Serum Lipase Amylase Ratio in Predicting Aetiology, Severity and Outcome of Acute Pancreatitis in a Tertiary Care Hospital

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Abstract

Background: Acute pancreatitis is a relatively common disease with variable prevalence in different countries. Different modalities are available for predicting aetiology, severity and outcome of acute pancreatitis with different sensitivity and specificity. Moreover, some are not widely available, some are very expensive. A single, cheap, widely available marker with high sensitivity and specificity is yet to be identified. The present study intends to find out the utility of serum lipase amylase ratio in predicting the aetiology, severity and outcome of acute pancreatitis.

Methods: This prospective, observational study was done at the Department of Gastrointestinal Hepatobiliary & Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, during the period of July 2014 to March 2016. A total of 71 patients with acute pancreatitis were included. Complete blood count, serum amylase, serum lipase, serum calcium, liver function test, renal function test, fasting lipid profile, ultrasonography of whole abdomen, CT scan of upper abdomen and arterial blood gas (ABG) were done in all patients. Statistical analysis was done with SPSS version 16.

Results: Among 71 patients, 23(32.4%) were due to biliary cause, 15(21.1%) were due to hypertriglyceridaemia, 4(5.6%) were due to alcohol and 22(31%) were due to unknown causes. 45 (63.4%) patients had mild attack, 10(14.1%) patients had moderate attack and 16(22.5%) patients had severe attack of acute pancreatitis. Out of 71 patients, 17(23.9%) developed complication whereas 54(76.1%) developed no complication. Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non-biliary pancreatitis was 2.39±0.84(p <0.001). Again, serum lipase amylase ratio in patients with acute alcoholic pancreatitis was 2.89±0.79 and in patients with non-alcoholic acute pancreatitis was 1.95±0.81 (p=0.002). Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±.65(p< 0.001). This study showed that serum amylase ratio was <2.0 in acute biliary pancreatitis and this ratio was >2.5 in acute alcoholic pancreatitis and in acute pancreatitis due to hypertriglyceridaemia. Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (p=0.273). Mean lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (p=0.357).

Conclusion: Role of serum lipase amylase ratio in predicting the aetiology and severity of acute pancreatitis has been addressed in several recent studies. This study was another attempt to achieve this goal. Predicting the aetiology of acute pancreatitis by such a cheap tool will guide further diagnostic work up and management strategy will avoid unnecessary investigations.

Key word: Serum lipase, serum amylase, acute pancreatitis.

Introduction:

The incidence of acute pancreatitis appears to be increasing. As the population is becoming increasingly overweight, the incidence of gallstones, the most common cause of acute pancreatitis is rising. The incidence of acute pancreatitis in England, Denmark, and the United States varies from 4.8 to 38 per 100,000 patients. However, estimates of incidence are inaccurate because the diagnosis of mild disease may be missed, and death may occur before diagnosis in 10% of patients with severe disease. Acute pancreatitis is defined physiologically as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ system.

Many conditions predispose to acute pancreatitis to varying degrees. Gall stone and alcohol are the most common causes. Other causes include hypertriglyceridaemia, hypercalcaemia, post ERCP, drugs, helminthes, pancreatic carcinoma, pancreatic divisum etc. The laboratory markers for diagnosing acute pancreatitis are serum levels of amylase and lipase. Serum Amylase rises within 6 to 12 hours of onset and is cleared fairly rapidly from the blood. It remains elevated for three to five days in uncomplicated attacks. Serum amylase activities may be normal in 19–32% of cases at the time of hospital admission, as a result of delayed presentation or exocrine pancreatic insufficiency—for example, secondary to chronic alcohol abuse. Serum amylose also may be falsely normal in hypertriglycerideremia-associated pancreatitis. The sensitivity of serum lipase for the diagnosis of acute pancreatitis is similar to that of serum amylase and is between 85% and 100%. Lipase may have greater specificity for pancreatitis than amylase. Serum lipase is always elevated on the first day of illness and remains elevated longer than the serum amylase. Serum lipase amylase ratio can be a useful
marker for predicting aetiology of acute pancreatitis. Devanath et al. (2009) showed that the sensitivity and specificity to predict alcoholic acute pancreatitis with lipase-amylase ratio at >4 was 84% and 59% respectively.7

Once the diagnosis is established, patients are classified as having mild, moderately severe or severe pancreatitis. The Atlanta criteria defines severity by the presence of organ failure or pancreatic necrosis on dynamic contrast-enhanced CT scan.4 Other acceptable markers of severe pancreatitis include three or more of Ranson’s 11 criteria for non-gallstone pancreatitis4 and an Acute Physiology and Chronic Health Evaluation (APACHE-II) score of greater than eight.10 Local complication of acute pancreatitis includes acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, acute necrotic collection (ANC) and walled-off pancreatic necrosis (WOPN). Other complications include splenic infarction splenic / portal vein thrombosis and gastric outlet dysfunction. Systemic complications include renal, circulatory or respiratory organ failure or exacerbation of serious pre-existing comorbidities.11 This study is intended to evaluate the relationship between serum lipase amylase ratio and acute pancreatitis, which may reveal the predictive value to determine the aetiology, severity and outcome of acute pancreatitis.

Materials and methods

The study was a hospital based prospective, observational and longitudinal study done at the department of Gastrointestinal Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, Bangladesh during the period of July 2014 to March 2016. Patients with acute pancreatitis aged above 18 years admitted to GHPD of BIRDEM General Hospital, Dhaka, were included in this study. Patients admitted with abdominal pain and diagnosed as acute pancreatitis by clinical history, physical examination and different imaging modalities were included in the study.

The following types of patients were excluded from this study: Known case of chronic kidney disease, chronic pancreatitis, patient unwilling to give voluntary consent to participate in the study and patient attending after 24 hours of onset of abdominal pain. Demographic and clinical variables were age, sex, BMI, duration of hospital stay, abdominal pain, severity of pain, radiation of pain, fever, co-morbid illness, smoking, alcohol, drug history, family history, history of previous attack, vital parameters and GCS score. Laboratory variables were hemoglobin level, haematocrit, WBC count, serum electrolyte, serum calcium, random blood sugar, HbA1c, blood urea, BUN, serum creatinine, liver function test, serum amylase, serum lipase, serum lipase amylase ratio, fasting lipid profile, serum LDH, ABG, CA 19.9, USG, CT scan findings.

Acute pancreatitis was defined by the presence of two of the following criteria: (1) symptoms, such as epigastric pain, consistent with the disease; (2) a serum amylase or lipase greater than three times the upper limit of normal; or (3) radiologic imaging consistent with the diagnosis, usually using CT or MRI. Biliary pancreatitis was considered when the patient with diagnosis of acute pancreatitis with no history of alcohol abuse and imaging techniques showing gall stones or biliary sludge. Biliary pancreatitis was also considered if serum ALT is > 150 U/L with a specificity of 96%.12 Hypertriglyceridaemia induced acute pancreatitis was defined when fasting serum triglyceride level within 24 hours of admission >1000 mg/dl.13

Alcoholic pancreatitis was defined when acute pancreatitis in a patient with history of heavy alcohol consumption (>50 gm/day) for more than 5 years was considered as acute alcoholic pancreatitis.13 Lipase amylase ratio was calculated on serum lipase and amylase values (expressed as multiples of the upper limit of normal), each of which was obtained on admission (preferably from the same sample) or at least within 24 hours of admission.7 Severity of pancreatitis was assessed by revised Atlanta criteria where mild acute pancreatitis was defined by absence of organ failure and local or systemic complication, moderately severe acute pancreatitis was defined by transient organ failure that resolves within 48 hours and/or local or systemic complications, severe acute pancreatitis was defined by presence of persistent single or multiple organ failure lasting for >48 hours.14

Outcome of acute pancreatitis was categorized into acute pancreatitis without any complication, acute pancreatitis with complication and death from sequel of acute pancreatitis. Organ failure was defined according to the Modified Marshall Scoring System, a universally applicable scoring system for identifying organ failure.

Data were collected in a pre-designed data-sheet which contains questionnaire, clinical findings and biochemical and imaging findings.
Statistical analysis
Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. The differences between groups were analyzed by unpaired t-test, chi-square (X²) test, and ANOVA test. Correlation between variables was measured by Spearman correlation coefficient test. A p-value <0.05 was considered as significant.

Ethical consideration
Prior to the commencement of this study, the research protocol was approved by the local ethical committee. The aims and objective of the study along with its procedure, alternative diagnostic methods, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient. It was assured that all records would be kept confidential and the procedure would be helpful for both the physician and patients in making rational approach regarding management of the case.

Results
A prospective observational study was carried out to evaluate serum lipase amylase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis. Total 71 patients with acute pancreatitis were enrolled in this study after admission in GHPD with certain inclusion criteria.

Table 1: Demographic, clinical and biochemical characteristics of the study population n(%) Parameters (n=71) Result

<table>
<thead>
<tr>
<th>Parameters (n=71)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.35±16.90</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>37(52.1)</td>
</tr>
<tr>
<td>Contributing factor</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>24(33.8)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>11(15.5)</td>
</tr>
<tr>
<td>DM</td>
<td>47(66.2)</td>
</tr>
<tr>
<td>OCP</td>
<td>5(7.0)</td>
</tr>
<tr>
<td>Tea/ coffee</td>
<td>49(69.0)</td>
</tr>
<tr>
<td>BMI</td>
<td>25.88±2.95</td>
</tr>
<tr>
<td>Clinical features</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>20(28.2)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>71(100.0)</td>
</tr>
<tr>
<td>Duration of hospital stay</td>
<td>7.8±2.5</td>
</tr>
<tr>
<td>Hct</td>
<td>32.9±7.5</td>
</tr>
<tr>
<td>HbA1c</td>
<td>7.8±1.7</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>21.7±7.2</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD. Values within the bracket are expressed as percentage.

Mean age of the patients was 44.35±16.90. 52.1% of the patients were male. Among the patients, 33.8% were smoker, 15.5% were alcoholic, 66.2% were diabetic, 7% patients used to take OCP and 69% patients used to take tea/coffee. 28.2% patients had fever where as all (100%) patients had abdominal pain. Mean duration of hospital stay was 7.8±2.5. Mean Hct level was 32.9±7.5, mean HbA1c was 7.8±1.7, mean blood urea level was 21.7±7.2 (table-1).

Table 2: Association between serum lipase amylase ratio and acute biliary pancreatitis

<table>
<thead>
<tr>
<th>Type of acute pancreatitis n(%)</th>
<th>L-A ratio (Mean±SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary pancreatitis 23(32.4)</td>
<td>1.40±0.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non biliary pancreatitis 48(67.6)</td>
<td>2.39±0.84</td>
<td></td>
</tr>
<tr>
<td>Total 71(100.0)</td>
<td>2.07±0.86</td>
<td></td>
</tr>
</tbody>
</table>

Unpaired t test was done to measure the level of significance.

Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non biliary pancreatitis was 2.39±0.84. This difference was statistically significant (p <0.001) (table-2).

Table 3: Association between serum lipase amylase ratio and acute alcoholic pancreatitis

<table>
<thead>
<tr>
<th>Type of acute pancreatitis n(%)</th>
<th>L-A ratio (Mean±SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic 9(12.7)</td>
<td>2.89±0.79</td>
<td>0.002</td>
</tr>
<tr>
<td>Non alcoholic 62(87.3)</td>
<td>1.95±0.81</td>
<td></td>
</tr>
<tr>
<td>Total 71(100.0)</td>
<td>2.06±0.89</td>
<td></td>
</tr>
</tbody>
</table>

Unpaired t test was done to measure the level of significance.
Severity of acute pancreatitis  n(%) L-A ratio p value

Hypertriglyceridaemia  28(39.4) 2.75±0.68 <0.001
Non-hypertriglyceridaemia  43(60.6) 1.62±0.65
Total  71(100.0) 2.06±0.89

Unpaired t test was done to measure the level of significance

Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±0.65. This difference was also statistically significant (p<0.001) (table-4).

Table 5: Association of serum lipase amylase ratio with severity of acute pancreatitis (based on revised Atlanta criteria)

Severity of acute pancreatitis  n(%) L-A ratio p value

Mild  45(63.4) 1.95±0.89 0.273
Moderately severe  10(14.1) 2.37±0.92
Severe  16(22.5) 2.22±0.70

ANOVA test was done to measure the level of significance

Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis, the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (p=0.273) (table-5).

Table 6: Association between serum lipase amylase ratio and outcome of acute pancreatitis

Outcome of acute pancreatitis  n(%) L-A ratio p value

No complications  53(74.6) 2.03±0.92 0.557
Complication  18(25.4) 2.17±0.68

Unpaired t test was done to measure the level of significance

Mean serum lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (p=0.557) (table-6).

Discussion

Acute pancreatitis is a relatively common disease with incidence of 5 – 80 per 100,000 population, although its prevalence varies in different countries. Different modalities are available for predicting aetiology, severity and outcome of acute pancreatitis with different sensitivity and specificity. Moreover some are not widely available, some are very expensive. A single, cheap, widely available marker with high sensitivity and specificity is yet to be identified. Serum lipase amylase ratio determined within first 24 hours of hospitalization may contribute in this regard. A prospective, longitudinal study was carried out to assess serum lipase amylase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis.

In this study, 71 patients diagnosed as a case of acute pancreatitis were included. Among them, 21(29.6%) patients were within 31-40 years age group and only 10(14.1%) patients were above 60 years of age. Mean age was 44.35±16.90 (mean±SD) with minimum age 18 years and maximum age 95 years (table 2). Among the patients, 37(52.1%) patients were male and 34(47.9%) patients were female (table 1). In a study by found the mean age of acute pancreatitis of 47 years among which 55 % were male and 45% were female. The mean age and sex difference of the above study correlate with this study.

It is observed that, there is a relation between DM and acute pancreatitis that may be due to hypertriglyceridaemia. In this study, majority (66.2%) of the patients had DM. This can be explained by the inclusion of patients from a tertiary level diabetic hospital. Out of 71, 24(33.8%) patients were smoker, 11(15.5%) patients were alcoholic. Mean BMI was 25.88±2.95. Mean haematoctrit after admission was 32.9±7.5. Mean blood urea nitrogen was 21.7±7.2 and mean HbA1c was 7.8±1.7. Average duration of hospital stay was 7.8±2.5 days.

In this study, 23(32.4%) cases were due to biliary pancreatitis, 15(21.1%) cases were due to hypertriglyceridaemia, 4(5.6%) cases were due to alcohol, 4(5.6%) cases were due to hypertriglyceridaemia and alcohol, 2 (2.8%) cases due to malignancy, 1(1.4%) case due to biliary and alcohol and 22 (31%) cases were due to unknown cause (figure 1). Al-Karawi et al found that 67.5% cases of acute pancreatitis were due to biliary cause; alcohol was responsible in 1.8% of cases and 17% cases were due to unknown cause. In another study, found gall stone as aetiology in 34.1% of cases and alcohol in 33.6% cases and hypertriglyceridaemia in 12.3% of cases. Low prevalence of alcohol as aetiology of acute pancreatitis in present study is due to social custom as well as religious belief. On the other hand, high prevalence of hypertriglyceridaemia in the present study is due to increased prevalence of DM among the study population.

This study showed more than half of the patients (63.4%) had mild acute pancreatitis according to revised Atlanta criteria, 14.1% cases had moderately severe attack and 22.5% of cases had severe attack of acute pancreatitis (figure 2). Cho et al. found 13% cases as severe acute pancreatitis, 8% cases as moderately severe and 79% cases as mild acute pancreatitis in their study which is similar to present study. Out of 71 patients, 17(23.9%) developed complication where as 54(76.1%) developed no complication. Albulushi et al.
found 32% patients that developed complication of acute pancreatitis in their study.\textsuperscript{16}

Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non biliary pancreatitis was 2.39±0.84. This difference was statistically significant (table 3; p <0.001). Again, serum lipase amylase ratio in patients with acute alcoholic pancreatitis was 2.89±0.79 and in patients with non alcoholic acute pancreatitis was 1.95±0.81. This difference was also statistically significant (table 4; p=0.002). Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±0.65. This difference was also statistically significant (table 5; p< 0.001).

This study showed that serum lipase amylase ratio was <2.0 in acute biliary pancreatitis and >2.5 in acute alcoholic pancreatitis and in acute pancreatitis due to hypertriglyceridaemia. Devanath et al. found serum lipase amylase ratio >4.0 in acute alcoholic pancreatitis and <4.0 in patients with acute pancreatitis due to biliary and miscellaneous causes.\textsuperscript{7} There is no study that showed lipase amylase ratio difference among patients with acute pancreatitis due to hypertriglyceridaemia and due to other causes.

Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (Table 6; p=0.273). Devanath et al. also didn’t find any statistically significant difference in lipase amylase ratio among different severity of acute pancreatitis.\textsuperscript{7}

Mean serum lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (table 8; p=0.557). Pezzilli et al. also found lipase amylase ratio unable to predict the outcome of acute pancreatitis.\textsuperscript{19}

Conclusion:

This study evaluated serum lipase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis. Serum lipase amylase ratio was <2.0 in acute biliary pancreatitis whereas this ratio was >2.5 in patients with acute pancreatitis due to alcohol and hypertriglyceridaemia. Serum lipase amylase ratio in mild AP was lower than that observed in moderately severe and severe AP; but this difference was not statistically significant. Again, serum lipase ratio was lower among patients who did not develop complication than those who developed complication; this difference also was not statistically significant. These findings were similar to other studies.

Serum lipase amylase ratio on admission of patients with acute pancreatitis may be used as a predictor of aetiology of acute pancreatitis. Further study is needed with larger sample size.

References: