Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Which simple laboratory test is better to differentiate acute complicated and noncomplicated appendicitis?

Akile Zengin[a,*], Yusuf Murat Bag[b], Mehmet Zeki Ogut[c], Kutay Saglam[c]

[a] *Malatya Training and Research Hospital, Department of Gastrointestinal Surgery, Malatya, Türkiye*
[b] *Van Training and Research Hospital, Department of Gastrointestinal Surgery, Van, Türkiye*
[c] *Inonu University, Faculty of Medicine, Department of General Surgery, Malatya, Türkiye*

ARTICLE INFO

Keywords:
Appendectomy
Abdominal pain
Serum marker
Prognosis

Received: Mar 15, 2022
Accepted: May 30, 2022
Available Online: 25.07.2022

DOI:
10.5455/annalsmedres.2021.12.661

Abstract

Aim: To investigate the clinical significance of the simple laboratory test values on differentiating complicated acute appendicitis.

Materials and Methods: We retrospectively examined the medical records of 216 acute appendicitis patients. Patients were divided into two groups according to pathological results (non-complicated (n=157) and complicated (n=59)). The demographic and clinical data, laboratory findings, length of hospital stay, and pathological results were compared between the two groups. Receiver operating characteristics (ROC) curves were performed to analyze the optimal cutoff value of numerical variables which were significantly differed between the group comparisons.

Results: The preoperative data were similar between the groups except for age. The length of hospital stay was longer and total/direct bilirubin levels higher in the complicated group (p=0.002, p=0.002, and p=0.002, respectively. The lymphocyte level and amylase level were lower in the complicated group (p=0.02 and p=0.004, respectively). ROC curve analysis provided a cutoff value of ≥0.89 mg/dL for total bilirubin, ≥0.43 mg/dL for direct bilirubin, ≤1.63% for lymphocyte and ≤46.5 U/L for amylase.

Conclusion: Preoperative higher total and direct bilirubin levels are able to predict complicated appendicitis. Preoperative higher serum amylase levels should not have a place in the differential diagnosis of complicated appendicitis. This means that if serum amylase is elevated in a patient with suspected acute appendicitis, it does not suggest acute complicated appendicitis.

Introduction

Acute appendicitis is the most common cause of acute surgical abdomen [1]. The distinction between acute complicated and uncomplicated appendicitis is important in the management of patients with suspected acute appendicitis. Because nowadays, patients with acute uncomplicated appendicitis can be followed conservatively with antibiotics, whereas patients with acute complicated appendicitis undergo surgery [2]. Delays in diagnosis and treatment increase the rates of perforation, morbidity, mortality, and prolong the length of hospital stay [1]. Ultrasonography (USG), computerized tomography (CT), and magnetic resonance imaging, which are preoperative diagnostic imaging methods, are easily accessible in central hospitals, but this is not always possible in rural areas. Preoperative diagnosis of acute appendicitis can be made rapidly with inexpensive laboratory tests [3]. However, specific biomarkers are needed to distinguish acute complicated and acute non-complicated appendicitis. Two of these biomarkers are the serum bilirubin level and serum amylase level. In this study, we aimed to investigate the diagnostic value of simple biomarkers on the clinical distinction of acute complicated and acute non-complicated appendicitis.

Materials and Methods

This study was approved by the local ethical committee (2021/2097). Two hundred and thirty-two patients underwent appendectomy between January 2017 and January 2019. The inclusion criteria were the age ≥18 years and the primary diagnosis of acute appendicitis. Sixteen patients were excluded due to diagnoses other than acute appendicitis (e.g. normal pathology, mucocele, mesenteric cyst, or elective appendectomy for plastron appendicitis), appendectomies performed as a part of another procedure (e.g. laparoscopic colon resection or gynecolog-

*Corresponding author:
Email address: dr.akile.zengin@gmail.com (Akile Zengin)

ical surgery), and concomitant liver or gall bladder diseases. Finally, two hundred and sixteen patients were included in the study. Age, gender, length of the symptoms, white blood cell count (WBC) (10^3/uL), mean platelet volume (MPV) (fL), platelet distribution width (PDW) (fL), platelet (Plt) count (10^3/uL), lymphocyte count (10^3/uL), platelet/lymphocyte ratio (PLR), red cell distribution width (RDW) (fl), serum Alanine amino transferase ALT (IU/L), serum Aspartate amino transferase AST (IU/L), serum total bilirubin (mg/dl) level (normal value between 0.2-1.2 mg/dl), serum direct bilirubin (mg/dl) level (normal value between 0-0.5 g/dl), serum amylase level (normal value between 20-120 (U/L)), radiological data (appendix diameter), length of hospital stay, and pathological data were analyzed retrospectively. The patients were divided into two groups as non-complicated (n= 157) and complicated (n=59) according to the pathological results. The pathological diagnoses of suppurative appendicitis, plastron appendicitis, perforated appendicitis, and gangrenous appendicitis were defined as complicated appendicitis. The pathological findings conformable with edematous, inflamed appendicitis were defined as non-complicated appendicitis. The venous blood samples were drawn within 1 hour of the patient's admission to the emergency department. The clinical diagnosis of acute appendicitis was done preoperatively by clinical findings, physical examination, laboratory tests, and imaging methods. USG was performed for all patients but, CT was used selectively. Appendix diameter was defined as the largest diameter measured on USG. Written informed consent was obtained from patients before surgery. All operations were performed laparoscopically.The operations were performed by the senior surgeon or training surgeons under the supervision of the senior surgeon. The details of the surgical procedure are as follows: The pneumoperitoneum was created from the subumbilical region by a Veres needle and the intraabdominal pressure was kept between 12-14 mmHg during the operation. A 10-mm trocar was inserted into the abdomen in the subumbilical region and the camera was introduced through this trocar. Two more trocars were positioned. The first one (5-mm) was placed in the midline just above the pubis and the second one (10-mm) in a point on the left side, symmetrical to the McBurney point. The appendicular artery was coagulated with an electrothermal bipolar vessel sealing device. Appendectomy was completed by using two handmade endoloops or polymer ligating clips and the appendix was extracted in a handmade bag made of a surgical glove [4].

Statistical analysis

We used the IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) for statistical analyses. The Shapiro-Wilk test was performed to determine the normality of the distribution of numerical variables. Numerical variables were defined as median (minimum-maximum) and were compared with the Mann–Whitney U-test. Categorical variables were defined as frequency (percentage) and were analyzed by using the chi-square tests. Receiver operating characteristics (ROC) curves were performed to analyze the optimal cutoff value of numerical variables which were significantly differed between the group comparisons. A two-sided P-value of less than 0,05 was considered significant.

Results

Table 1 shows the demographic data, preoperative findings, and postoperative variables of the patients. Most of the patients were male (n=116, 53.7%). There were no significant differences between the groups in terms of gender, the length of symptoms, WBC value, MPV value, PDW value, plt value, PLR, RDW value, ALT, AST, and preoperatively measured appendix diameter. The patients in the complicated group were older (p=0.01). The complicated group had significantly lower amylase and lymphocyte levels (p=0.004 and p=0.02, respectively) and significantly higher total/direct bilirubin levels (p=0,002/p=0,002, respectively) compared to the non-complicated group. And also the length of hospital stay was significantly longer in the complicated group (p=0,002). ROC curve analysis of lymphocyte count, serum total/direct bilirubin levels, and serum amylase levels in predicting the acute complicated appendicitis are shown in Table 2. All parameters were able to predict acute complicated appendicitis, but the serum total bilirubin level ≥0.89 mg/dL was the strongest. Serum direct bilirubin level ≥0.43 mg/dL was the most specific parameter, while serum amylase level ≤46.5 U/L was the most sensitive parameter.

Discussion

In this study, we found that patients with acute appendicitis were more likely to be complicated when serum amylase value was ≤46.5 U/L, serum total bilirubin value was ≥0.89 mg/dL, and serum direct bilirubin value was ≥0.43. Serum total bilirubin value was better than the others in predicting acute complicated appendicitis.

Acute complicated appendicitis (perforated, gangrenous, plastron) is about 20-30% of all acute appendicitis [5]. Acute complicated appendicitis is related to increased postoperative complications rate, delayed recovery, prolonged hospital stay, and increased medical financial charge [6]. Clinical findings and physical examination are the important scales of acute appendicitis diagnosis, although the various diagnostic methods are available. Additionally, laboratory tests are leading in the diagnosis of acute appendicitis [7].

Some previous studies stated that increased serum bilirubin level was able to predict appendix perforation [1,8]. Bacterial transmigration after acute appendicitis causes the release of proinflammatory cytokines. These cytokines are carried to the liver via the superior mesenteric vein and cause inflammation, hepatic abscess, or liver failure [9]. This results in increased serum bilirubin levels and decreased bilirubin breakdown in the liver [10]. In the literature, there are publications defending the idea that all elevations of serum bilirubin levels can be considered a marker of perforated appendicitis, while a normal serum bilirubin level does not exclude perforation [2,10,11]. In this study, we concluded that elevated serum total and direct bilirubin levels are predictors of acute complicated appendicitis. In contrast to this, Adams et al. found no significant difference between acute perforated and non-perforated appendicitis (p = 0.326) in serum bilirubin level

Table 1. Demographic data, preoperative findings and postoperative variables of the patients.

	Study group (n=216)	Noncomplicated appendicitis group (n=157)	Complicated appendicitis group (n=59)	P value
Gender (male)	116 (53.7%)	80 (51%)	36 (61%)	0.18
Age (year)	32 (17-86)	30 (17-86)	35 (18-85)	0.01
Length of symptoms (hour)	24 (1-240)	24 (1-120)	24 (4-240)	0.7
WBC (10^3/uL)	12.5 (3.9-28.2)	12.5 (3.9-23)	13.5 (5.4-28.2)	0.2
MPV (fL)	10.2 (6.6-14.5)	10.2 (6.8-14.3)	10.1 (6.6-14.5)	0.8
PDW (fL)	12.3 (8.3-23.9)	12.3 (8.3-21.6)	12.2 (9.6-23.9)	0.8
Plt (10^3/uL)	242 (16-462)	248 (53-462)	240 (16-340)	0.4
Lymphocyte (10^3/uL)	1.9 (0.4-5.8)	2 (0.4-5.8)	1.6 (0.4-4.1)	0.02
PLR	120.5 (8-810)	116.2 (21.1-810)	126.7 (8-555.8)	0.1
RDW (fl)	12.9 (11-117)	12.9 (11-117)	12.9 (11.3-17.2)	0.7
Total bilirubin (mg/dl)	0.67 (0.19-3.73)	0.61 (0.19-2.33)	0.88 (0.24-3.73)	0.002
Direct bilirubin (mg/dl)	0.25 (0.10-1.46)	0.23 (0.10-0.70)	0.30 (0.10-1.46)	0.002
ALT (IU/L)	17 (6-243)	16 (6-83)	19 (6-243)	0.1
AST (IU/L)	20 (10-247)	19 (10-74)	20 (10-247)	0.4
Amylase (U/L)	52 (14-174)	57 (14-174)	46 (22-117)	0.004
Appendix diameter on USG (mm)	9 (4-120)	9 (4.5-120)	10 (4-15)	0.07
Length of hospital stay (day)	2 (1-15)	1 (1-13)	2 (1-15)	0.002
Pathology	216 (100%)			
Acute appendicitis		157 (100%)		
Suppurative appendicitis			30 (50.8%)	
Plastron appendicitis			3 (5%)	
Perforated appendicitis			24 (40.7%)	
Gangrenous appendicitis			2 (3.5%)	

WBC: White blood cell MPV: Mean platelet volume PDW: Platelet distribution width Plt: Platelet PLR:Platelet/ lymphocyte ratio RDW: Red cell distribution width ALT: Alanine amino transferase AST: Aspartate amino transferase USG: Ultrasonography.

Table 2. ROC curve analysis of predictors of acute complicated appendicitis.

		95% CI					
	AUC	Lower limit	Upper limit	Sensitivity	Specificity	Cut-off value	P value
Lymphocyte count (10^3/uL)	0.602	0.519	0.685	50.8%	70.3%	$\leq$ 1.63	0.022
Amylase (U/L)	0.633	0.545	0.721	50.9%	73.3%	$\leq$ 46.5	0.004
Total bilirubin (mg/dl)	0.642	0.558	0.725	50.0%	73.7%	$\geq$ 0.89	0.002
Direct bilirubin (mg/dl)	0.638	0.551	0.724	35.6%	88.2%	$\geq$ 0.43	0.002

ROC: Receiver operating characteristics 95% CI: 95% confidence interval.

however there was a difference between normal appendix and acute appendicitis [12].

A high serum amylase level does not occur only in acute pancreatitis but also in non-pancreatic acute abdomen [13]. Cholecystitis, gastroenteritis, parotitis, intestinal obstruction, pancreatic duct or bile duct obstruction, peptic ulcer perforation, ectopic pregnancy are some causes of non-pancreatic acute abdomen [14]. In a case report, a 60-year-old morbidly obese patient was followed up with biliary pancreatitis due to high serum amylase level (1029 IU/L), and the autopsy revealed that the cause of death was perforated appendicitis and related generalized peritonitis [13]. Starch-degrading organisms in the infected appendix are blamed for the increase in serum amylase levels [14]. As a result of this study, contrary to the literature, no relationship was found between higher amylase levels and acute complicated appendicitis. And also we found that patients with lower serum amylase level were more likely to have acute complicated appendicitis.

Study limitations

There are some limitations to our study. First, this study was retrospective Second, the number of patients included, and the data obtained were limited. Third, the associations of total and direct bilirubin value with prognosis and postoperative complications were not examined.

Conclusion

Patients with acute appendicitis may have complicated one if there have elevated serum total/direct bilirubin. The cut-off values were 0.89 mg/dl and 0.43 mg/dl, respectively. In addition, higher serum amylase levels should not have a place in the differential diagnosis of complicated appendicitis. This means that if serum amylase is elevated in a patient with suspected acute appendicitis, it does not suggest acute complicated appendicitis.

Ethics approval

This study was approved by the Inonu University ethical committee (2021/2097).

References

1. Goudar BV, Kanchan VR. Elevated serum bilirubin in acute appendicular perforation as a newer serum marker: a diagnostic validation test. Int Surg J. 2020;7(2):414–8.
2. Eddama MMR, Fragkos KC, Renshaw S, Aldridge M, Bough G, Bonthala L, et al. Logistic regression model to predict acute uncomplicated and complicated appendicitis. Ann R Coll Surg Engl. 2019;101(2):107–18.
3. Doğan S, Kalafat UM, Bildik B, Sarıcı İŞ, Cander B. Diagnostic Value of C-Reactive Protein/Albumin Ratio to Differentiate Simple Versus Complicated Appendicitis. Eurasian J Emerg Med. 2020;19(3):178-83.
4. Isik A, Demiryilmaz I, Yilmaz I, Firat D, Cimen O, Eken H. Effectiveness of manual knotting at laparoscopic appendectomy. Gazi Med J. 2016;27(1):19–20.
5. Bedel C. Diagnostic value of basic laboratory parameters for simple and perforated acute appendicitis. Turk J Clin Lab. 2018;9(4):266–71.
6. Ünal Y. A new and early marker in the diagnosis of acute complicated appendicitis: immature granulocytes. Ulus Travma Acil Cerrahi Derg. 2018;24(5):434–9.
7. Sand M, Trullen XV, Bechara FG, Pala XF, Sand D, Landgrafe G, et al. A prospective bicenter study investigating the diagnostic value of procalcitonin in patients with acute appendicitis. Eur Surg Res. 2009;43(3):291–7.
8. Atahan K, Üreyen O, Aslan E, Deniz M, Çökmez A, Gür S, et al. Preoperative diagnostic role of hyperbilirubinaemia as a marker of appendix perforation. J Int Med Res. 2011;39(2):609–18.
9. MoulaBux K, Parveen S, Iqbal M, Mehboob A. The effect of acute complicated appendicitis on liver function test. Pak J Med Sci. 2021;37(2):351-4.
10. Kanlioz M, Karatas T. The Relationship of Perforated Appendicitis with Total and Direct Bilirubin. Cureus. 2019;11(12).
11. Käser SA, Fankhauser G, Willi N, Maurer CA. C-reactive protein is superior to bilirubin for anticipation of perforation in acute appendicitis. Scand J Gastroenterol. 2010;45(7–8):885–92.
12. Adams HL, Jaunoo SS. Hyperbilirubinaemia in appendicitis: the diagnostic value for prediction of appendicitis and appendiceal perforation. Eur J Trauma Emerg Surg. 2016;42(2):249–52.
13. Forster MJ, Akoh JA. Perforated appendicitis masquerading as acute pancreatitis in a morbidly obese patient. World J Gastroenterol WJG. 2008;14(11):1795-6.
14. Salih IK, Al-Dabbagh AJ, Hassan QA. The Value of Inflammatory Markers in Acute Appendicitis: A diagnostic accuracy study. Pak J Med Health Sci. 2017;11(4):1607–11.