



Evaluation of tumor necrosis factor- α (TNF- α) and C-reactive protein over lipase amylase ratio for acute pancreatitis in north Indian population

Authors

Sweta Kumari¹, Amod Kumar² Musarrat Parveen³, Amitesh Kumar,*S.S.Haque⁴,
Md.Tanweeruddin⁵

¹Department of Biochemistry, Vardhman Institute of Medical Sciences, Pavapuri, Nalanda

²Department of Clinical Pathology, Patna Medical College and Hospital, Patna India

³Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna-14

⁴Department of Biochemistry, ⁴Indira Gandhi Institute of Medical Sciences, Patna-14

⁵Department of Anaesthesiology and Critical care, ECR, Danapur

*Corresponding Author

Dr S.S.Haque

Department of Biochemistry, Indira Gandhi Institute of Medical Sciences, Patna-14

Abstract

Acute pancreatitis is an acute inflammatory disease of pancreas. Pancreatitis is due to premature, intra-pancreatic activation of pancreatic proenzymes. Increased levels of serum amylase and lipase establish the diagnosis of acute pancreatitis. Aim of the study was to determine the ratio of serum lipase to serum amylase (L/A) along with TNF- α and CRP in acute pancreatitis patients in north Indian population. The mean lipase/ amylase ratio (4.17 ± 1.27 U/L) levels are significantly higher in severe acute pancreatitis. The study showed no significant age difference between group A (N=60; mean age 40.25 ± 12.31 years) and control group B (N=60; mean age 37.92 ± 9.69 years). Out of 60 patients of acute pancreatitis, 32 were having severe disease with CRP level between 96-192 mg/l while in mild disease 18 patients were having severe disease with CRP level between 24-48 mg/L and only 10 patient were having normal CRP level i.e. below 8 mg/L, and TNF- α in case of acute pancreatitis 12.20 ± 3.32 compared to control (9.86 ± 4.57) pg/ml The lipase/ amylase ratio is a good predictor factor and is useful in distinguishing acute episode of alcoholic from non-alcoholic acute pancreatitis. It may useful in predicting the severity of acute pancreatitis.

Keywords: Acute pancreatitis; lipase; amylase; lipase/ amylase ratio (L/A).

Introduction

For the diagnosis of acute pancreatitis (AP) an elevated serum pancreatic enzyme has been reported. In 1932 Cherry and Crandl first described an association between pancreatic injury and elevated serum lipase levels [1]. AP is regarded as a kind of an inflammatory disorder induced by many various causes nowadays.

Inflammatory mediators is another very important pathophysiologic mechanism of AP. It was reported that acinar cell itself like leukocyte can produce cytokine such as tumor necrosis factor α (TNF- α) in AP and this cytokine influence the patterns of acinar cell death. The proposed mechanisms of TNF- α induced pancreas injury are direct pancreas duct cell injury, formation of

microthrombus, ischemia, hemorrhage, necrosis and edema. The neutralization of TNF- α with an antibody produced a mild improvement in the parameters and can significant reduction in mortality and enhance the therapeutic effectiveness of octreotide for treatment of necrotizing AP in experimental studies. During this inflammatory response multiple substances are released which play an important role in disease pathogenesis they are called Acute Phase Protein. Serum IL-6 has been shown to be a useful index of the severity of acute pancreatitis⁽⁴⁻⁷⁾. So my aim of the study was to determine combined use of serum lipase and amylase ratio along with IL-6 and CRP in the evaluation of diagnosis and the prognosis of acute pancreatitis in north Indian population

Materials and Methods

This was a retrospective study conducted on patients attending the clinics of Gastroenterology, Emergency medicine and Department of Biochemistry, Vardhman Institute of Medical Sciences, Pavapuri, Nalanda. A written informed consent was obtained from all the patients before the screening in the study.

In our study we have selected one hundred fifty patients (90 male, 60 female) with acute pancreatitis in which 60 were alcoholic and 90 were non-alcoholic between age group of 18-70 yrs.

Inclusion criteria

All the patients with acute pancreatitis were included in the study. 60 patients had an etiology of pancreatitis by alcoholism (with an average alcohol intake of 85 g and above), 90 patients with etiology of pancreatitis of biliary origin. The diagnosis of AP is based on the evidence of two or more combination of the following presentations: at least three folds increase in serum amylase and / or lipase levels, in addition to history of upper abdominal pain and further confirmed by ultrasonography and/ or CT performed during the hospital stay.

Exclusion Criteria

Patient with chronic pancreatitis excluded from the study.

All patients with questionable diagnosis of other possible abdominal conditions and incomplete data collections were excluded in this study.

Patient with intestinal perforation, cholecystitis, acute intestinal obstruction, mesenteric Ischemia, MI, renal colic etc. excluded from the study.

Methods

The serum amylase was estimated by enzymatic kinetic method using 2-chloro-4-nitrophenyl – alpha maltotrioxide as substrate^[8-10]. The serum lipase was estimated by enzymatic color test method by using Olympus AU-400 automated analyzer. IL-6 values were assessed using ELISA and CRP by Agglutination method (Biosystem SA, Barcelona, Spain) at admission. When the serum sample containing a significant level of CRP is mixed with the latex, visible agglutination occurs.

The reference range of serum amylase was 40-150 U/L and the reference range of serum lipase in adults age 60 and younger was 10-150 U/L and in adults older than age 60 was 20-180 U/L. Samples were taken between 24 and 48 h after the onset of symptoms corresponding with the rise in IL levels in body.

Results are presented as mean \pm S.D. for parametric data and as percentage for nonparametric data. The statistical analysis was done using two sample 't' test and chi square test. The level of significance was measured at $p < 0.05$.

Results

One hundred fifty patients (90 male, 60 female) with acute pancreatitis have been studied in which 60 were alcoholic and 90 were non-alcoholic between age group of 19-75 yrs.

The patients with acute pancreatitis were divided into two groups Group A and Group B .Group B is treated as a control groups. Patient with chronic pancreatitis were excluded from the study.

Table No.1: Age distribution of patients in Group A and Group B

Age (Years)	Group A		Group B		Remarks
	No. of cases	Percentage (%)	No. of cases	Percentage (%)	
9-19	3	5.0	0	0.0	t= 1.16 P value > 0.05 Non-Significant
20-29	7	11.7	18	30.0	
30-39	21	35.0	15	25.0	
40-49	16	26.7	20	33.3	
50-59	7	11.7	6	10.0	
60-69	5	8.3	1	1.7	
70-79	1	1.7	0	0	
80-89	0	0	0	0	
Total	60	100.0	60	100.0	
Mean±SD	40.25±12.31		37.92±9.69		

Out of 60 cases of alcoholic acute pancreatitis under study, the maximum numbers of patients were in age-group of 30 to 39 years (35.0%) and minimum were in the age group of 70-79(1.7%).

And in control group the maximum numbers of patients were in age-group of 40 to 49 years (33.3%) (table 1) and minimum were in the age group of 60-69(1.7%).

Table No.3: Sex distribution of patients in Group A and Group B

Sex	Group A		Group B		Total	Remarks
	No. of cases	Percentage	No. of cases	Percentage		
Male	55	91.7	46	76.7	101	χ ² = 5.26 P value= 0.02 Significant
Female	5	8.3	14	23.3	19	
Total	60	100.0	60	100.0	120	

The result of sex distribution was significant statistically (table 3). Out of 60 cases of alcoholic acute pancreatitis males (91.7%) outnumbered

females (8.3%) in this study. Sixty normal healthy individuals, comprising of 46 males and 14 females served as control group.

Table No. 7: Comparison of mean Lipase, Amylase and L/A ratio in Group A (N=60) and Group B (N=60).

Parameters	Group	Mean	SD	Difference of mean	d. f.	t	P
Lipase (U/L)	A	2283.78	792.58	2218.52	59.02	21.68	<0.001
	B	65.27	11.01	-	-	-	-
Amylase (U/L)	A	659.97	312.19	591.10	59.23	14.65	<0.001
	B	68.87	13.82	-	-	-	-
L/A ratio	A	3.78	1.29	2.80	63.60	16.44	<0.001
	B	0.98	0.26	-	-	-	-

The mean serum lipase levels were significantly ($P < 0.001$) higher in alcoholic acute pancreatitis (group A) in comparison to normal healthy individuals/control group (group B). Serum lipase values were significantly higher in alcoholic group (2283.78 ± 792.58 U/L) in comparison to normal healthy individuals/control group B (65.27 ± 11.01U/L).The mean serum amylase levels were significantly higher ($P < 0.001$) in alcoholic acute pancreatitis (group A) in comparison to normal healthy individuals/control group (table 7). The mean lipase/amylase (L/A) ratio

(3.78±1.29) was significantly higher in group A (alcoholic acute pancreatitis) than control group/group B (0.98±0.26).

Table

Sr.No	Number of patients	CRP levels
1.	32	96-192 mg/l
2.	18	24-48 mg/l
3.	10	Below 8 mg/l

Discussion

In our study, the maximum numbers of acute pancreatitis (AP) patients were in age-group of 30 to 39 years (35.0%) and minimum were in the age

group of 70-79(1.7%). This study was similar to the results of Wu et al reported that most of these cases with acute pancreatitis were between the ages of 21 to 40 years old.^[11] The total number of cases in group A (alcoholic AP) were 60 (40%) and the total number of cases in group C (non-alcoholic AP) were 90 (60%) (table 3). The number of non-alcoholic acute pancreatitis seemed to be marginally higher than alcoholic pancreatitis that is not comparable to western literature, where alcohol is the most common cause of acute pancreatitis ^[12-20]. Our study findings were concurrent with others ^[21] with respect to the alcoholic pancreatitis being predominantly seen in males (91.7%) when compared to females while the non-alcoholic AP was higher amongst the females (60%) in comparison to males. Probably the reason could be that the percentage of alcoholics reported ^[22] is lower in females when compared to males in Indian population. And the reported cases of AP in females for other causes of pancreatitis such as biliary is much higher than the alcoholic variety. Serum lipase values were significant higher in alcoholic group/group A (2283.78±792.58 U/L) in comparison to non-alcoholic/group C (1224.88±705.62 U/L).

Serum amylase values were significantly higher in non-alcoholic group (1080.86±687.73 U/L) in comparison to alcoholic group (659.47±312.19 U/L) that was similar to previous studies ^[23,24] The possible reason for these results could lie in the different pathophysiology occurring in alcoholic vs. biliary AP. Whether acute alcoholic pancreatitis occurs in a normal pancreas or in a pancreas that has already been altered by chronic pancreatitis is unclear. The mean lipase/amylase (L/A) ratio (3.78±1.29) was significantly higher in group A (alcoholic acute pancreatitis) than group C (1.45±0.86).

Our results show that serum lipase / amylase ratio with a cut off value fixed at 3.0, can assist in differentiating alcoholic AP from non-alcoholic AP. Our results are similar to the study ^[25] that has stated the lipase / amylase ratio > 3 was seen

more often in AP / acute chronic pancreatitis than biliary AP. However, in their study the amylase and lipase were not significantly different in the two groups. One of the study ^[26] showed that serum lipase / amylase ratio with a cut off value fixed at 4.0, can assist in differentiating alcoholic AP from non-alcoholic AP. Thus, our results indicate that the L/A ratio are useful to distinguish alcoholic from nonalcoholic acute pancreatitis.

Conclusion

We would like to conclude that the serum lipase to amylase ratio greater than 3.0 could be used to differentiate between alcoholic and non-alcoholic AP and serum lipase to amylase ratio with a cut off of 3.0 or greater is useful to differentiate the severe AP from milder AP. Hence, the lipase/ amylase ratio is a good predictor factor and is useful in distinguishing acute episode of alcoholic from non-alcoholic acute pancreatitis. It may be useful in predicting the severity of acute pancreatitis.

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