ORIGINAL ARTICLE

USEFULNESS OF LIPASE / AMYLASE RATIO IN ACUTE PANCREATITIS IN SOUTH INDIAN POPULATION

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ABSTRACT

This retrospective study was conducted to assess the serum lipase / amylase ratio in acute pancreatitis for South Indian population attending the clinics of Gastroenterology and Emergency medicine in the last five years. One thousand one hundred and thirty two patients (768 males and 364 females) with acute pancreatitis (AP) were selected for the study. The diagnosis of AP was based on clinical evaluation, Computed Tomography (CT) findings and biochemical parameters such as serum lipase and amylase. Based on the etiology, the groups were divided into alcoholic, biliary and miscellaneous AP. Based on CT findings, groups were divided into mild, moderate and severe AP. Serum lipase, amylase and lipase / amylase ratio were calculated and statistically analyzed. Serum lipase levels in alcoholic group (3226.3 ± 1384.7) were significantly lower in comparison to biliary (6064.5 ± 1640.8) group though the levels were not significantly different from miscellaneous group (2132.3 ± 1210). Serum amylase values were significantly lower in alcoholic group (923.4 ± 557.5) in comparison to biliary (1736.2 ± 390.7) and there was significant difference between alcoholic and miscellaneous group (535.8 ± 477.6). The serum lipase / amylase ratio > 4 occurred in alcoholic group than with biliary and miscellaneous group. The sensitivity and specificity to predict alcoholic AP with lipase / amylase ratio at >4.0 was 84 % and 59 % respectively. In conclusion the serum lipase to amylase ratio greater than 3.0 could be used to differentiate but keeping the cut off at 4.0 would be of higher sensitivity without much change in specificity. The serum lipase to amylase ratio with a cut off of 3.0 or greater is not useful to differentiate the severe AP from milder AP. Hence, serum amylase and lipase are important for evaluation of pancreatitis though it is not a gold standard for the diagnosis or assessment of severity of acute pancreatitis.

KEY WORDS

Lipase / amylase ratio, Acute pancreatitis, Alcoholic pancreatitis, Biliary pancreatitis.

INTRODUCTION

Acute Pancreatitis (AP) is usually a short-lived inflammatory response to pancreatic gland injury. Typical symptoms include abdominal pain, nausea and vomiting with an increase in the serum levels of digestive zymogens including amylase and

lipase. Biliary disease and alcohol abuse are the two main etiological factors. From a clinical point of view, the course of alcoholic and biliary AP is the same; however, because endoscopic retrograde cholangiopancreatography associated with endoscopic sphincterotomy can prevent further complications in patients with severe biliary pancreatitis, it is important to recognize early the biliary origin of the disease. On the other hand, identification of alcoholic origin of pancreatitis can prevent interventional procedures not useful in this kind of patients. Gumaste et al (1) proposed that the serum lipase/amylase ratio of greater than 2 could differentiate acute episodes.

In our study, we hypothesized that lipase to amylase ratio of

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greater than 3.0 can be used to differentiate between alcoholic and non-alcoholic pancreatitis. Further the lipase to amylase ratio of greater than 3.0 can be used to differentiate severe AP from mild and moderate forms of AP. The aims and objectives of the study were to (a) To collect data of patients diagnosed with acute pancreatitis in the past 5 years. The data should include age, sex, etiological factors proposed, CT findings and serum lipase and amylase. (b) To categorize patients based on etiological factors into alcoholic and non-alcoholic and calculate the serum lipase to amylase ratio. (c) To categorize patients based on the ultrasound findings and calculate their serum lipase to amylase ratio.

MATERIALS AND METHODS

We conducted a retrospective study on patients attending the clinics of Gastroenterology and Emergency medicine between May 2003 and May 2008. The data were retrieved from the medical records of the patients and compiled for the study. The study is on hospital-based south Indian population.

One thousand one hundred and thirty two patients (768 male and 364 female) with AP were selected for study. 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. The majority of patients had come as out patient with a history of abdominal pain of 2 to 3 days with varying degree that were eventually admitted to the hospital. All patients with questionable diagnosis of other possible abdominal conditions and incomplete data collections were excluded in this study. All patients with clinical presentations suggestive of chronic pancreatitis such as pancreatic duct dilatation, calcifications and malabsorption were excluded.

576 patients had an etiology of pancreatitis by alcoholism (with an average alcohol intake of 75 g and above), 341 patients with etiology of pancreatitis of biliary origin and 215 patients were secondary to / associated with trauma, dyslipidemia, end stage renal disease and diabetes mellitus (labeled as miscellaneous). The CT findings of 261 patients were retrievable and were classified as per Balthazar criteria (2) into three groups: Grade Mild (n = 88): normal, local or diffuse enlargement of the pancreas; Grade Moderate (n = 82): pancreatic gland abnormalities associated with peripancreatic inflammation; Grade Severe (n = 91): fluid collection in one or more location and / or the presence of gas in or adjacent to the pancreas. The serum amylase and lipase concentration were analyzed at admission. The lipase to amylase ratio was calculated after converting the values of serum lipase and amylase values into multiples of upper reference limit that was used. The lipase / amylase ratio were also correlated with ultrasound findings. The serum lipase and amylase were analyzed on DAE Behring automated analyzer with its dedicated reagents. The photometric technique for serum amylase was done using CNPG3 substrate (3). The lipase was done by method of Neumann et al (4). Statistical analysis was performed using ANOVA tests, Non parametric test and Z test for comparison of the three groups based on severity by statistical package SPSS. The $p < 0.05$ was considered as statistically significant.

RESULTS

Our study showed that alcoholic acute pancreatitis patients (n = 1125; 44 ± 9.6 years) were significantly younger than those with biliary (n = 578; 62.1 ± 14.3 years) and miscellaneous pancreatitis (n = 429; 58.5 ± 6.3 years). The mean serum amylase levels were significantly lower in alcoholic group in comparison to non-alcoholic groups. Serum amylase values (reference values: 25 to 115 U/L) were

Table 1 : Levels of serum lipase / amylase ratio in different groups

	Alcoholic AP	Biliary AP	Miscellaneous AP
Number of patients (n)	576	341	215
Age (years)	44 ± 9.6	62.1 ± 14.3	58.5 ± 6.3
Male / Female ratio	569 / 7	116 / 125	88 / 127
Serum amylase (U/L) (reference interval : 25 – 115 U/L)	$923.4 \pm 557.5^*$	$1736.2 \pm 390.7^*$	$535.8 \pm 477.6^*$
Serum lipase (U / L) (reference interval : 114 – 286 U/L)	$3226.3 \pm 1384.7^*$	$6064.5 \pm 1640.8^*$	2132.3 ± 1210
Serum lipase / amylase ratio	$4.25 \pm 2.33^*$	$1.5 \pm 0.61^*$	$2.44 \pm 1.6^*$

The values are expressed as Mean $\pm$ SE. * $p < 0.05$, Statistically significant difference observed in serum amylase and serum lipase / amylase ratio between alcoholic, biliary and miscellaneous AP. Statistically significant difference observed in serum lipase between alcoholic and biliary AP, miscellaneous and biliary group but there was no statistically significant difference between miscellaneous and alcoholic AP groups ('p' value = 0.07)

significantly lower in alcoholic group (923.4 ± 557.5) in comparison to biliary (1736.2 ± 390.7) and there was significant difference between alcoholic and miscellaneous group (535.8 ± 477.6). Similarly, the mean lipase levels (reference values: 114 to 286 U/L) were significantly lower in alcoholic group (3226.3 ± 1384.7) in comparison to the biliary group (6064.5 ± 1640.8) but there was no significant difference between alcoholic and miscellaneous group (2132.3 ± 1210). However, the serum lipase levels were higher in comparison with serum amylase levels in all the groups. And the serum lipase / amylase ratio > 4 occurred in alcoholic group than with biliary and miscellaneous group. This has been summarized in Table 1.

The patients with mild AP were significantly older than those with moderate and severe AP. And the number of patients with alcoholic AP with severe pancreatitis was significantly higher compared to pancreatitis with other etiology. There was no significant difference between serum amylase values in all the three groups (grouping based on CT findings). There was no significant difference in lipase and lipase / amylase ratio between mild and severe pancreatitis. However, there was significant difference observed in lipase and lipase / amylase ratio when the moderate and severe pancreatitis was compared. This is summarized in the Table 2.

At serum lipase / amylase ratio > 3.0 , the sensitivity and specificity for predicting alcoholic AP was 76% and specificity of 64 % while the positive predictive value was 54.9% and negative predictive value was 78.9 %. At serum lipase / amylase ratio > 4.0 , the sensitivity and specificity for predicting alcoholic AP was 84 % and 59 % respectively while the positive and negative predictive value were 43.3 % and 65 % respectively. At serum lipase / amylase ratio > 3.0 , the sensitivity and specificity of AP to predict severe AP was 68.9% and 52 % respectively while the positive and negative

predictive value are 38% and 56% respectively. With serum lipase / amylase ratio > 4.0 , the sensitivity and specificity of AP to predict severe AP was 54 % and 48.7 % respectively while the positive and negative predictive value are 27.6 % and 42 % respectively.

DISCUSSION

In our study, the number of alcoholic pancreatitis seemed to be marginally higher than non-alcoholic pancreatitis that is comparable to western literature (5, 6, 7). The patients with alcoholic AP were relatively younger than non- alcoholic AP patients. The alcoholic AP patients were ranging between 34 to 54 years while the non-alcoholic AP ranges between 52 to 72 years. Similar findings were observed in other studies (8, 9, 10). The reason for younger age group of alcoholic AP could be attributed to the initiation of alcohol consumption and its dependence at very early age (11). Our study findings were concurrent with others (12) with respect to the alcoholic pancreatitis being predominantly seen in males when compared to females while the biliary AP was higher amongst the females in comparison to males. Probably the reason could be that the percentage of alcoholics reported (13) is lower for 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.

Our study showed that there was significant difference in serum amylase and lipase values when alcoholic AP was compared with non-alcoholic AP. Though the amylase and lipase values were lower in alcoholic AP when compared to biliary group but the values were higher in alcoholic AP in comparison to miscellaneous group that was similar to previous studies (1, 9, 10). However these studies showed that the raised amylase levels were significantly lower in alcoholic AP in comparison

Table 2: Relationship between CT findings and lipase / amylase values

	Grading based on CT findings (Balthazar's criteria)		
	Mild	Moderate	Severe
Alcoholic AP	19	16	65
Biliary AP	48	46	14
Miscellaneous AP	21	20	12
Age	54 ± 9.72	43.9 ± 2.67	41 ± 3.9
Serum Amylase	1245 ± 368.7	1436 ± 664.3	989.6 ± 469.8
Serum Lipase	3669.2 ± 1623.4	6204.8 ± 1589.6	$1684.5 \pm 1899.4^*$
Serum Lipase / Amylase ratio	2.85 ± 0.48	5.42 ± 1.17	$1.52 \pm 1.03^*$

The values are expressed as Mean $\pm$ SE. * $p < 0.05$ statistically significant difference between Moderate and Severe AP.

Table 3: Comparison with different cut off for serum lipase / amylase ratio to distinguish alcoholic from non-alcoholic (combination of biliary and miscellaneous) AP

	Serum lipase / amylase ratio	
	> 3.0	> 4.0
Sensitivity	76 %	84 %
Specificity	64 %	59 %
Positive predictive value	54.9 %	43.3 %
Negative predictive value	78.9 %	65 %

to biliary AP and the serum lipase concentrations were not significantly different in these studies. Similar to another study (8), our observations showed that serum lipase levels were found to be elevated with a significant difference between alcoholic and non-alcoholic AP groups (biliary and miscellaneous). However, there was a certain degree of overlap in the serum lipase levels in alcoholic and miscellaneous AP and these groups didn't show a significant difference unlike the biliary group. Our results show that serum lipase / amylase ratio with a cut off value fixed at 4.0, can assist in differentiating alcoholic AP from non-alcoholic AP. The lipase / amylase ratio >4.0 is observed in alcoholic AP while the biliary and miscellaneous group have ratios less than 4.0. However, there would be considerable overlap when the lipase/ amylase ratio is fixed at lower values. Our results are similar to another study (14) that concluded serum lipase / amylase ratio fixed a cut-off value of 4.2 yielded a specificity of 57% and sensitivity of 96%. This is similar to our reports that showed sensitivity of 84 % and specificity was 59 % with lipase / amylase ratio > 4.0.

One of the study (15) has stated that the lipase / amylase ratio > 3 was seen more often in AP / acutized chronic pancreatitis than biliary AP. However, in their study the amylase and lipase were not significantly different in the two groups. In the original work by Gumaste et al (1), the lipase / amylase ratio greater than 2.0 was reported to have the specificity of 78 % whereas in another (10) study, the specificities were 50

Table 4: Comparison with different cut off for serum lipase / amylase ratio to distinguish severe from non-severe (combination of mild and moderate) AP

	Serum lipase / amylase ratio	
	> 3.0	> 4.0
Sensitivity	68.9 %	54 %
Specificity	52 %	48.7 %
Positive predictive value	38 %	27.6 %
Negative predictive value	56 %	42 %

% and 78 % for lipase / amylase ratio values > 2 and > 3.0 respectively. The sensitivity for both these lipase / amylase ratio values was < 70%. Similar to a previous study (8), our results showed that serum amylase is unable to distinguish between various degrees of severity in the acute pancreatitis since there was no statistical difference in the values between mild and moderate / severe pancreatitis. Further serum lipase and lipase / amylase ratio showed a significant difference between moderate and severe AP. The serum lipase / amylase ratio was found to be highest in moderate AP. In severe AP, due to widespread inflammatory reactions and tissue destruction, the clinical course is more severe and hence the pancreatic enzyme levels are lower.

In our study, majority of the patients with alcoholic AP had severe AP with serum amylase and lipase levels lower than the mild and moderately severe AP. However, the most of biliary AP patients presented with mild AP had serum amylase and lipase levels higher than the severe AP and this is similar to previous reports (16). According to earlier reports (16, 17), a typical attack of alcoholic AP presents with relatively lower amylase levels than a non-alcoholic patient who present with acute gall stone pancreatitis. 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. One of the studies (18) suggested that acute alcoholic pancreatitis develops in a pancreas already affected by chronic pancreatitis but their study did not support that in alcoholics chronic pancreatitis derives from AP.

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 but keeping the cut off at 4.0 would be of higher sensitivity without much change in specificity. The serum lipase to amylase ratio with a cut off of 3.0 or greater is not useful to differentiate the severe AP from milder AP. Hence, serum amylase and lipase are important for evaluation of pancreatitis though it is not a gold standard nor can be used for the assessment of severity of acute pancreatitis.

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