

Original Research Article

Diagnostic accuracy of serum lipase and amylase as biomarkers for acute pancreatitis

Anil Kumar*, Sangeeta Kapoor

Department of Biochemistry, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

Received: 02 March 2018

Accepted: 29 March 2018

***Correspondence:**

Dr. Anil Kumar,
E-mail: dr.netin@gmail.com

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ABSTRACT

Background: Currently, majority of clinicians ask for both amylase and lipase for diagnosis of acute pancreatitis but a large number of health care facilities in India still have facility for only amylase. Aim was to find which single marker to be used in for diagnosis of acute pancreatitis.

Methods: Patients seeking care at emergency department for acute abdominal pain during the period from July 2016 to June 2017 formed the study population. The serum lipase and amylase were taken from 1725 patients. Diagnostic accuracy, sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios were calculated.

Results: Sixteen patients had amylase above 3-fold elevation, while there were 26 such patients in the lipase group. The sensitivity and specificity of amylase at 3-fold above normal limit were 62.8% and 99.2% while those of lipase were 96.1% and 99.1% respectively. Both amylase and lipase had high accuracy index in the area under the ROC curve (0.990 and 0.997 respectively).

Conclusions: In this study, serum lipase had better diagnostic accuracy as compared to serum amylase. In resource-constrained settings with limited lab and radiological facilities, serum lipase should be preferred over serum amylase for diagnosis of acute pancreatitis.

Keywords: Acute pancreatitis, Amylase, Diagnostic biomarkers, Lipase

INTRODUCTION

It's well known fact that acute pancreatitis is a common surgical emergency. Acute pancreatitis, the inflammatory disorder of the pancreas, is one of the most common gastrointestinal causes of hospital admission.

The overall mortality rate can be as low as 5% but mortality rate can raise up to 20-25% due to severe complications which may require admission to intensive care unit.^{1,2} An essential part of acute pancreatitis' management is the evaluation of pancreatic enzymes, specifically serum amylase and lipase. Serum amylase has been used as a diagnostic tool for acute pancreatitis

since long. It is well known for its low cost and easy assay technique.³ Though it has low sensitivity, ranging from 55-84%.⁴ The occasional failure to detect a rise in serum amylase is due to the short half life of the enzyme or depleted pancreatic tissue in some patients, e.g. chronic pancreatitis. Besides, there is a long list of differential diagnosis of hyperamylasemia.⁵

Currently, majority of clinicians ask for both amylase and lipase for diagnosis of acute pancreatitis. But its hard fact that a large number of health care facilities in India still have facility for only amylase as it is the only enzymatic marker available. Therefore, keeping scenario of resource-constrained settings with limited lab and

radiological facilities in mind, it was planned to evaluate diagnostic accuracy of serum lipase and amylase as biomarkers for acute pancreatitis. Thus, the aim of the study was to find which single marker to be used in for diagnosis of acute pancreatitis.

METHODS

The present study was planned and executed by the Department of Biochemistry in collaboration with emergency and radiology departments of a tertiary care teaching center of western Uttar Pradesh. Patients seeking care at emergency department for acute abdominal pain during the period from July 2016 to June 2017 formed the study population. Only those cases were included in the study whose blood samples were drawn and acute pancreatitis was suspected. Those cases who were clinically unlikely to be acute pancreatitis and with normal amylase and lipase were presumed not having acute pancreatitis. Such cases were excluded from this study. Subjects with coexistent pathologies like parotid disease, intracranial haemorrhage, end-stage renal disease, causing the rise in amylase or lipase were also excluded.

The laboratory data of amylase and lipase were retrieved for study subjects who presented during study period with acute abdominal pain and blood taken for the above investigation. Clinical records and reports of the study subjects served as study tools. Their clinical records were then traced and retrieved from Medical Records Department (MRD), the central laboratory, biochemistry department and radiology department. The diagnosis of acute pancreatitis requires two of the following three features, characteristic abdominal pain, levels of serum amylase or serum lipase, or both, that are three or more times the upper limit of normal and findings of acute pancreatitis on computed tomography. For the purpose of this study, the gold standard method was defined as those with clinical diagnosis of acute pancreatitis supported by radiological evidence, either by ultrasonography (USG) or computed tomography (CT). Patients with a confirmed diagnosis of acute pancreatitis were listed down. Their

records were examined if the cases fulfilled the criteria of the gold standard. Samples were collected within 12 to 38 hours of onset of abdominal pain. A serum amylase level 2 or 3 time above normal is considered to be acute pancreatitis. The assays for both amylase and lipase were made by autoanalyzer Erba-XL-600 (Transasia Biomedicals).

The study adhered to the tenets of the Declaration of Helsinki for research in humans. All the proforma were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done by dividing subjects into 2 groups, 2-fold and 3-fold rise above normal levels both in amylase and lipase. These groups were defined as indeterminate as their blood results were not high enough to support a diagnosis of pancreatitis.

Diagnostic accuracy was calculated by plotting area under curve (AUC) in the receiver operating characteristic curve (ROC). A 2-way table was also formulated with sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios calculated. The ROC was constructed using the Stats Direct program. Wilcoxon method was used for the estimation of the AUC of the ROC curves. Medcalc was used for the comparison of area under the ROC curve.

RESULTS

A total of 1725 patient presented to emergency department with acute abdominal pain during the study period and blood samples were taken. The total number of patients with amylase level above normal value was 144 while that for lipase was 218. Notably, 117 patients had amylase result above normal but below 2-fold elevation, while there were 182 such patients in the lipase group. Sixteen patients had amylase above 3-fold elevation, while there were 26 such patients in the lipase group. Distribution of study subjects as per levels of amylase and lipase are presented in Table 1.

Table 1: Distribution of study subjects as per levels of serum amylase and lipase.

Variables	Serum amylase	Serum lipase
Within normal limit	1581 (91.65%) CI: 91.02-93.14%	1507 (87.36%) CI: 85.20-89.01%
Above normal limit (amylase >141 U/L, lipase >51 U/L)	144 (8.35%) CI: 6.98-9.26%	218 (12.64%) CI: 12.03-14.14%
Between upper limit and 2-fold elevation (indeterminate)	117 (6.78%) CI: 5.82-7.84%	185 (10.72%) CI: 9.42-10.87%
Above 2-fold elevation (amylase >282 U/L or lipase >102 U/L)	26 (1.50%) CI: 1.20-2.16%	37 (2.14%) CI: 1.58-2.54%
Above 3-fold elevation (amylase >423 U/L or lipase >153)	16 (0.92%) CI: 0.61-1.42%	26 (1.51%) CI: 0.98-1.83%
CI=95% confidence interval		

A total of 17 patients had their clinical diagnosis as acute pancreatitis.

However, on reviewing their clinical records, only 11 patients had positive radiological evidence of acute pancreatitis. Among these clinical pancreatitis patients, two of them had severe abdominal or epigastric pain but initially both amylase and lipase levels were normal. Subsequent blood tests after hospital admission showed raised amylase and lipase levels. However, CT abdomen in both showed unremarkable changes in the pancreas. Four patients had amylase level in the indeterminate

group but two of them had 2-fold elevation in lipase and the other two had 3-fold elevation. On the other hand, no patient with lipase level in the indeterminate group had amylase level raised above 2-fold.

The sensitivity and specificity of amylase at 3-fold above normal limit were 62.8% and 99.2% while those of lipase were 96.1% and 99.1% respectively. The sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios at both 2-fold and 3-fold levels, with confidence intervals are shown in Table 2.

Table 2: Sensitivity, specificity, PPV, NPV, positive and negative LR.

Variable	Amylase		Lipase	
	>423 U/L	>282 U/L	>153 U/L	>102 U/L
Sensitivity	0.628 CI:0.378-0.785	0.744 CI:0.617-0.936	0.961 CI:0.732-0.984	1.000 CI:0.822-1.000
Specificity	0.992 CI:0.986-0.995	0.991 CI:0.974-0.995	0.991 CI:0.986-0.995	0.986 CI:0.978-0.989
PPV	0.421 CI:0.245-0.594	0.362 CI:0.223-0.460	0.421 CI:0.264-0.583	0.311 CI:0.198-0.418
NPV	0.997 CI:0.993-0.999	0.998 CI:0.995-1.000	0.999 CI:0.993-0.999	1.000 CI:0.997-1.000
LR (+ve)	112.32 CI:65.472-184.528	78.015 CI:52.852-109.452	113.264 CI:78.315-162.154	66.744 CI:50.854-84.477
LR (-ve)	0.372 CI:0.197-0.645	0.175 CI:0.063-0.445	0.043 CI:0.012-0.322	0

PPV=positive predictive value, NPV=negative predictive value, LR (+ve) =positive likelihood ratio, LR (-ve) =negative likelihood ratio

Both amylase and lipase had high accuracy index in the area under the ROC curve (0.990 and 0.997 respectively). On plotting ROC curve of amylase, the AUC was 0.990 with 95% confidence interval 0.983- 0.996, p<0.001 and cut-off value at 180. Similarly, on plotting ROC curve of lipase, the AUC was 0.997 with 95% confidence interval 0.989- 0.997, p<0.001 and cut-off value at 141. But the difference between the AUC of these two graphs was not statistically significant.

DISCUSSION

Serum amylase has been used as a diagnostic tool for acute pancreatitis since the 1920s. Lipase assay was first introduced in 1986 in USA and claimed to achieve a sensitivity of 80% and specificity of 60%.⁶ Thomson et al, in 1987 found the sensitivities of both amylase and lipase were 67-100%, while the specificities were 85-98% and 83-98% respectively.⁷ Smith et al, in 2005 showed that the sensitivity and specificity of amylase were 69% and 96% respectively.⁸

In this study, we observed that the sensitivity and specificity of amylase at 3-fold above normal limit were

62.8% and 99.2% while those of lipase were 96.1% and 99.1% respectively. A cut-off of three folds of the upper limit of reference has improved the diagnostic criteria for acute pancreatitis by increasing the sensitivity and specificity of both amylase and lipase tests.^{9,10}

Clave P et al, in his prospective study used different diagnostic cut-off points to diagnose acute pancreatitis, and found no difference found between serum amylase and lipase in terms of diagnostic accuracy as measured by the area under the Receiver Operating Curve (ROC).¹¹ On the other hand, another study by Chase CW et al, observed that patients admitted with acute abdominal pain indicated that serum lipase offered a better diagnostic efficiency than amylase (94% versus 91%), despite the tests having similar degrees of specificity and sensitivity.¹²

Given that the levels of lipase remain raised for a longer time than that of amylase, a prospective study by Treacy J et al, looking at the level of amylase and lipase during the first day in comparison to the third day of presentation of acute abdominal pain observed that serum lipase had a better degree of sensitivity and specificity for

diagnosing acute pancreatitis during both early and late stages of the disease.¹³

Our findings are in contrast to the literatures review by Beauregard et al. He indicated that several prospective and retrospective studies did not find any significant diagnostic advantage of lipase over amylase in term of specificity, sensitivity and accuracy.¹⁴ Another study by Gomez D et al, is also in concordance with our observations. He observed that majority of patients with acute pancreatitis had raised levels of both amylase and lipase (97%), however, raised lipase levels were seen between 95 and 100 % of patients based on the aetiology.

In our study, 84 % of patients of acute pancreatitis had both amylase and lipase raised and 100 % of acute pancreatitis patients had lipase raised, irrespective of aetiology. Our findings confirm the results of other studies by Thomson et al, Agrawal et al who observed higher sensitivity and specificity of serum lipase in diagnosis of acute pancreatitis compared to serum amylase.^{7,15} Measuring both lipase and amylase to determine the etiology of acute pancreatitis has been a matter of debate. Gumaste VV et al, in his prospective study on 20 patients concluded that a ratio of lipase to amylase serum level greater than two is indicative of alcoholic acute pancreatitis.¹⁶ A few retrospective studies have found that a lipase to amylase ratio of more than five is indicative of alcoholic pancreatitis (sensitivity 31%, specificity 100%).¹⁷ In contrast, the ratio of lipase to amylase in other studies did not correlate with the cause of acute pancreatitis.¹⁸ The sensitivity, specificity, accuracy, and positive and negative predictive values of lipase to amylase ratios were ineffective in determining the etiology of acute pancreatitis.¹⁹

Currently there are other serum markers being utilized. Pancreatic isoamylase is one of such example. A few others are serum trypsin, elastase-1, phospholipase A2 and urine amylase. Serum trypsin and elastase are of interest because of their longer half life, thus having a more prolonged elevation allowing detection even with delayed presentation.¹¹ Therefore, they are used only in doubtful cases or delayed presentation and may need another enzyme for comparison.

CONCLUSION

In light of above discussion, it can be concluded that serum lipase had better diagnostic accuracy as compared to serum amylase. In resource-constrained settings with limited lab and radiological facilities, serum lipase should be preferred over serum amylase for diagnosis of acute pancreatitis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumar A, Kapoor S. Diagnostic accuracy of serum lipase and amylase as biomarkers for acute pancreatitis. *Int J Res Med Sci* 2018;6:1721-5.