

Original Research Article

A study of Adenosine Deaminase and Gamma Glutamyl Transpeptidase in Acute Pancreatitis


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Abstract

Background: Acute pancreatitis is an important cause of morbidity and mortality worldwide. Alcohol and gallstone disease remain the commonest causes of acute pancreatitis but metabolic abnormalities, obesity and genetic susceptibility are thought to be increasingly important etiological factors. Serum enzymes amylases and lipase are used as conventional biomarkers of acute pancreatitis.

Objectives: To assay serum enzymes amylase, lipase, adenosine deaminase (ADA) and gamma glutamyl transpeptidase (GGT) in acute pancreatitis of alcoholic and non-alcoholic etiology. The present study also aimed to find the correlation among the enzymes.

Materials and methods: The study subjects were categorized as non-alcoholic acute pancreatitis (n=30), alcoholic acute pancreatitis (n=30) and healthy controls (n=30). Levels of amylase, lipase, adenosine deaminase and gamma glutamyl transpeptidase were estimated in serum samples by standard spectrophotometric methods.

Results: The levels of amylase, lipase, ADA and GGT were significantly higher in acute pancreatitis patients than controls. With respect to amylase and lipase, more pronounced increase was seen in non-alcoholic than the alcoholic acute pancreatitis patients. Increase in GGT was more in alcoholic acute pancreatitis while increase in ADA was comparable in acute pancreatitis of alcoholic and non-

alcoholic etiologies. Serum amylase showed significant positive correlation with lipase, GGT and ADA in alcoholic acute pancreatitis and with lipase in non-alcoholic acute pancreatitis.

Conclusion: Serum levels of enzymes amylase, lipase, ADA and GGT served sensitive markers of acute pancreatitis. Future studies employing larger sample size and differentiating various etiologies of acute pancreatitis, findings correlation among enzyme biomarkers are required.

Key words

Acute pancreatitis, Adenosine deaminase (ADA), Amylase, Gamma glutamyl transpeptidase (GGA).

Introduction

Acute pancreatitis is an important cause of morbidity and mortality worldwide. Alcohol and gallstone disease remains the commonest causes of acute pancreatitis but metabolic abnormalities, obesity and genetic susceptibility are thought to be increasingly important etiological factors [1]. The prompt diagnosis of acute pancreatitis and stratification of disease severity is essential in taking appropriate treatment [1].

Serum amylase and lipase activities are considered the most convenient biochemical tests for the diagnosis of acute pancreatitis [2]. However, serum amylase has low clinical specificity since increased values are also found in a number of acute intraabdominal disorders and in several extrapancreatic conditions [3]. Acute pancreatitis is sometimes a difficult to diagnose because it must be differentiated from other acute intraabdominal disorders with similar clinical findings. In differential diagnosis, elevation of serum lipase activity is a more specific diagnostic finding than increase in serum amylase activity [3].

Gamma glutamyl transpeptidase (GGT) is a sensitive indicator of the presence of hepatobiliary disease and more often serum GGT activity is elevated in alcoholics. Increase in serum GGT is also seen in acute and chronic pancreatitis [3, 4]. Serum GGT has been proposed to be a sensitive biomarker of acute biliary and alcoholic pancreatitis [5, 6]. Adenosine deaminase (ADA) an enzyme of the purine metabolism has been used in the differential diagnosis of pleural effusion. ADA has been looked upon as a marker of cell

mediated immune response. Studies suggested the possible role of ADA in inflammatory disease of the pancreas [7].

There is a need for studies which correlates the changes in serum enzymes in acute pancreatitis; there is paucity of such studies done on Indian population. Hence, the present study was taken up to assess the activities of serum enzymes ADA and GGT in acute pancreatitis and correlate the findings with clinical diagnosis and etiological factors.

Material and methods

The study was carried out at MNR Medical College and Hospital, Sangareddy, Medak, Telangana from June 2014 to May 2015. A total 80 patients with clinically diagnosed acute pancreatitis were subjected and patients were divided into 2 groups of alcoholic pancreatitis and non-alcoholic pancreatitis. Thirty age and sex matched controls were included.

Inclusion criteria

- Patients with clinically diagnosed acute pancreatitis.
- Age between 19-60 years.

Exclusion criteria

- Pancreatic diseases other than acute pancreatitis.
- Systemic diseases or infections.
- Hepatobiliary diseases without secondary pancreatic diseases.

A total five ml of blood was collected from acute pancreatitis and healthy controls, taking aseptic precautions. From the collected blood, serum

was separated and following parameters were assayed.

- **Amylase:** by kinetic spectrophotometric method using Ethylidene G7-p Nitrophenol as substrate [3].
- **Lipase:** By kinetic spectrophotometric method using 1, 2 O-dilauryl-rac-glycero-3-glutaric acid (6-methyl-resorufin) ester as substrate [3].
- **GGT:** By kinetic spectrophotometric method using gamma-glutamyl-p-nitroanilide as substrate [3].

- **ADA:** By kinetic spectrophotometric method using adenosine as substrate [3].

Results

Among the study subjects, overall 25% were females. There were four females in non-alcoholic pancreatitis group and no females in alcoholic pancreatitis group. The average age of study subjects was 39 years with a standard deviation of 9. (**Table - 1** and **Table - 2**)

Table – 1: Serum levels of Amylase, Lipase, GGT and ADA.

| | Group-I (Non-alcoholic pancreatitis) (n=30) | Group-II (alcoholic pancreatitis) (n=30) | Group-3 (Healthy controls) (n=30) |
|----------------|--|---|--|
| Amylase (IU/L) | 644± 132* | 424± 65* | 55± 16 |
| Lipase (IU/L) | 847±183* | 518± 125* | 33±17 |
| GGT (IU/L) | 49.6±10.1* | 116±31* | 29±8.5 |
| ADA (IU/L) | 31±9.5* | 29±9* | 13±5.8 |

Table - 2: Correlation among amylase, lipase, GGT and ADA in alcoholic and non-alcoholic pancreatitis patients.

| Correlation | Non-alcoholic pancreatitis | | Alcoholic pancreatitis | |
|--------------------|-----------------------------------|-----------|-------------------------------|-----------|
| Amylase- Lipase | r = 0.877 | P < 0.001 | r = 0.927 | P < 0.001 |
| Amylase-GGT | r = 0.033 | P = 0.880 | r = 0.780 | P < 0.001 |
| Amylase-ADA | r = 0.172 | P = 0.443 | r = 0.877 | P < 0.001 |
| Lipase- GGT | r = 0.137 | P = 0.533 | r = 0.794 | P < 0.001 |
| Lipase- ADA | r = 0.273 | P = 0.330 | r = 0.053 | P = 0.834 |
| GGT-ADA | r = 0.178 | P = 0.416 | r = 0.052 | P = 0.828 |

The patients with acute pancreatitis showed significantly higher serum levels of amylase and lipase, when compared to healthy controls. The increase in amylase and lipase was more pronounced in non-alcoholic acute pancreatitis patients than their alcoholic cohorts. Increase in amylase was 11.7 fold and increase in lipase was 25.5 fold in non-alcoholic pancreatitis patients. In alcoholic acute pancreatitis, the increase in serum levels of amylase and lipase were 7.7 fold and 15.7 fold respectively. The results were statistically highly significant (P < 0.001).

Serum level ADA showed significant increase by 2.4 fold and 2.2 fold respectively, in non-alcoholic and alcoholic acute pancreatitis patients. There was no significant difference in ADA levels of alcoholic and non-alcoholic pancreatitis patients. Serum GGT showed significant increase of 1.7 fold and 4 fold respectively in non-alcoholic and alcoholic acute pancreatitis patient. The increase was more pronounced in alcoholic patients than the non-alcoholic cohorts in comparison to controls.

The correlation analysis showed that there was significant positive correlation between serum amylase and lipase in both alcoholic and non-

alcoholic acute pancreatitis patients. In alcoholic acute pancreatitis patients, amylase showed significant correlation with ADA and GGT and lipase showed correlation with GGT.

Discussion

The present study has made an attempt to analyze the serum levels of amylase, lipase, GGT and ADA in Acute pancreatitis patients. The study observed that there was significant elevation of serum levels of all these enzymes in alcoholic and non-alcoholic acute pancreatitis patients.

Serum amylase originates from salivary gland and pancreatic sources. Hence, it has less specificity than lipase with respect to diagnosis of acute pancreatitis [8, 9, 10]. In acute pancreatitis, the rise in serum amylase activity occurs within 5 to 8 hours of symptom onset, activity returns to normal by the third or fourth day. In acute pancreatitis, a fourfold to six fold elevation of amylase above the upper reference limit is usual, with maximal concentration attained in 12 to 72 hours. As compared with serum amylase level in alcoholic acute pancreatitis was higher by 7.7 fold and in non-alcoholic acute pancreatitis was higher by 11.7 fold, when compared to mean serum amylase on healthy controls. Serum lipase increased by 25.5 and 15.7 fold respectively, in non-alcoholic and alcoholic pancreatitis group and the lipase showed significant correlation with amylase in both the groups [11].

In previous study by tenner and Steinberg, the serum amylase at admission was lower, serum lipase was within normal limit and the lipase to amylase ratio was higher in patients with alcoholic pancreatitis. They observed that higher the lipase: amylase ratio, greater the specificity of alcohol as the etiology of acute pancreatitis (1.3) and alcoholic acute pancreatitis (1.2) in comparison to controls (0.6). Some other studies have reported increased serum levels of amylase and lipase levels in acute pancreatitis of biliary and alcoholic etiology. They also reported that

enzyme levels were comparable in acute pancreatitis of both biliary and alcoholic etiology and lipase: amylase ratio differentiated between alcoholic (ratio > 3) and biliary etiologies [12]. In the present study, the amylase and lipase levels were significantly higher in non-alcoholic etiology than the alcoholic etiology of acute pancreatitis and the ratio of lipase: amylase was comparable between two etiologies. This has a small sample size and did not do a differential diagnosis of non-alcoholic etiologies as there was a very small number of pancreatitis of biliary etiology (6 Out of total 30 patients with non-alcoholic etiology of acute pancreatitis).

Serum GGT was significantly higher in alcoholic and non-alcoholic acute pancreatitis in comparison to controls. The increase was more in alcoholic group (4 fold) than non-alcoholic groups (1.7 fold). Elevation of serum GGT activity is found in patients with alcoholic hepatitis and in heavy drinkers. Serum GGT is also considered as an indicator of hepatobiliary diseases [3]. studies by Coffey, et al. [13] suggested that the biliary pancreatitis triad of serum GGT ≥ 40 U/L, ALT ≥ 150 U/L and lipase $\geq 15 \times$ ULN, within 48 hours of presentation may be used as simple clinical predictors of ABP in children; and children with values falling below 2 or 3 of these thresholds are very unlikely to have AP due to a biliary cause. Serum GGT showed positive correlation with amylase and lipase in acute pancreatitis of alcoholic etiology [13].

Activity of ADA in serum was significantly higher in acute pancreatitis patients when compared to healthy controls. The magnitude of increase in serum ADA was marginally higher in non-alcoholic (2.4 fold) than alcoholic (2.2 fold) acute pancreatitis. How the difference between 2 groups was statistically insignificant. In a study by Ibis, et al. [5], Serum ADA levels were significantly higher in acute and chronic pancreatitis and pancreatic cancer patients compared to the controls. The present study has observed that serum ADA showed a significant positive correlation with serum amylase in

alcoholic acute pancreatitis patients but, such correlation was not seen in acute pancreatitis of non-alcoholic etiology.

This study has its own limitations. The sample size was small, non-alcoholic etiologies were not differentiated and other enzymes related to liver function were not assayed. The levels of lipase were not estimated during the time of admission in some cases. Hence, calculation of lipase: amylase ratio might not have reflected the actual scenario and limited the diagnostic utility of this ratio. However, with in the limitations the study has demonstrated sensitivity of enzymes lipase and amylase in the diagnosis of acute pancreatitis and correlation of the conventional marker amylase with lipase, GGT and ADA.

Conclusion

The present study has observed significant increase in serum enzymes amylase, lipase, GGT and ADA in alcoholic and non-alcoholic acute pancreatitis patients. This study also showed significant correlation of serum amylase with other enzymes GGT, Lipase and ADA. the enzyme GGT has shown more pronounced increase in alcoholic acute pancreatitis than non-alcoholic acute pancreatitis suggesting its utility as an additional biochemical to be estimated in case of acute pancreatitis of alcoholic etiology. Future studies employing larger sample size and assessing the clinical utility of enzymes in differential diagnosis of acute pancreatitis of various etiologies are required.

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