas under the AUC curve for AST, ALT, and ALP in the diagnosis of acute appendicitis were 0.536, 0.617, and 0.486, respectively, which showed their inefficiency for diagnosing appendicitis. In addition, the means of AST and ALP in patients with and without a diagnosis of appendicitis were not significantly different, but in patients who were diagnosed as having appendicitis, the mean ALT was significantly higher. However, a combination of serum bilirubin, ALT, and ANC levels showed the highest area under the curve levels (0.898, 95% confidence interval, 0.835-0.962, p<0.001) with a 86% diagnostic accuracy in the diagnosis of appendicitis (16).

In the study by Nevler, an increase in liver ALT was observed in patients suffering from appendicitis versus the normals, but in the present study, an increase in AST was observed. In the present study, the area under the AST curve was 0.63, which was slightly higher than the mentioned study. In addition, the area under the ALT curve was 0.43, which was lower than the above study. Sufficient efficiency and accuracy of ALT and AST in diagnosing appendicitis were consistent. The discrepancy between some of the results of our study and those of the above-mentioned studies is probably due to the differences regarding the study populations in terms of demographic variables, underlying diseases, racial differences, and the type of appendicitis.

In Farooqi *et al*'s study, among 1,008 patients having symptoms of appendicitis, the acute appendicitis diagnosis in 700 patients was proven by pathological findings. In people with the diagnosed acute appendicitis, the mean serum ALT was significantly higher than patients without a diagnosis of appendicitis, but there was not any significant difference in terms of AST between the two groups. In addition, the mean ALT did not show any significant difference in people with acute and perforated acute appendicitis. The AUC for ALT for diagnosing acute appendicitis was 0.569, which lacked the necessary

efficiency to diagnose appendicitis (9). In the present study, similar to the above study, ALT and AST did failed to have the necessary efficiency to diagnose appendicitis. However, unlike the above study, the area under the AST curve was higher and AST displayed a significant discrepancy between the two groups with and without appendicitis, which is probably due to the differences in the studied populations. Furthermore, in the above study, similar to the present study, the levels of liver enzymes in the complicated and non-complicated types were not significantly different. While there are various theories about the reason for increased liver enzymes in patients with appendicitis, their increase may be in response to inflammatory processes in the body and damage to liver cells. Although more than half a century ago, the association of elevated liver enzymes and bilirubin levels with severe appendicitis infection was explained by Miller and Irvine, the mechanisms leading to the observed increase in bilirubin and liver enzymes are not yet fully understood (25). According to our experiment data, the mean serum glutamic-oxaloacetic transaminase (AST) was significantly different in the three groups (normal, simple appendicitis, and complicated) ($p<0.19$), but the mean serum glutamic pyruvic transaminase (ALT) failed to show a significant difference. The differential test showed that there was a significant difference between the two appendicitis groups and the normal group in AST ($p<0.05$), but not between the two appendicitis groups. The p-values of AST and ALT were 0.17 and 0.2, respectively. Therefore, the means of ALT and AST in different types of complicated appendicitis were not significantly different. The frequency of abnormal ALT and AST values was not significantly different based on the pain duration, pain site, and leukocytosis.

The two main pathogens isolated in acute appendicitis include *Bacteroides fragilis* and *Escherichia coli (E.coli)*, which cause endotoxemia and hepatic dysfunction due to infection and inflammation (26). Exposure to *E.coli* lipopolysaccharides results in an inflammatory cascade that regulates bile transporters, reduces hepatic metabolism, increases nitric oxide synthase-dependent NO (iNOS) production, and impairs apoptotic function of the hepatobiliary system (27). Animal models have also shown that both bacteria alter microcirculation and hepatic sinus damage (28). We demonstrated that in patients suffering from appendicitis, there was a significant increase in levels of AST, which may possibly occur due to the inflammatory reaction present in liver cells or liver injury. In a study by Khan *et al* on 50 patients undergoing appendectomy, it was reported that elevated AST and ALP fail to have high diagnostic value in acute appendicitis, while high ALT may be useful in potentially suspected cases of acute appendicitis (29).

Based on our trial results, using the ROC curve to determine the diagnostic accuracy of AST and ALT (with lower normal values < 31 in women, < 41 in men for ALT, < 31 in women and < 37 in men for AST), it was found that AST with area under the ROC=0.623, $p=0.005$, sensitivity of 0.61%, and specificity of 0.53% lacked the necessary diagnostic accuracy.

In a study of 80 patients with appendicitis, Yadav and Chandra stated that the liver enzymes, *i.e*, AST, ALT, and ALP increased, respectively in 28.75, 32.5, and 82.5% of patients, respectively. The sensitivity and specificity of ASR were 30.6 and 100%, respectively. The sensitivity and specificity of ALT were 34.6 and 100%, respectively. Also, the sensitivity and specificity of ALP were 80%, and 40%, respectively. The positive predictive values of AST, ALT, and ALP were 100, 100, and 95.45%, respectively. Finally, it was stated that liver function tests have good predictive properties and values, but low sensitivity can be utilized alongside the clinical examination and additional laboratory tests to evaluate people diagnosed with suspected acute appendicitis (4). The findings of a recent study were in line with our results. In the study conducted by Mishra *et al*, among patients with and without a pathological diagnosis of appendicitis, the prevalence of high AST were 43 and 3, ALT 5 and 1, and ALP 6 and 0, respectively. The sensitivity of AST, ALT, and ALP in the diagnosis of appendicitis were 25.7, 8.3, and 10%, respectively, and their specificity were 50, 83.3, and 100%, respectively, and the predictive value were 94, 100, and 100, respectively, indicating their low sensitivity (19). So far, numerous studies have been performed to find the biological causes or markers to diagnose patients with appendicitis, propose a

differential diagnosis, and reduce the number of patients experiencing surgical treatments (7). Efforts have also been made to identify biomarkers to differentiate between complicated and uncomplicated appendicitis. To date, many biomarkers associated with appendicitis and its complications have been identified, the most important and documented of which are WBC, CRP, bilirubin, and to some extent, liver enzymes. The mentioned biomarkers have generally shown high specificity despite the low sensitivity (30,31). The combination of biomarkers may increase diagnostic accuracy. For example, in a combined study, bilirubin, white blood cell count, and ALT had the highest predictive value in diagnosing appendicitis (9). In another study, a combination of serum bilirubin, ALT, and ANC levels showed the highest AUC levels (0.898, 95% confidence interval, 0.835-0.962, $p<0.001$) with an 86% accuracy in the diagnosis of appendicitis (25). However, the relevant biomarkers, unaccompanied or accompanied, may not be utilized as the main differential tool, but as an adjunct to the patients' clinical manifestations and symptoms.

Conclusion

Based on the results of the Kruskal-Wallis test, the mean AST was significantly different in the three groups (simple and complicated appendicitis and normal group) ($p=0.019$), but the mean of ALT failed to show a significant difference. A differential test showed that AST was significantly different between the simple and complicated appendicitis groups and the normal group ($p<0.05$), but no significant difference was observed between the complicated and simple appendicitis groups. In a comparison between the four groups of people suffering from appendicitis complications, the p-values for AST and ALT were 0.17 and 0.2, respectively, therefore the means of SPGT and AST in different types of appendicitis complication were not significantly different. The frequency of abnormal ALT and AST values was not significantly different based on the duration of pain, site of pain, and leukocytosis. Using the ROC curve to determine the diagnostic accuracy of AST and ALT, it was revealed that AST with AUC = 0.623, $p=0.005$, sensitivity=0.61%, and specificity=0.53% fail to have the required diagnostic accuracy (due to the very low sensitivity, and specificity and the area under the curve less than 0.7). On the other hand, ALT with AUC=0.43 and $p=0.16$ was found inefficient for diagnosing appendicitis due to specificity and sensitivity close to zero and the area under the curve of less than 0.5. According to the results of this study, it seems that increased AST may be increased in simple/complicated appendicitis in contrast to normal group. But regarding AUC curve data, AST and ALT do not have the necessary diagnostic accuracy and efficiency to diagnose acute appendicitis and predict its complications. Further research should be established to clarify the definite and exact impacts.

References

1. Shogilev DJ, Duus N, Odom SR, Shapiro NI. Diagnosing appendicitis: evidence-based review of the diagnostic approach in 2014. West J Emerg Med 2014 Nov;15(7):859-71.

2. Carr NJ. The pathology of acute appendicitis. Ann Diagn Pathol 2000 Feb;4(1):46-58.

3. Laal M, Granpaye L, Khodadi F, Salavatipour A, Sadeghi AR. Sonography versus the Alvarado Scoring System for the diagnosis of acute appendicitis. Tehran Univ Med J.2008;66(6):408-12.

4. Yadav S, Chandra K. Liver function test as a marker for acute appendicitis. Janaki Med College J Med Sci 2015;3(1):31-6.

5. Al-Abed YA, Alobaid N, Myint F. Diagnostic markers in acute appendicitis. Am J Surg 2015 Jun;209(6):1043-7.

6. Hosseini MM, Safdari R, Shahmoradi L, Javaherzadeh M. Better diagnosis of acute appendicitis by using artificial

intelligence. ISMJ 2017 Aug 10;20(4):339-48.

7. Aslanabadi S, Mofidi MA, Yosef Nezhad O, Maghsoodi H. Diagnostic Value of C-Reactive Protein for Detection of Acute Appendicitis in Adults. Razi J Med Sci 2009 Dec 10;16(2):44-9.

8. Kaya B, Sana B, Eris C, Karabulut K, Bat O, Kutanis R. The diagnostic value of D-dimer, procalcitonin and CRP in acute appendicitis. Int J Med Sci 2012;9(10):909-15.

9. Farooqui W, Pommergaard HC, Burcharth J, Eriksen JR. The diagnostic value of a panel of serological markers in acute appendicitis. Scand J Surg 2015 Jun;104(2):72-8.

10. Berenji M, EshaghHoseini N, GhaziSaeadi R, Vagharian V. Association rate of leukocytosis increased CRP and ESR with acute appendicitis. Ebnesina 2010 Apr 10;13(1):24-7.

11. Rouzrokh M, Fard FE, Momeni N, Tavassoli A. Diagnostic role of ESR, CRP, leukocytosis and Neutrophil/ Lymphocyte in peripheral blood smear in children under 14 with acute appendicitis. Pajoohandeh J 2011 Apr 10;16(1):42-6.

12. Falcone Jr RA. Appendicitis. Pediatr Clin Advisor 2007;50-1.

13. Humes D, Simpson J. Acute appendicitis. BMJ 2006 Sep 9;333(7567):530-4.

14. Acharya A, Markar SR, Ni M, Hanna GB. Biomarkers of acute appendicitis: systematic review and cost–benefit trade-off analysis. Surg Endosc 2017 Mar;31(3):1022-31.

15. Kryzauskas M, Danys D, Poskus T, Mikalauskas S, Poskus E, Jotautas V, et al. Is acute appendicitis still misdiagnosed? Open Med 2016 Jul 22;11(1):231-6.

16. Alhamdani YF, Rizk HA, Algethami MR, Algarawi AM, Albadawi RH, Faqih SN, et al. Negative Appendectomy Rate and Risk Factors That Influence Improper Diagnosis at King Abdulaziz University Hospital. Mater Sociomed 2018 Oct;30(3):215-20.

17. Alvarez-Alvarez F, Maciel-Gutierrez V, Rocha-Muñoz A, Lujan J, Ploneda-Valencia C. Diagnostic value of serum fibrinogen as a predictive factor for complicated appendicitis (perforated). A cross-sectional study. Int J Surg 2016 Jan;25:109-13.

18. Emmanuel A, Murchan P, Wilson I, Balfe P. The value of hyperbilirubinaemia in the diagnosis of acute appendicitis. Ann R Coll Surg Engl 2011 Apr;93(3):213-7.

19. Mishra BM, Nayak MK, Mishra S, Sahu P, Das D. Role of liver function test parameters in acute appendicitis and its complication: a prospective study. Int Surg J 2018 Dec 27;6(1):193-7.

20. Prystowsky JB, Pugh CM, Nagle AP. Appendicitis. Curr Probl Surg 2005 Oct;42(10):694-742.

21. Farrokh Tehrani D, Layegh P. Evaluation of CT scan in patients suspicious for acute appendicitis with negative or equivocal sonographic findings. Medical J Mashhad Univ Med Sci 2015;58(8):466-72.

22. Nyuwi KT, Singh CG, Khumukcham S, Rangaswamy R, Ezung YS, Chittvolu SR, et al. The role of serum fibrinogen level in the diagnosis of acute appendicitis. J Clin Diagn Res 2017 Jan;11(1):PC13.

23. Menteş O, Eryılmaz M, Harlak A, Oztürk E, Tufan T. The value of serum fibrinogen level in the diagnosis of acute appendicitis. Ulus Travma Acil Cerrahi Derg 2012 Sep;18(5):384-8.

24. Saadati K, Mahdi E. Prevalence of acute appendicitis complications in patients diagnosed with acute appendicitis admitted to Shafi'i Hospital and undergoing surgery. J Zanjan Med Sci 1996;1(22):34-45.

25. Nevler A, Berger Y, Rabinovitz A, Zmora O, Shabtai M, Rosin D, et al. Diagnostic Value of Serum Bilirubin and Liver Enzyme Levels in Acute Appendicitis. Isr Med Assoc J 2018 Mar;20(3):176-81.

26. Stringer MD. Acute appendicitis. J Paediatr Child Health 2017 Nov;53(11):1071-6.

27. Han X, Fink MP, Uchiyama T, Yang R, Delude RL. Increased iNOS activity is essential for hepatic epithelial tight junction dysfunction in endotoxemic mice. Am J Physiol Gastrointestinal Liver Physiol 2004 Jan;286(1):126-36.

28. Rink R, Kaelin C, Giammara B, Fry D. Effects of live Escherichia coli and Bacteroides fragilis on metabolism and hepatic pO2. Circ Shock 1981;8(5):601-11.

29. Khan S. Effect of Acute appendicitis on routine Liver function Tests. J Institute Med 2008;30(1):41-5.

30. McGowan DR, Sims HM, Zia K, Uheba M, Shaikh IA. The value of biochemical markers in predicting a perforation in acute appendicitis. ANZ J Surg 2013 Jan;83(1-2):79-83.

31. Burcharth J, Pommergaard H, Rosenberg J, Gögenur I. Hyperbilirubinemia as a predictor for appendiceal perforation: a systematic review. Scand J Surg 2013;102(2):55-60.