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Research Article

COMPARING TRADITIONAL SERUM AMYLASE WITH RELATIVELY NEW LIPASE IN ACUTE PANCREATITIS

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ABSTRACT: Acute pancreatitis is most often diagnosed clinically and by blood tests rather than expensive radiological methods. Among the blood tests, amylase and lipase are frequently used to diagnose acute pancreatitis. In this retrospective study, we compare amylase versus lipase in terms of sensitivity and specificity with ROC curve analysis.40 established cases of acute pancreatitis were chosen. Day 1 measurements of serum amylase and lipase were noted. Values ≥3 times the upper limit of normal were considered to have acute pancreatitis. 40 age and sex matched controls were also chosen. Cases and controls were compared statistically.Receiver operating characteristics (ROC) curves were constructed for amylase and lipase. Area under the curve (AUC) for amylase was 0.85 and for lipase 0.92. At a cut off level of 122U/L, serum amylase had a sensitivity of 64.5% and specificity of 91%. On the other hand, serum lipase had a sensitivity of 67.5% and specificity of 97.5% at a cut-off level of 58U/L. Our study clearly shows that sensitivity and specificity of serum lipase is better than that of serum amylase and hence proves that lipase is a better marker for acute pancreatitis than amylase.

Key words: Amylase, Area under Curve (AUC), Lipase, Pancreatitis, ROC (Receiver Operating Characteristics) curve, Sensitivity, Specificity

INTRODUCTION

Acute pancreatitis is an inflammatory condition of the pancreas which is usually reversible and resolves without causing any structural disruption. But the severity of the disease varies from a mild self-limiting illness to a catastrophic event causing multi-organ failure, sepsis leading to death. Many mild cases may go undiagnosed. Acute pancreatitis accounts for 7-10% of cases presenting with abdominal pain.

Pathophysiology

Gallstones and alcohol abuse account for most (>90%) of the cases of acute pancreatitis. Gallstones cause obstruction of pancreatic duct, impairing the blood flow to pancreatic cells leading to ischemic cellular injury. This may predispose to activation of the pancreatic proteolytic enzymes. The exact mechanism by which alcohol causes pancreatic injury is not known, but it is thought to be causing direct injury or by releasing free radicals.The free radicals in turn activate the pancreatic proenzymes. The lesser common causes include drugs (azathioprine, mercaptopurine, didanosine, oestrogens, antibiotics (sulfonamides, erythromycin, tetracycline), anticonvulsants such as valproateetc), blunt trauma to the abdomen, infections (mumps, hepatitis, hepatitis viruses), metabolic causes (hypertriglyceridemia, hypercalcemia, uremia, diabetic ketoacidosis) and iatrogenic causes (ERCP induced pancreatitis).

Also, people with specific type of mutation called Anti-monocyte Chemoattractant Protein-1 (MCP-1) mutation, are eight times more prone to develop acute pancreatitis than the general population. MCP-1 is an inflammatory chemokine which normally targets monocytes and T-lymphocytes. Mutated MCP-1 is known to cause acute or chronic pancreatitis by causing mononuclear infiltration (Marra, 2005).

Ultimately, there is inappropriate/premature activation of precursor enzymes, the zymogens in the pancreatic cells. Usually trypsinogen is the first to be activated to trypsin. Later, trypsin activates most of the other proenzymes causing localized inflammation - pancreatitis. The activated enzymes destroy pancreatic acinar cells resulting in the release of cytokines which will enhance the local inflammatory response as well as systemic/extrapancreatic inflammatory response. This is responsible for the systemic complications in acute pancreatitis such as multi organ dysfunction and ARDS (Manso et al., 2007). A balance between the pro-inflammatory and anti-inflammatory factors determines the severity of acute pancreatitis. Patients with acute pancreatitis present with acute abdominal pain in the epigastric region often radiating to the back, which lasts for several hours. Laboratory tests reveal elevated serum amylase &lipase and are still being used for the diagnosis of acute pancreatitis (Munoz and Katerndahl, 2000). Abnormal liver function tests include elevated serum bilirubin levels, elevated serum transaminases and alkaline phosphatase (ALP). A threefold elevation of alanine transaminase (ALT) in the presence of acute pancreatitis is helpful in diagnosing gallstone pancreatitis. But estimation of bilirubin and alkaline phosphatase has not been proved to be useful (Tenner et al., 1994).

Amylase: There are several types of amylase enzyme: α, β and γ. Human tissues predominantly have α-amylase(E.C. 3.2.1.1.), which is produced by the pancreas and salivary glands. The main function of amylase is to cleave starch at the internal 1,4 α-glycosidic linkages in the process of digestion resulting in the formation of smaller carbohydrates such as maltose and glucose. Following acute pancreatitis, serum amylase rises in the first 24 hours of onset of symptoms and returns to normal in 3-5 days (Matullet al., 2006). However, depending on the severity, it may remain in circulation for 5-10 days. A diagnosis of acute pancreatitis can be made if serum amylase (or lipase) levels ≥3 times the upper limit of normal (Banks and Freeman, 2006).

Lipase: Lipase hydrolyzes triglycerides. There are several forms of lipase such as pancreatic lipase, hormone sensitive lipase and lipoprotein lipase. Pancreatic lipase hydrolyses triglycerides in the gastrointestinal tract to monoglycerides and free fatty acids. Hormone sensitive lipase is an intracellular lipase, hydrolyses triglycerides of the adipose tissue. Lipoprotein lipase hydrolyses circulating triglycerides present on chylomicrons and VLDL.

A diagnosis of acute pancreatitis can be made if serum lipase (or amylase) levels ≥3 times the upper limit of normal (Banks and Freeman, 2006). Its level increases within 4-8 hours, peaks at 24 hours and stays longer in circulation – for 1-2 weeks (Cartier et al., 2006). If amylase or lipase levels remain elevated for many weeks, it is usually due to persistent pancreatitis, blockage of pancreatic duct or development of pancreatic pseudocyst (Banks and Freeman, 2006).

The aim of this study was to compare amylase and lipase in terms of their sensitivity and specificityand analyze which one is more reliable in the clinical setting of acute pancreatitis.Our study is one of the very few retrospective studies done in a south Indian population where the diagnostic accuracy of serum amylase and lipase in cases of acute pancreatitis was evaluated by ROC analysis.

MATERIALS AND METHODS

This was a retrospective study conducted by obtaining laboratory data of the enzymes lipase and amylase from case records with the help of MRD (Medical Records Department). Data of over a period of 2 years was collected. Data was obtained from established cases of acute pancreatitis, where the diagnosis had been made clinically andby laboratory tests. 40 cases of acute pancreatitis in the age group of 30 to 65 years were included in the study.Patients with any associated pathology that might cause elevation of serum amylase and lipase such as renal failure, parotid disease, peptic ulcer, cardiac diseases, pneumonia, ovarian tumours, salpinigitis, intestinal obstruction, appendicitis etc. were excluded from the study. 40 age and sex matched controls were also involved in the study. The controls were chosen from patients attending ENT and Ophthalmology OPDs with nonpancreatic illnesses. Venous blood samples had been collected on the day of admission, processed and analyzed soon after. Analysis of serum for the enzymes had been done using autoanalyzer.

Methodology:

Estimation of amylase was done by an IFCC approved enzymatic rate method (Lorentz, 1998).

Estimation of lipase was done based on a kinetic method (Panteghini and Bonora 1996)

Diagnosis: Patients with serum amylase and lipase levels ≥3 times the upper limit of normal were considered to have pancreatitis (Banks and Freeman, 2006).

The laboratory reference ranges considered were as follows:

Serum amylase: 24 – 125 U/L

Serum Lipase: 32 – 60 U/L

Results were tabulated on an Excel sheet and statistical analysis was done using SPSS software.

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RESULTS

A total of 40 cases were included in this study along with 40 controls. Among these 40 cases, 27 were males and 13 were females.

Six patients (15%) admitted to regular alcohol intake.

On comparison of the mean values of serum amylase and lipase with that of controls, a significant difference (P<0.01) was noted (Table 1). The same is represented in a bar diagram (Fig 1).

Enzyme values (of Day 1) were evaluated by ROC (Receiver Operating Characteristic) curves to compare the diagnostic accuracy of serum amylase v/s serum lipase.

The area under the curve (AUC) for serum amylase was 0.85 and AUC for serum lipase 0.92 (Fig 2). The cut-off (threshold) for serum amylase was 122U/L, at which the sensitivity was 64.5% and specificity was 91%. The cut-off (threshold) for serum lipase was 58U/L, at which the sensitivity was 67.5% and specificity was 97.5% (Table 2).

The values show that serum lipase is more sensitive and specific than serum amylase to pancreatitis and also the superiority of the ROC curve of serum lipase over that of serum amylase.

Table 1: Comparison of Amylase and Lipase in two groups studied

	Cases	Control	P value
Amylase	219.35±57.90	65.73±31.55	<0.01
Lipase	141.25±68.99	32.88±13.07	<0.01

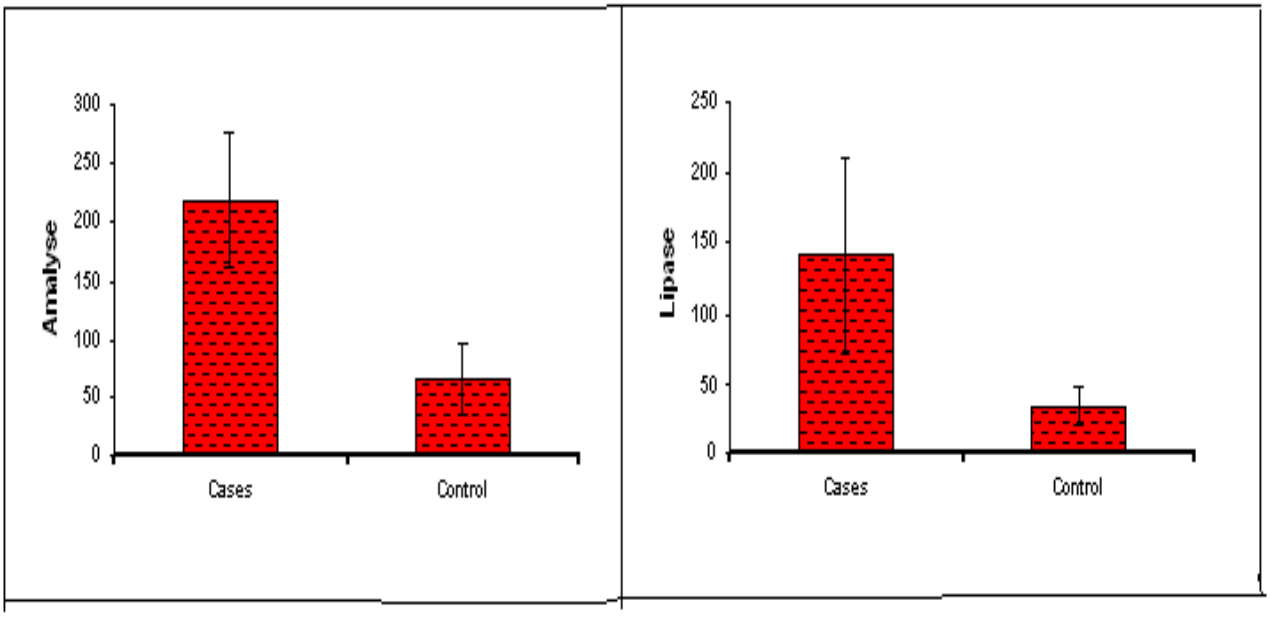

Fig1: Bar diagram showing amylase and lipase levels in cases and controls

Table 2: ROC curve analysis for Amylase and Lipase

Cases v/s Control	Cut-off	Sensitivity	Specificity	AUC	P value
Amylase	122U/L	64.5	91.0	0.85	<0.01
Lipase	58U/L	67.5	97.5	0.92	<0.01

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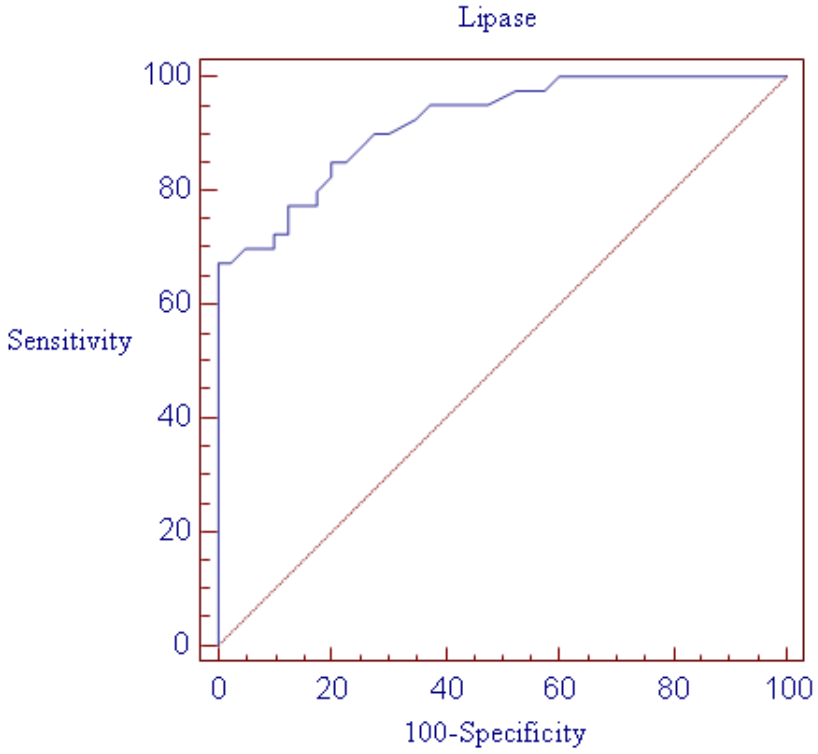

Fig 2: ROC curve for Lipase

Table 3: Causes of Hyperamylasemia

Acute or chronic pancreatitis
Pancreatic pseudocysts
Pancreatic trauma
Carcinoma of the pancreas
Recent ERCP procedure
Cholecystitis, cystic fibrosis
Choledocholithiasis
Parotitis
Chronic liver disease – alcoholism
Renal failure – due to reduced metabolic clearance
Intestinal diseases – Mesenteric infarction, intestinal obstruction, peritonitis, appendicitis
Macroamylasemia
Ruptured ectopic pregnancy
Salpingitis
Fallopian / ovarian cysts
Ectopic amylase production – from Carcinoma lung/ovary/colon/breast / multiple myeloma
Eating disorders: anorexia nervosa and bulimia nervosa
Acidosis – ketoacidosis or non-ketotic acidosis
Drugs – ciprofloxacin, morphine, codeine
Rare causes: SLE, pneumonia, burns, abdominal aortic aneurysms, OP poisoning

Table 4: Causes of Hyperlipasemia

Acute or chronic pancreatitis
Gall bladder disease
Intestinal obstruction
Renal insufficiency
Peptic ulcer disease
Obesity

DISCUSSION

Most of the cases of acute pancreatitis in our study were due to gall stone disease (81%). About 15% of the cases were due to alcoholism. The remaining few cases were due to metabolic causes, infections and trauma.

Our study revealed that serum lipase had a better sensitivitywhen compared to serum amylase. The result of our study is similar to the one done by Gomez D et alin 2012, which was a retrospective study where they included 151 patients with acute pancreatitis, and the results showed that lipase had a sensitivity of 96.6% and amylase had a sensitivity of 78.6% (Gomez et al., 2012).Another study done by Keim V et al showed that lipase had a sensitivity of 100% and specificity of 95% on day 1, which, however reduced on days 2-3 for the diagnosis of acute pancreatitis (Keim et al., 1998). According to Lott et al, serum lipase has a clinical sensitivity in excess of 80% for acute pancreatitis (Lott et al., 1986). But there are many factors that reduce the sensitivity of amylase. According to Matull et al, amylase sensitivity is reduced by its late presentation. Amylase sensitivity is also reduced by hypertriglyceridemia and chronic alcoholism (Matull et al., 2006). Excessive triglycerides in serum will interfere with the assay of amylase and yield false low results (Yadav et al., 2002). Triglycerides will not interfere with lipase measurement (Matull et al., 2006). So sensitivity of Lipase for AP is better than that of amylase. Our study also showed that specificity of serum lipase is better than that of amylase. The study done by Gomez et al showed that serum lipase had a higher specificity than serum amylase for diagnosing acute pancreatitis (Gomez et al., 2012). Gumaste et al conducted a study in 1993 involving 95 cases with acute abdominal pain. They estimated serum amylase and lipase and compared them in patients with nonpancreatic abdominal pain and acute pancreatitis. They found that serum lipase had a better sensitivity (100%) and specificity (99%) in detecting acute pancreatitis than serum amylase in differentiating nonpancreatic abdominal pain from acute pancreatitis (Gumaste et al., 1993). A retrospective study conducted by Chang et al in a large population revealed that serum amylase and lipase both had high specificities but serum lipase had far higher sensitivity to diagnose acute pancreatitis than serum amylase, unlike the results of our study (Chang and Chung, 2011). Usually, only 40% of serum amylase is of pancreatic origin and the remaining is of salivary origin (Dubagunta et al., 2001). Therefore, the elevation of serum amylase suggests several pancreatic as well as extrapancreatic pathologies (Table 3). This reduces the specificity of serum amylase for using it as a marker for diagnosing acute pancreatitis.Usually what is measured is total amylase in serum and not the specific pancreatic isoenzyme, which will of great significance when measured.However, the degree of elevation of either total serum lipase or amylase does not indicate the severity of disease. (Lankisch et al.,1999). The pancreas is the primary source of serum lipase (triacylglycerol acyl-hydrolase; EC 3.1.1.3), unlike that of amylase. Lipase levels are not elevated in salivary pathologies. Hence, serum lipase specificity is more than that of serum amylase. Even serum lipase is not considered very specific for the pancreas as it is elevated in other intra-abdominal pathologies as well, but extrapancreatic causes for hyperlipasemia are very few (Table 4). This factor contributes to the higher specificity of serum lipase.

Many clinicians earlier used to find the combined estimation of serum amylase and lipase beneficial. But of late, researchers are finding amylase to be not of much worth and that amylase estimation may be totally replaced by lipase estimation. In fact, many studies have shown that the estimation of lipase alone will be profitable (Gomez et al., 2012).

CONCLUSION

Although serum amylase is a commonly used marker for acute pancreatitis, it has many disadvantages such as poor sensitivity and that its level increases in serum much later during the disease process when compared to serum lipase. Serum lipase is more sensitive and specific than serum amylase to acute pancreatitis and also helps in the early detection of the disease. Therefore, serum lipase is superior to serum amylase as a marker for the diagnosis of acute pancreatitis.Serum lipase estimation alone is sufficient to confirm or rule out acute pancreatitis.

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