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RESEARCH ARTICLE

EVALUATION OF SERUM CREATININE AND LIPASE/AMYLASE RATIO IN ACUTE PANCREATITIS

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ABSTRACT

Background: Acute Pancreatitis is usually a short-lived inflammatory response to pancreatic gland injury. This study had been proposed to distinguish the etiology of acute pancreatitis by serum lipase/amylase ratio and association between serum creatinine and development of pancreatic necrosis in patients with acute pancreatitis.

Materials & Methods: Total five hundred and thirty patients (352 males and 178 females) with acute pancreatitis were selected for the study. The diagnosis of acute pancreatitis was based on clinical evaluation, Computed Tomography findings and biochemical parameters. Based on the etiology, the groups were divided into alcoholic, biliary and miscellaneous. Pancreatic necrosis was assessed by contrast-enhanced computed tomography. Serum creatinine, lipase, amylase and lipase / amylase ratio were calculated and statistically analyzed.

Results: At serum lipase/amylase ratio>4.0, sensitivity and specificity for predicting alcoholic group was 61.3 % and 56.0 % respectively. Using 48 h serum creatinine>1.8 mg/dl for pancreatic necrosis, the sensitivity, specificity, positive and negative predictive values were 48.0%, 96.4%, 58.0% and 83.6% respectively.

Conclusions: Serum lipase to amylase ratio greater than 4.0 could be used to differentiate between alcoholic and non-alcoholic patients. An increase in serum creatinine within the first 48 h is strongly associated with the development of pancreatic necrosis.

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INTRODUCTION

Acute pancreatitis (AP) is a complex process in which pancreatic enzyme activation causes local pancreatic damage, resulting in an acute inflammatory response. Biliary disease and alcohol abuse are the two main etiological factors (Papachristou *et al*., 2007). The recognition of the cause is important for the therapeutic approach. Patients with biliary disease can sometimes benefit from endoscopic sphincterotomy and whenever possible, should undergo cholecystectomy before discharge to prevent the recurrence of AP (Nealon *et al*., 2004). The alcoholic patient will require counseling or other form of treatment not to drink again. These differences in therapeutic approaches justify the search for noninvasive tests that can assist the clinical history and imaging in the differential diagnosis of these two causes of pancreatitis. It was reported that patients with acute alcoholic pancreatitis had serum concentrations of amylase lower than those with nonalcoholic pancreatitis, but the serum lipase concentrations were similar in the both forms of the disease (King *et al*., 1995). The serum lipase/amylase (L/A) ratio was significantly higher in alcoholic acute pancreatitis than in the nonalcoholic form of the disease. On the basis of these findings Gumaste *et al.* proposed that this index (L/A ratio >2) could differentiate acute episodes of alcoholic from those nonalcoholic acute pancreatitis (Gumaste *et al*., 1991). Pancreatic necrosis (PNec) is a condition associated with severely diminished blood flow to the pancreas, resulting in segmental pancreatic parenchymal ischemia and infarction. Pancreatic Necrosis occurs in approximately 15 % of AP patients and is detected by the loss of vascular enhancement on computerized tomography (CT) (Isenmann and Beger, 1999;

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Beger *et al*., 1997). We hypothesize that severe intravascular volume depletion and the associated stress response that diminishes visceral blood flow and leads to pancreatic necrosis will also affect the kidneys, resulting in an increase in serum creatinine levels. Therefore, the present study was planned to verify the efficacy of lipase/amylase ratio in the evaluation of different etiologies of acute pancreatitis and association between serum creatinine and development of pancreatic necrosis in acute pancreatitis patients.

MATERIALS AND METHODS

A retrospective study was conducted on patients attended the Clinics of Gastroenterology Department and Emergency Medicine at S.M.S. Medical College and Associated Group Hospitals, Jaipur from April 2010 to April 2013. The data was retrieved from the medical records of the patients and compiled for the study. Total 530 patients with acute pancreatitis were selected for this study, out of which 352 were male and 178 were female. The diagnosis of AP was based on the presence of two of the following three features: (i) abdominal pain characteristic of AP, (ii) serum amylase and / or lipase ≥ 3 times the upper limit of normal, and (iii) characteristic findings of AP on abdominal CT scan. The majority of patients had come as outpatient with a history of abdominal pain of 2 to 3 days with varying degree that were eventually admitted to the hospital. Patients were recruited within 24 h of the time of admission. The institutional ethics committee approved the study and informed consent was obtained from the study subjects. First time point chosen for all the study parameters data analysis in this study was at hospital admission and the second for serum creatinine was within 48 h of admission. Pancreatic necrosis was assessed by contrast-enhanced computed tomography (CECT). Evidence of PNec on CT was defined as lack of enhancement of pancreatic parenchyma with contrast. Seventy seven patients had CECT evidence of PNec.

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. Out of total 530 AP patients, 230 patients had an etiology of pancreatitis by alcoholism (with an average alcohol intake of 75 g and above), 180 patients with etiology of pancreatitis of biliary origin and 120 patients were secondary to / associated with trauma, dyslipidemia, end stage renal disease and diabetes mellitus (labeled as miscellaneous). Serum amylase, lipase and creatinine were analyzed by Kinetic Method using GALG2-CNP (Henry and Chiamori, 1960), Turbidometric UV-method (Ziegenhorn *et al*., 1979) and Mod. Jaffe's Kinetic Method (Jaffe *et al*., 1886) respectively. All tests were performed on fully autoanalyzer AU–400 by Olympus. 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. Statistical analysis was performed using ANOVA tests; Non parametric test and Z test for comparison of the three groups by statistical package SPSS. The $p < 0.05$ was considered as statistically significant. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for lipase/amylase ratio and 48 h serum creatinine.

RESULTS

In the present study, alcoholic acute pancreatitis patients (n = 230; 42±9.2 years) were significantly younger than those with biliary (n = 180; 60.1±13.9 years) and miscellaneous pancreatitis (n = 120; 56.5±6.2 years). Serum amylase values (reference values: 25-110 U/L) were significantly lower in alcoholic AP (889.3±525.5) as compared to biliary AP (1656.2±465.7) and there was significant difference between alcoholic and miscellaneous AP (458.4±395.5). Similarly, the mean lipase levels (reference values: 115-270 U/L) were significantly lower in alcoholic AP (3345.1±1350.5) as compared to the biliary AP (6292.8±1550.0) but no significant difference was observed between alcoholic and miscellaneous group (2312.4±1280.2).

Table 1. Values of Serum Lipase/Amylase Ratio in Different Groups

	Alcoholic AP	Biliary AP	Miscellaneous AP
Number of Patients (n)	230	180	120
Pancreatic Necrosis	33	26	18
No Pancreatic Necrosis	197	154	102
Age (Years)	42±9.2	60.2±13.9	56.5±6.2
Male/Female ratio	225/5	75/105	52/68
Serum Amylase (U/L) (reference interval : 25 – 110 U/L)	889.3±525.5*	1656.2±465.7*	458.4±395.5*
Serum Lipase (U/L) (reference interval : 115 – 270 U/L)	3345.1±1350.5*	6292.8±1550.0*	2312.4±1280.2
Serum Lipase/Amylase ratio	4.42±2.15*	1.41±0.58*	2.23±1.4*

Values are expressed as Mean±SE. *P<0.05, Statistically significant difference observed in serum amylase and serum lipase/amylase ratio between alcoholic, biliary and miscellaoneus AP. Statistically significant difference observed in serum lipase between alcoholic and biliary AP, miscellaneous and biliary group but no statistically significant difference observed between miscellaneous and alcoholic AP.

Table 2. 48 hour Serum Creatinine in Acute Pancreatitis patients with and without pancreatic necrosis

	Pancreatic Necrosis (n=77)	No Pancreatic Necrosis (n=453)
>1.8mg/dl	37	3
≤1.8mg/dl	40	450

Serum lipase / amylase ratio was significantly increased (>4.0) in alcoholic AP as compared to biliary and miscellaneous AP (Table 1). When serum lipase / amylase ratio was > 2.0, the sensitivity and specificity for predicting alcoholic AP was 90.5% and specificity of 39.3 % while the positive predictive value was 38.0% and negative predictive value was 86.4 %. At serum lipase /amylase ratio > 4.0, the sensitivity and specificity for predicting alcoholic AP was 61.3 % and 56.0 % respectively while the positive and negative predictive value were 32.6 % and 75.5 % respectively (Table 3).

Table 3. Sensitivity and Specificity for lipase/amylase ratio in acute alcoholic and non-alcoholic (biliary and miscellaneous) pancreatitis

	Serum Lipase/Amylase Ratio	
	>2.0	>4.0
Sensitivity (%)	90.5	61.3
Specificity (%)	39.3	56.0
Positive Predictive Value (%)	38.0	32.6
Negative Predictive Value (%)	86.4	75.5

Table 4. Sensitivity and Specificity for 48 hour Serum Creatinine as predictive tests for the development of Pancreatic Necrosis

	Serum Creatinine >1.8 mg/dl
Sensitivity (%)	48.0
Specificity (%)	96.4
Positive Predictive Value (%)	58.0
Negative Predictive Value (%)	83.6

Serum creatinine level after 48h of admission was>1.8mg/dl in 37 patients out of 77 patients with pancreatic necrosis and in only 3 patients out of 453 patients without pancreatic necrosis (Table 2). Using the 48 h serum creatinine >1.8 mg/dl for pancreatic necrosis, the sensitivity, specificity, positive and negative predictive values were 48.0%, 96.4%, 58.0% and 83.6% respectively (Table 4).

DISCUSSION

In our study, the number of alcoholic AP seemed to be marginally higher than non-alcoholic AP that is comparable to western literature (Bernard *et al*., 1999; Renner *et al*., 1985 and Uhl *et al*., 1996). Alcoholic AP patients were relatively younger than non- alcoholic AP patients. Alcoholic AP patients were ranging between 32 to 52 years while non-alcoholic AP ranges between 50 to 74 years. Similar findings were observed in other studies (Kuo-Chin Chang *et al*., 2005; King *et al*., 1995 and Tenner *et al*., 1992). Reason for younger age group of alcoholic AP could be attributed to the initiation of alcohol consumption and its dependence at very early age (http://www.addictionindia.org/image-ttkh/alcohol-related-harm-in-india-afact-sheet.pdf). Our study findings were concurrent with others with respect to the alcoholic AP being predominantly seen in males as compared to females while the biliary AP was higher amongst the females as compared to males (Fan *et al*., 1988). Probably the reason could be that the percentage of alcoholics reported 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 (http://www.nimhans.kar.nic.in/deaddiction/lit/female%20alcoholics.pdf). According to the present study there was significant difference in serum amylase and lipase values when alcoholic AP was compared with non-alcoholic AP. Though amylase and lipase values were lower in alcoholic AP when compared to biliary AP but values were higher in alcoholic AP as compared to miscellaneous AP that was similar to previous studies (King *et al*., 1995 and Tenner *et al*., 1992). However these studies showed that raised amylase levels were significantly lower in alcoholic AP as compared to biliary AP but serum lipase concentrations were not significantly different in these studies. In this study, 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 serum lipase levels in alcoholic and miscellaneous AP and these groups didn't show a significant difference unlike biliary AP. Serum lipase/amylase ratio with a cut off value fixed at 4.0 can assist in differentiating alcoholic AP from non-alcoholic AP. 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. Sensitivity and specificity for L/A ratio>4.0 was 84% and 59% (Devanath *et al*., 2009). Kazmierczak *et al* found that the L/A ratio > 4.2 had a sensitivity of 96 % but a low specificity of 57 % (Kazmierczak *et al*., 1995). In another study serum lipase/amylase ratio fixed a cut-off value of 4.2 yielded a sensitivity of 64.8% and specificity of 34.2% (Kuo-Chin Chang *et al*., 2005). We found sensitivity of 61.3% and specificity was 56.0 % with lipase / amylase ratio > 4.0. Gumaste *et al.* suggested that L/A ratio value >2 had a sensitivity and specificity for diagnosing acute alcoholic pancreatitis of 91.0 % and 78.0 %, respectively (4). We found the sensitivity was 90.5 % but the specificity was low (39.3%). The negative predictive rate is 86.4 % in L/A ratio > 2 mean that if L/A ratio less than 2, the alcoholic pancreatitis is estimated about 13%.

The development of PNec is a major contributing factor to morbidity and mortality of AP, especially when PNec becomes infected (21). Early identification of patients at risk for PNec should lead to preventative measures, such as vigorous fluid resuscitation, whereas early recognition of developing PNec will alter management to address this complication, such as increased vigilance for the development of infection in necrotic pancreatic tissue and consideration of the use of antibiotic and/or enteral nutrition therapy (Ratschko *et al*., 1999). Here we identified rising Cr levels as a factor that is closely associated with the development of PNec. A critical finding of our study is that an elevated serum Cr of >1.8 mg/dl within 48 h of admission is strongly associated with the development of PNec. We hypothesize that elevated Cr during early hospitalization reflects visceral organ injury and is strongly associated with the presence of PNec. However, it is also important to recognize that serum Cr has significant limitations. Although very specific, only 37 out of 77 patients who developed PNec yielded an elevated Cr resulting in a low sensitivity of 48.0 %. In another study, Pancreatic necrosis was present in 62 (13%) of the patients. Serum creatinine levels (abnormal ≥2 mg/dl) on admission and after 24 and 48 h were evaluated vs. the presence or absence of pancreatic necrosis.

Sensitivity rates varied between 14 and 23%, specificity between 95 and 97% (23).

Conclusion

Serum lipase to amylase ratio greater than 4.0 could be used to differentiate between alcoholic and non-alcoholic AP. Hence, serum amylase and lipase are important for evaluation of pancreatitis though it is not a gold standard. Early recognition of subjects at high risk for PNec and identification of patients with a high likelihood of unidentified PNec are important goals in determining optimal management of patients with AP. our study demonstrates that a serum Cr >1.8 mg / dl within 48 h of admission is strongly associated with the development of PNec.

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