ABSTRACT
A case control study was undertaken in a tertiary medical care hospital to find out the significance of measurement of serum amylase and lipase activity as an indicator of chronic alcoholism. Out of total 100 subjects, 50 healthy individuals were taken as control group and 50 cases of chronic alcoholics with clinical manifestations of chronic alcohol abuse were taken as test group. The fasting plasma glucose (FPG), serum amylase, serum lipase, and serum gamma glutamyl transferase were estimated by colorimetric methods. The mean serum amylase, serum lipase, and serum gamma glutamyl transferase activities in control group and the test group were found to be 61.64±13.15 U/L and 156.14±152.94 U/L; 61.84±14.07 U/L and 268.48±175.13 U/L; 38.84±18.01 U/L and 170.5±110.88 U/L respectively with a significance of P<0.001. Mean fasting plasma glucose is found to be lower in the test group compared to the control group though both are within normal reference interval. The study suggests that serum amylase and lipase activities are increased in individuals with history of chronic alcohol abuse compared to normal individuals and can be used as markers of chronic alcoholism along with serum gamma glutamyl transferase activity.

Keywords: Case control study, Amylase, Lipase, Gamma glutamyl transferase

INTRODUCTION
Chronic alcoholism is a chemical/biological disease that is primary, progressive, chronic and fatal characterized by an incessant craving for increased tolerance of physical dependence upon and loss of control over drinking alcohol. It is a disease with a known pathology and an established bio molecular signal transduction pathway. The American Medical Association (AMA) had declared alcoholism as an illness in 1956. In 1991, The AMA further endorsed the dual classification of alcoholism by the International Classification of Diseases under both psychiatric and medical sections. Chronic alcoholism is primary since it is not related to another disease. It has its own diagnosis and own pathology. It is also a chemical disease because it breaks down differently in the stomach and has an entirely different effect on the brain of the alcoholic than on the non-alcoholic. It is biological in the sense that the chemical predisposition is inherited. Heavy alcohol use is one of the most common causes of both acute and chronic pancreatitis. While pancreatitis has been known to occur after a single episode of heavy alcohol use, prolonged heavy drinking is common in most cases. Acute alcoholic pancreatitis is characterized by the abrupt onset of abdominal pain, nausea, vomiting, and increased levels of serum or urine pancreatic enzymes.

Amylases are group of hydrolases that split carbohydrates having glucose monomers bonded by α-1,4 glycosidic linkage. It has two isomers – salivary (S) and pancreatic (P) amylases. Amylase is present in a number of organs and tissues. The greatest concentration is present in the pancreas (P – type), where the enzyme is synthesized by the acinar cells and then secreted into the intestinal tract by way of the pancreatic duct system. The salivary glands also secrete a very potent amylase (S – type) to initiate hydrolysis of starch in the mouth and oesophagus. The enzyme is also found in colostrums, tears and milk. The serum amylase concentration reflects the balance between the rates of amylase entry into and removal from the blood. Hyperamylasemia can result either from an increased rate of entry of amylase into the circulation and/or a decreased metabolic clearance of this enzyme. The pancreas and salivary glands have amylase

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concentrations that are several orders of magnitude greater than that of any other normal tissue, and these two organs probably account for almost all of the serum amylase activity in normal persons. A variety of techniques are now available to distinguish pancreatic from salivary-type isoamylase. Pancreatic hyperamylasemia results from an insult to the pancreas, ranging from trivial (cannulation of the pancreatic duct) to severe (pancreatitis). In addition, loss of bowel integrity (infarction or perforation) causes pancreatic hyperamylasemia due to absorption of amylase from the intestinal lumen. Hyperamylasemia due to salivary-type isoamylase is observed in conditions involving the salivary glands. In addition, this type of hyperamylasemia occurs in conditions in which there is no clinical evidence of salivary gland disease, such as chronic alcoholism, postoperative states (particularly postcoronary bypass), lactic acidosis, anorexia nervosa or bulimia, and malignant neoplasms that secrete amylase. Hyperamylasemia can also result from decreased metabolic clearance of amylase due to renal failure or macroamylasemia (a condition in which an abnormally high-molecular-weight amylase is present in the serum). Patients with abdominal pain and a markedly elevated serum amylase (more than three times the upper limit of normal) usually have acute pancreatitis, and additional serum enzyme testing is not helpful. Patients with smaller elevations of serum amylase often have conditions other than pancreatitis, and measurement of a serum enzyme more specific for the pancreas (pancreatic isoamylase, lipase or trypsin) is frequently of diagnostic value in such patients.¹

Lipase is an enzyme that catalyses the breakdown of triglycerides.² In addition to pancreatic acinar cells, lipase is found in the gastrointestinal tract, including the oesophagus, duodenum, stomach and colon.² Lipase has also been described in the liver, heart, lungs and leukocytes.²,³ Pancreatic lipase content is approximately 100 times that of the small intestine and liver, and the pancreas to serum lipase concentration gradient is close to 20 000.²

Lipase levels may be increased in Acute pancreatitis, Perforated or penetrating peptic ulcer, Obstruction of pancreatic duct by stone, Drug-induced spasm of sphincter of Oddi, Chronic pancreatitis, Pancreatic pseudocyst, Pancreatic malignancy, Gastric malignancy or perforation, Acute cholecystitis, Small bowel obstruction, Intestinal infarction, Cystic fibrosis, Inflammatory bowel disease, Acute and chronic renal failure, Organ transplantation, particularly associated with a complication (organ rejection, cyclosporine toxicity, cytomegalovirus infection), Alcoholism, Diabetic ketoacidosis, Intracranial hemorrhage, Lymphoma, Chronic liver disease, and after endoscopic retrograde cholangiopancreatography.⁴

MATERIALS AND METHODS
The present study is a case control study on a group of 100 individuals equally divided into age and sex matched healthy non-alcoholics (controls) and alcoholics (cases or tests) taken randomly from different socioeconomic status. The study was conducted in the department of Biochemistry, Assam Medical College and Hospital, Dibrugarh, Assam in collaboration with various clinical departments. Control group consists of normal healthy individuals without any history or symptoms referable to disease of any system and who are non-alcoholics. Subjects of the test (case) group were amongst those who attended OPD as well as who were admitted in the neurology, medicine, surgery and psychiatry wards of Assam Medical College and Hospital with different types of clinical manifestations of chronic alcohol abuse.

Exclusion criteria of the test group:
- Non-alcoholic liver disease
- Diabetes Mellitus
- Hyperlipidemia
- Viral hepatitis
- Cirrhosis of liver
- Non-alcoholic pancreatic disease
- Carcinoma of liver/pancreas
- Drug induced liver disease
- Alcoholism, Diabetic ketoacidosis, Intracranial hemorrhage, Lymphoma, Chronic liver disease, and after endoscopic retrograde cholangiopancreatography.

RESULTS AND OBSERVATION
Age and sex distribution of the subjects: It was found that maximum numbers of cases in chronic alcoholic (test) group were in the age group of 31 – 40 years (48%) and this was followed by the age group of 41 – 50 years (28%). No case was found below 20 years and above 60 years of age. Out of 50 cases there were 45 males and 5 females. Male preponderance was observed with a ratio of 9:1.

<table>
<thead>
<tr>
<th>Table 1 Age and sex distribution of the subjects</th>
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<tbody>
<tr>
<td>Variables</td>
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<tr>
<td>Age in years</td>
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<tr>
<td>Sex</td>
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Figure 1 shows the age distribution of the control and test group. Figure 2 shows the sex distribution of the control and test group.

Table 2 Range, mean and standard deviation (SD) of fasting plasma glucose, Serum amylase, Serum lipase and serum GGT in control and test subjects

<table>
<thead>
<tr>
<th>Different parameters</th>
<th>Controls (No. 50)</th>
<th>Test (No. 50)</th>
<th>P – value</th>
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</thead>
<tbody>
<tr>
<td>Fasting plasma Glucose (mg%)</td>
<td>Range 74 - 109</td>
<td>Mean 92.58</td>
<td>SD (+) 9.61</td>
</tr>
<tr>
<td>Serum amylase (U/L)</td>
<td>36 - 84</td>
<td>Mean 61.64</td>
<td>SD (+) 13.15</td>
</tr>
<tr>
<td>Serum Lipase (U/L)</td>
<td>38 - 89</td>
<td>Mean 61.84</td>
<td>SD (+) 14.07</td>
</tr>
<tr>
<td>Serum GGT (U/L)</td>
<td>14 - 82</td>
<td>Mean 38.84</td>
<td>SD (+) 18.01</td>
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</table>

Table 2 shows that mean fasting plasma glucose in the control group were higher (92.58 mg%) than the test group (84 mg%) though both are within normal reference interval. Mean serum amylase activity in control group is lower (61.64 U/L) than the test group (156.14 U/L). Also mean serum lipase in control group is lower (61.84 U/L) than the test group (268.48 U/L). Mean serum GGT in control group is lower (38.84 U/L) than the test group (170.5 U/L).

Figure 3 shows the statistical difference in parameters FPG, serum amylase, serum lipase and serum GGT between control and test group.

DISCUSSION

In the present study, highest number of cases were found in the fourth decade that is between 31 – 40 years (48%) followed by fifth decade that is between 41 – 50 years (28%). Wilsnack RW et al found men and women in three age groups (18–34, 35–49, 50–65) showed the prevalence of drinkers, former drinkers, and lifetime abstainers; and the prevalence of high-frequency, high-volume, and heavy episodic drinking among current drinkers. It is also found that among 50 numbers of chronic alcoholics, 45 were males and 5 were females with a male preponderance of 9:1.

The findings regarding the gender distribution of alcoholism is similar with the study by Wilsnack RW et al.9

Fasting plasma glucose is found to be within normal reference interval in both the control (92.58 mg%) and test (84 mg%) groups. The mean serum amylase is found to be higher in test group (156.14 U/L) when compared to control group (61.64 U/L) with a P value of <0.001. d’Emden et al found hyperamylasemia in asymptomatic alcoholics.10 Pelletier G et al11 studied the prevalence of hyperamylasemia in 100 patients with chronic alcoholism. Moderate hyperamylasemia was found in 15 patients. After one week of hospitalization, serum amylase was still elevated in 11 of 14 alcoholic patients. Hyperamylasemia was due to an increase in the isoamylase P in 5 cases, in the isoamylase S in 7 cases, and in both forms in 3 cases. Activities of serum lipase and isoamylase P were roughly parallel. Only two out of 8 patients with elevated isoamylase P had chronic pancreatitis. The salivary origin of elevated isoamylase S was suspected in only one out of 10 patients. This work shows that the origin of moderate hyperamylasemia, observed in alcoholic patients, is often extrapancreatic. It is suggested that the dosage of serum lipase simpler than that of isoamylases, may be routinely used in chronic alcoholic patients for diagnostic purposes.

Maruyama K et al12 found that in the group with abnormally high total serum amylase on admission, levels were decreased after abstinence. In patients with pancreatic disorders in this group,
abstinence leads to a decrease in total serum amylase, but in patients with no such disorders, total serum amylase increases temporarily due to increases in salivary isoamylase. In the group with normal total serum amylase on admission, levels increased sharply after abstinence, and both pancreatic isoamylase and salivary isoamylase contributed to the gains. In the group with low total serum amylase, a sharp increase of 2-fold or more was noted after abstinence, and a major contributor was pancreatic isoamylase. The ratio of urine amylase to total serum amylase gradually declined, indicating clearly that abstinence led to a decrease in the excretion of amylase in urine.

The mean serum lipase activity in the test group (268.48 U/L) is higher than the control group (61.84 U/L) with a P value of <0.001. According to Gumaste VV et al13, using an elevated serum amylase level to diagnose acute pancreatitis in an alcoholic patient with abdominal pain may not be appropriate, because hyperamylasemia is common in asymptomatic alcoholics without acute pancreatitis. To determine whether serum lipase also suffers from the same drawback, they undertook a prospective study involving 202 asymptomatic alcoholics admitted to the detoxification unit of their hospital. Sixty-six of the 202 patients had serum lipase levels above the normal range (0-213 U/L). Of these 66, 55 (83%) had levels that were one to two times normal, while 11 patients had levels ranging between two and three times normal. No patient exceeded three times the normal level. This background information is important in the interpretation of serum lipase levels in alcoholic patients with abdominal pain.

Pezzilli R et al14 found that Among occasional drinkers, serum amylase levels were abnormally high in 6 subjects (13%), whereas serum pancreatic isoamylase and lipase were abnormally high in one, (2%). In chronic alcoholics without abdominal pain serum amylase and lipase were abnormally high in 10 subjects (14%) but serum pancreatic isoamylase in only 7 (10%). In patients with acute alcoholic pancreatitis, serum amylase and pancreatic isoamylase were abnormally high in 16 of the 17 patients (94%), whereas serum lipase was abnormally high in all.

The mean serum GGT in the test group (170.5 U/L) is found to be higher than the control group (38.84 U/L) in the present study. Ishii H et al15 also got a similar finding. His findings suggested that enhanced hepatic and intestinal GGT activities may contribute, at least in part, to an increased level of serum GGT frequently seen in chronic alcoholics.

CONCLUSION

It has become evident from the above discussions that though a variety of factors influence the serum concentrations of amylase and lipase, chronic ethanol abuse having a profound effect on almost all the organs of the body, contributes greatly into increase in the levels of these two enzymes in the general circulation. On the light of all foregoing observations and discussions along with the statistical evaluations, it is established that serum amylase and lipase activities are definitely increased resulting in a higher lipase to amylase ratio in the chronic alcoholics and present the affirmative conclusion that serum amylase and lipase are altered with a fixed proportion under chronic ethanol abuse but is still insufficient to directly link any definite organ or system under the observed changes. A further prospective study would be helpful to evaluate the exact contribution of chronic ethanol abuse responsible for this clinical chemical constellation, especially in patients without abdominal pain, as multiple factors and conditions can lead to a state of hyperamylasemia and hyperlipasemia.

Ethical clearance: Taken

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Conflict of interest: Nil

Contribution of authors:

REFERENCES