



Evaluation of Diagnostic Threshold of Amylase and Lipase Enzymes in Diagnosis of Acute Pancreatitis and Their Sensitivity and Specificity

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Abstract

Objectives: Every sudden and non-traumatic disorder with a major clinical manifestation in the abdomen is considered as an acute abdomen and requires urgent surgery, considering the fact that it is a cause of acute pancreatitis, which is usually associated with increased blood amylase and lipase levels. Therefore, the diagnostic value of amylase, lipase enzymes, their sensitivity, and specificity along with their positive and negative predictive value in the diagnosis of acute pancreatitis were evaluated.

Materials and Methods: This descriptive-analytical study examined 244 patients who referred to Imam Reza and Sina Hospitals of Tabriz. The diagnostic values of two thresholds of 110 and 550 IU/L for amylase, and 80 and 400 IU/L for lipase were studied.

Results: The results showed that 142 (58.2%) of the patients were female. The mean age was 57.97 ± 21.22 years old. Eighty-one patients (33.2%) had acute pancreatitis. At a cut-off of 110 IU/L, the sensitivity, specificity, positive predictive value, and negative predictive value of amylase enzyme were 0.762, 0.407, 0.736 and 0.988 and at a cut-off of 550 IU/L, they were 0.598, 0.943, 0.876 and 0.77, respectively. In the case of lipase, at cut-offs of 80 and 400 IU/L, the sensitivity of 0.84 and 0.519, the specificity of 0.552 and 0.847, positive predictive value of 0.482 and 0.627, negative predictive value of 0.874 and 0.87.

Conclusions: The results showed that as the detection threshold increased, the specificity of tests increased, but the sensitivity decreased. In addition, studying the level of lipase and amylase enzymes can help in the diagnosis of acute pancreatitis.

Keywords: Pancreatitis, Amylase, Lipase, Cut off, Sensitivity, Specificity

Introduction

Acute abdominal pain is an emergency condition in patients referred to the emergency or surgery department and the blood test is usually used for diagnosis. Acute pancreatitis is an inflammatory pancreatic disease with or without fibrosis, which is affected by several factors such as gallstones, alcohol use, trauma, infection and, in some cases, heredity. Often, patients with acute pancreatitis suffer from other complications, such as septic shock, as well as renal and pulmonary failure, which is significantly associated with morbidity and mortality (1). Gallstones and alcohol addiction are the causes of 80% to 90% of the cases and the remaining 10% to 20% have resulted from an idiopathic disease or various causes, such as trauma, surgery, drugs, inheritance, infection and toxins (2).

Usually, most acute pancreatitis attacks occur with intense pain after eating; the pain is usually epigastric, but it can occur in any part of the abdomen or the lower chest. It is described as a stabbing or shooting pain in the back, which can be removed by bending forward. After

the onset of pain, nausea and vomiting occur and nausea continues after gastric emptying (3).

Since pancreatic acinar cells synthesize, store, and secrete a large number of digestive enzymes (such as amylase, lipase, trypsinogen and elastase), the level of these enzymes increases in pancreatitis. Usually, at the outbreak of the disease, the serum amylase concentration increases, reaching its peak in a few hours, and its reduction to normal levels take 3 to 5 days. However, in patients with hyperlipidemia, amylase might be at the normal level (4). In patients with acute abdominal pain, serum amylase and lipase test are widely used as the initial diagnostic test (5). In addition, in acute pancreatitis, the level of lipase is 5 to 10 times higher than normal levels, and the lipase level is elevated 24 to 48 hours after the pancreatitis attack and returns to normal after 5 to 7 days (6).

The accuracy level of lipase and amylase tests in detecting acute pancreatitis is significantly related to the selective diagnostic thresholds (2,5,7-11). However, some researchers have also reported that the measurement



of amylase levels is not necessary for diagnosing acute pancreatitis (12,13).

Some researchers believe that for confirming acute pancreatitis, amylase levels should be more than normal in at least 3 consecutive tests so that the occurrence of pancreatitis can be confirmed (4). It was suggested that the specificity and the sensitivity rate of lipase are higher in the diagnosis of acute pancreatitis (14,15). Therefore, with respect to different expressed ideas, this study aimed to determine the diagnostic value of amylase, lipase, sensitivity, specificity, positive and negative predictive values of each one in the diagnosis of acute pancreatitis in the patients hospitalized in Sina and Imam Reza hospitals of Tabriz during 2013 to 2014.

Materials and Methods

The present study was conducted as a descriptive and analytical study on the patients hospitalized in Imam Reza and Sina hospitals of Tabriz during 2013 to 2014. Patients who simultaneously received both amylase and lipase tests were studied in this study. Based on the diagnostic criteria, patients with pancreatitis were included in the study and patients without pancreatitis were excluded. Two cutoffs were used for evaluating the patients. The first cut-off for amylase was 110 IU/L and 80 IU/L for lipase, and the second, 5 times more than the normal range, was 550 IU/L for amylase and 400 IU/L for lipase. All the studied variables were introduced in the researcher-made checklist, all the information used was recorded confidentially, and there was no treatment interference. All data were introduced into SPSS statistical software version 22.00 and was analyzed statistically.

Finally, sensitivity, specificity and positive, as well as the negative predictive value of lipase and amylase were

evaluated in the diagnosis of acute pancreatitis.

Results

In this study, 244 patients with abdominal pain were studied, which included 102 males and 142 females. The mean age was 57.97 ± 21.22 years old, ranging from less than 10 to over 80 years old. The study results showed that amylase and lipase levels in the patients with acute pancreatitis were significantly higher compared to all patients (Table 1).

The results of Table 2 showed that in patients with acute pancreatitis, the cut-off rates above 550 and 400 IU/L were significantly higher compared with all patients, for amylase and lipase, respectively.

The results of studying the role of amylase in the diagnosis of acute pancreatitis showed that it has good sensitivity, specificity and negative predictive value, at a cut-off of 110 IU/L but it lacks suitable diagnostic power due to its positive predictive value. The results indicated that there is high specificity, negative predictive value, positive predictive value, and ROC but low sensitivity at a cut-off of 550 (Table 3 and Figure 1).

The study results of the lipase enzyme role in the diagnosis of acute pancreatitis showed that it has a high sensitivity and negative predictive value, at a cut-off of 80 IU/L, but it has low diagnostic power due to its specificity level and positive predictive value. The results demonstrate that the cut-off of 400 IU/L has a high specificity, negative predictive value, and a good ROC, but its sensitivity and positive predictive values are low (Table 4 and Figure 2).

Discussion and Conclusions

The accuracy of lipase and amylase tests in detecting acute pancreatitis depends on the selective diagnostic thresholds, and with respect to different diagnostic thresholds in these tests, different sensitivity and specificity can be obtained, and the diagnostic accuracy of these tests depends on the sensitivity and specificity at the selected threshold (7).

Researchers have stated that routine amylase and lipase measurements cannot have a good diagnostic value in the diagnosis of acute abdominal pain, and it can be a

Table 1. Amylase and Lipase Levels in All the Patients and the Patients With Acute Pancreatitis

Enzymes	All Patients	Acute Pancreatitis	P Value
Amylase	179.98±301.92	451.42±374.35	0.021
Lipase	241.00±424.22	460.77±646.55	0.016

Table 2. Frequency of Different Levels of Amylase and Lipase in All the Patients and Patients With Acute Pancreatitis

Group	Amylase (IU/L), No. (%)			Lipase (IU/L) No. (%)		
	110<	110-550	550>	80<	80-400	400>
All patients	137 (56.1)	72 (29.5)	35 (14.3)	103 (42.2)	74 (30.3)	67 (27.5)
Acute pancreatitis	17 (21.0)	31 (38.3)	33 (40.7)	13 (16.0)	26 (32.1)	42 (51.9)

Table 3. The Levels of Sensitivity, Specificity, PPV, NPV, and ROC Curve Level for Amylase

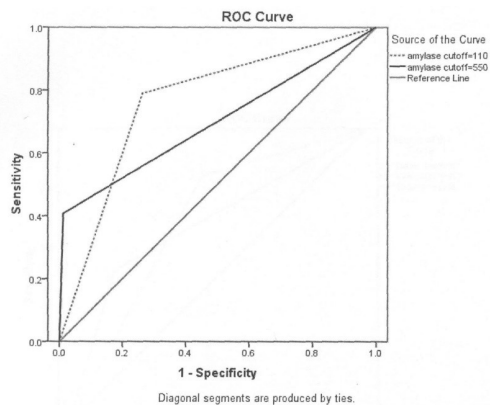
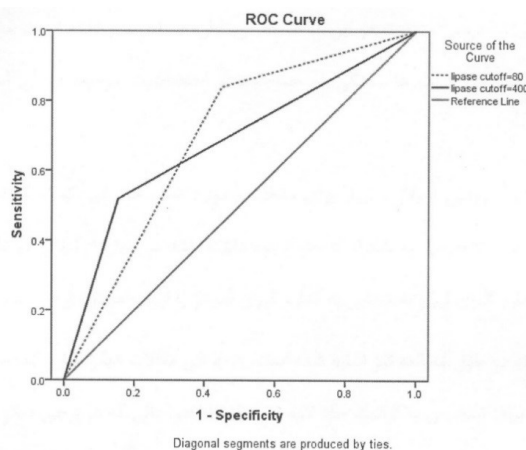
Cut off (IU/L)	Real Positive	Real Negative	False Positive	False Negative	Sensitivity	Specificity	PPV	NPV	ROC Curve	
									Level	P Value
110	64	120	43	17	0.790	0.736	0.598	0.876	0.763	0.001
550	33	161	2	48	0.407	0.988	0.943	0.770	0.698	0.001

Abbreviations: PPV, positive predictive value; NPV, negative predictive value

Table 4. Sensitivity, Specificity, PPV, NPV, and ROC Curve Levels for Lipase

Cut off (IU/L)	Real Positive	Real Negative	False Positive	False Negative	Sensitivity	Specificity	PPV	NPV	ROC Curve	
									Level	P Value
80	68	90	73	13	0.840	0.552	0.482	0.874	0.696	0.001
400	42	138	25	39	0.519	0.847	0.627	0.780	0.683	0.001

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

**Figure 1.** ROC Curve for Amylase Values.**Figure 2.** ROC Curve for Lipase Values.

good diagnostic test only in the cases where the risk of acute pancreatitis is likely (16). Some researchers do not consider the amount of amylase and lipase enzymes necessary for diagnosing acute pancreatitis (13), while some others believe that evaluating these two enzymes is necessary for the diagnosis of acute pancreatitis (7). In addition, some researchers have found it adequate to evaluate lipase assessments for the diagnosis of acute pancreatitis, arguing that the selective cut-off is effective in the sensitivity and specificity of this test (11).

The results of a study showed that the average age of the subjects was 49.6 years, the highest prevalence was in middle-aged people, with the age of more than 45 (5). The results found by the researchers showed that of 508 patients studied, 108 (35%) patients had acute pancreatitis, of whom 36% were males and 64% were females. In

addition, in the present study, 81 (33.2%) people had acute pancreatitis, of whom 41.8% were male and 58.2% were female. In total, the incidence rate of acute pancreatitis was higher in women than men, probably suggestive of the prevalence of triglycerides and inactivity in women. The age of the patients ranged from 50 to 70 years old, which was consistent with our study, while in another study, the age ranged from 30 to 70 years old, which is probably due to the incidence of triglyceridemia and inactivity in women.

The results of the researches showed that, for diagnosing acute pancreatitis, the amount of amylase should be greater than normal levels in at least 3 successive tests. However, as its cut-off level increases to 1000 IU/L (three times more than the normal maximum), its specificity increases to about 95%, but its sensitivity decreases to 61% (4). In addition, the results of the present study showed that increasing the cut-off rate from 110 to 550 IU/L reduced the sensitivity from 79% to 49%, and increased the specificity from 74% to 99%. The results also showed that the negative predictive value was higher at both cut-offs, while the positive predictive value lacked good diagnostic value at a cut-off of 110 IU/L, unlike the cutoff of 550 IU/L which had a good diagnostic value. The study results indicated that high and low cut-offs have good diagnostic value for diagnosing the healthy cases, and the results are consistent with the results of previous researchers in this field.

Serum lipase retains its high levels for a longer time compared with serum amylase, having a good sensitivity in terms of diagnosis in the patients who develop the symptoms later. Factors such as triglyceridemia, Furosemide medication, and others can affect lipase levels, though the lipase seems to be more accurate than amylase in terms of diagnosis. The researchers reported that the specificity of lipase enzyme levels at a cut-off of 600 IU/L was 95% and its sensitivity was 55 to 100% and with the increase of cutoff to above 600 IU/L, its specificity increased, while its sensitivity reduced (4).

The results of the present study also showed that as the cut-off increases from 80 to 400 IU/L, the test specificity increases from 55% to 85% as well, and the sensitivity decreases from 84% to 52%. While both cut-offs had good negative predictive value, they had low positive predictive value; hence, they lacked a good diagnostic value.

It was indicated that the cut-off 5 times more than normal range has 99% specificity and 39% sensitivity,

and a positive predictive value of 50% and the cut-off 3 times more than normal range has 99% specificity and 50% sensitivity, and a positive predictive value of 51%. In the case of lipase, the cut-off 5 times more than normal has 98% specificity and 57% sensitivity, and a positive predictive value of 50%. In addition, at a cut-off 3 times higher than the normal range, the specificity was 97% and sensitivity was 64%, and the positive predictive value was 41% (5).

The results of the present study showed that as the cutoff for amylase decreases from 550 to 110 IU/L, the sensitivity increases from 40% to 79% and the specificity decreases from 99 to 74% and the negative predictive value increases from 77% to 87%, and the positive predictive value decreases from 61% to 43%. In the case of lipase, as the cut-off decreases from 400 to 80 IU/L, the sensitivity increases from 52% to 84%, and the specificity decreases from 85% to 55%, the negative predictive value increases from 78 to 87%, and the positive predictive value decreases from 58% to 44%. The study results indicate that lower and higher cut-offs are better predictors of healthy and disease cases, respectively.

The results of the study by researchers showed that at a cut-off of 110 IU/L for amylase, the positive predictive value was 38%, and the negative predictive value was 95%. Moreover, at a cut-off of 240 IU/L for lipase, the positive predictive value was 78% and the negative predictive value was 99% (7), which was inconsistent with the results of the present study. The results of previous studies also suggested that these tests serve better in predicting healthy people, but clinical symptoms should be used in identifying the patients. Researchers reported that as the cut-off for amylase increases, the specificity and the sensitivity rates amount to 95% and 60%, respectively (2).

The results of the present study showed that the diagnostic power of amylase (the surface below ROC curve) at cut-offs of 110 and 550 IU/L were 76% and 70%, respectively, while the diagnostic power of lipase at cut-offs of 80 and 400 IU/L were 70% and 68%, respectively. The results show that the diagnostic power at a cut-off of 110 IU/L for amylase and 80 IU/L for lipase is more appropriate. At a cut-off of 240 IU/L for amylase, the sensitivity, specificity, and the diagnostic power were 69%, 89% and 76%, respectively, and at a cut-off of 800 IU/L for lipase, the sensitivity, specificity, and the diagnostic power were 80%, 84% and was 82%, respectively (17).

The results of the present study showed that if clinical signs of pancreatitis occur, a slight increase in lipase is also sufficient for diagnosis. Also, the results showed that as the diagnostic threshold increases, the specificity of the tests increases as well, while their sensitivity decreases. Moreover, negative predictive values were acceptable at different diagnostic thresholds, while the positive predictive value was unacceptable, except at a cut-off of 550 IU/L for amylase, inconsistent with the clinical results; however, the results of this study showed that the

levels of lipase and amylase enzymes can be helpful in the diagnosis of acute pancreatitis.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The ethical committee of Islamic Azad University approved the study (Ethical No. IR.IAU.TABRIZ.REC.1396.89).

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