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Serum Hyperamylasemia as a prognostic indicator of acute viral hepatitis and cirrhosis of liver

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ABSTRACT

Liver disease is a condition that causes liver inflammation or tissue damage and affects liver function. Liver functions tests are abnormal in various liver diseases such as hepatitis, cirrhosis and end stage liver disease. The study of pancreatic enzymes for prognostic purpose in evolving liver disease is gaining ground and act as prognostic indicator for liver diseases. Present study has been planned to assess the serum amylase status in 50 patients of acute viral hepatitis and 50 patients of cirrhosis of liver in comparison to 50 normal healthy control subjects. Levels of serum amylase were determined by CNP- G3 kinetic method. The serum levels of amylase were significantly raised ($p<0.0001$) in patients compared to control group and levels were observed to be constantly increased with increased severity of liver diseases. The probable cause of variation in serum amylase enzymes in acute viral hepatitis and cirrhosis of liver is its anatomical proximity and common egress system through Ampulla of vater into the duodenum.

Key words: *Serum Amylase, Liver cirrhosis, Viral hepatitis, Pancreatic enzyme*

INTRODUCTION:

Acute viral hepatitis is a distinct clinical syndrome that can be caused by five separate, unrelated viruses. Clinically, acute viral hepatitis is marked by symptoms of malaise, nausea, poor appetite, vague abdominal pain, and jaundice and biochemically, by abrupt increases in serum Bilirubin and aminotransferase levels (Ergasa., 2007)

Cirrhosis is the end result of liver injury characterized by distortion of the hepatic architecture by extensive fibrosis and the formation of regenerative nodules with chronic inflammation of the liver tissues. Cirrhosis may result from, alcoholic liver disease, biliary cirrhosis and chronic liver injuries including infectious, autoimmune, toxic, and metabolic causes (Collier et al., 2010) Several enzymes are available to diagnose the liver diseases such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and γ glutamyl transpeptidase(Hoofnangle., 2007) another diagnostic enzyme of significance can be Amylase, as the pancreatic juice containing pancreatic amylase and pancreatic lipase passes via intercalated and excretory duct to be collected by two ducts- duct of "Wirsung" and duct of "Santorini". The duct of Wirsung is the major pancreatic duct formed by joining of small intercalated and excretory duct and joins with the common bile duct to form Ampulla of Vater also known as hepatopancreatic duct, which opens through the duodenal papilla into second part of duodenum (Jain., 2010) Anatomic alterations of the pancreaticobiliary junction are rare anomalies which cause various pathological conditions in the biliary tract and the pancreas, and may be associated with serum pancreatic amylasemia (Kamisawa et al., 2003). Amylase is an enzyme which helps in digestion of carbohydrates. Pancreas and salivary glands are main source of amylase enzyme and Liver plays an important role in amylase metabolism. It's thought that circulating pancreatic enzymes are removed by reticulo-endothelial system and Liver is suspected to be a major organ for amylase removal (Donaldson et al., 1979 and Rosenblum et al., 1982)

Level of serum amylase increased concomitantly with the progression of liver disease in patients with hepatitis B and hepatitis C (Katakura et al., 2005)

This review emphasizes the biological mechanisms behind these serological alterations, the possible causes, the clinical implications and the diagnostic approach and the existing reports do indicate the importance of estimating amylase in various liver diseases. However, the trend of amylase activity is not clear in different forms of liver diseases. Therefore the present study has been planned in this direction.

MATERIAL AND METHOD

Study Subjects

In the present study Hundred patients of liver disease i.e. Fifty patients of cirrhosis of liver and fifty patients of acute viral hepatitis diagnosed clinically on the basis of presenting features those

could be included to determine a diseased liver, some of those external signs are a coated tongue, bad breath, skin rashes, itchy skin, flushed facial appearance, jaundice, dark urine, pale stool, fluid in the abdominal cavity, pain from the biliary tract or pancreas and enlarged gallbladder, ultrasonographical presentation, biochemical and microbiological investigations were selected from OPD and Wards of Department of Medicine, Guru Nanak Dev Hospital, Amritsar. Fifty age and sex matched healthy individuals were taken as control from the general population. Patients and controls voluntarily participated for the study. The control subjects were healthy, with no past History of any liver disease, or any medication. This study was approved by the institutional ethical committee" we certify that concerning the ethical use of human volunteers were followed during the research." These controls and patients had no history of heart, Diabetes, renal, neurological, thyroid, pancreatic or bone disorders.

Sample Collection

5 ml of fasting venous blood was taken from liver disease patients and normal individuals under aseptic conditions. The blood was allowed to clot for half an hour and then centrifuged at 2500 rpm to collect the serum.

The pancreatic function tests were measured by using a semi automated biochemistry analyzer on the same day of sample collection. The serum amylase was measured by CNP -G3 the kinetic method using reagents provided in kit by Transasia biomedical (India).[14] 2-Chloro-4-nitrophenyl-α-maltotrioside (CNP-G3) is a direct substrate for determination of α-amylase activity.

$$10\ \text{CNP-G}_3 \longrightarrow \text{CNP} + \text{CNP-G}_2 + 9\ \text{Maltotriose} + \text{Glucose}$$

The rate of 2-Chloro-4-nitrophenyl formation can be monitored at 450 nm and is proportional to the α- amylase activity in the specimen.

OBSERVATION AND RESULTS:

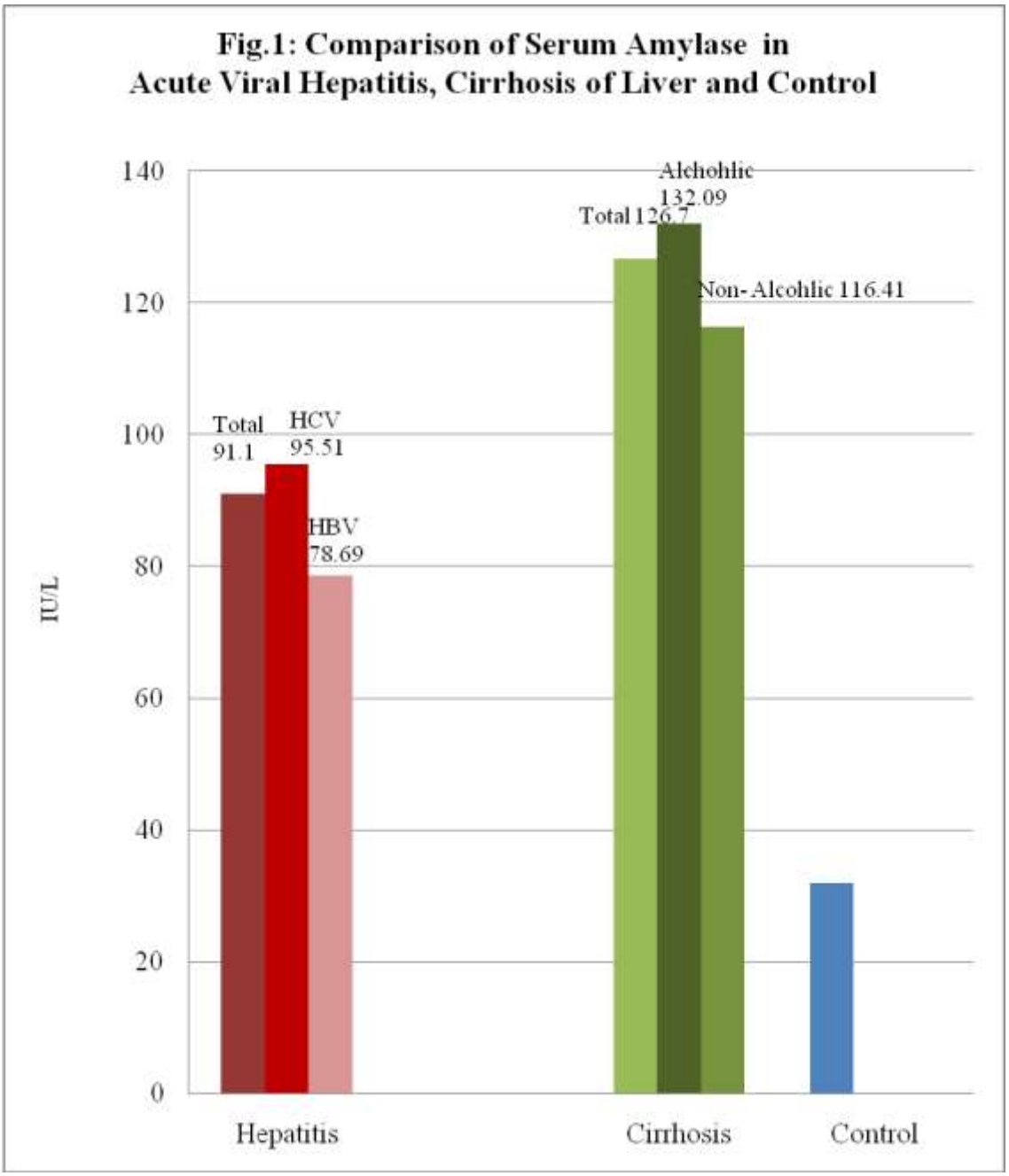
Serum amylase level in 50 patients of acute viral hepatitis, 50 patients of cirrhosis of liver were estimated and compared to that of 50 normal healthy control subjects. Classification of patients based on acute viral hepatitis B, hepatitis C, alcoholic cirrhotic and non alcoholic cirrhotic patients. The mean level of Serum Amylase in patients of acute viral hepatitis (n=50) were estimated and compared to that of normal individuals (n=50) (Table-1). It was observed that serum Amylase levels were significantly ($p<0.0001$) raised in all patients of acute viral hepatitis, viral hepatitis C (n=37) ($t= 6.401$, $p<0.0001$) and viral hepatitis B patients (n=13) ($t=6.458$, $p<0.0001$) when compared to that of normal individuals. Further there was no

significant variations (t=0.790, p=0.433) in serum amylase levels when hepatitis C virus patients (n=37) were compared to that of hepatitis B virus patients (n=13). In cirrhotic patients (n=50) it was observed that serum amylase levels were significantly raised in alcoholic cirrhotic patients (n=33) (t=4.2394, p <0.0001) and non alcoholic cirrhotic patients (n=17) (t=3.97, p <0.0001) when compared to that of normal individuals. Further, there were no significant variations (t= 0.3263, p=0.7456) in serum amylase levels when patients of alcoholic cirrhosis were compared to that of non alcoholic cirrhosis.

TABLE-1 Variations in Serum Amylase levels in Acute viral Hepatitis and Cirrhosis of liver.

Parameter / Individuals	Serum Amylase (Normal value 90 IU/L)			
	Range	Mean± SD	t value	p value
o Control n =50	13-38	31.82±5.63		
* Hepatitis n =50	18-328	91.1±65.7	9.7825	**<0.0001** **o** v/s *
** Hepatitis C virus n= 37	18-328	95.51±70.19	6.401	**<0.0001** **o** v/s **
***Hepatitis B virus n= 13	18-192	78.69±51.31	6.458	**<0.0001** **o** v/s ***
# Patients of cirrhosis (Total) n = 50	34-850	126.7±193.1	3.46	**<0.0001** **o** v/s #
## Patients of alcoholic cirrhosis n = 33	35-850	132.09±167.40	4.239	**<0.0001** **o** v/s ##
### Patients of non alcoholic cirrhosis n =17	34-625	116.41±147.24	3.971	**<0.0001** **o** v/s ###

(t= 0.790, p=0.433) **v/s ***
(t= 0.326, p=0.7456) ## v/s ###



Comparative study of serum amylase, SGOT, SGPT, ALP and γ GGT revealed that with increase in serum amylase and lipase activity there was concomitant increase in SGOT, ALP and γGGT levels in patients with acute viral hepatitis. Moreover in cirrhosis of liver levels of SGOT, SGPT, ALP started declining at the end stage of cirrhosis whereas, activity of serum amylase and lipase leads to increase more significantly with increased severity of cirrhosis. However, no definite relationship of serum amylase and lipase with γ GGT was observed.

TABLE-2 Comparative study of Serum Amylase, SGOT, SGPT, ALP and GGT in acute viral hepatitis and cirrhosis of liver.

Parameter			Amylase	SGOT	SGPT	ALP	GGT
	Value of amylase/No. of patients		Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD
Acute Viral Hepatitis	<90	n=29 (58%)	48.65±19.47	74.137±41	90.551±47.09	120.89±108.6	65.62±55.39
	90-300	n=20 (40%)	140.9±47.64	74.35±39.86	88±46.616	122.2±55.68	107.2±85.68
	>300	n=1 (2%)	328	137	59	202	194
Cirrhosis	<90	n=32 (64%)	54.90±14.62	63.71±43.97	73.25±37.94	123.90±80.36	72.5±58.46
	90-300	n=14 (28%)	156.64±47.9	76.85±45.79	90.857±50.39	151.57±56.61	71.92±43.69
	>300	n=4 (8%)	597±221.95	48.75±51.87	64±16.950	92.5±51.87	108.75±80.84

DISCUSSION:

An increase in the serum concentration of pancreatic enzymes serum amylase is commonly an expression of inflammatory or neoplastic pancreatic disease. However, an elevation of pancreatic enzymes, generally mild, may be a non-specific phenomenon without any clinical implication.Our data also indicate in patients diagnosed with acute viral hepatitis infection the levels of serum amylase were significantly raised without any pancreatic disease Vissere et al. 1999 and Lang et al. 1995. Lechi et al., 1984 reported hyperamylasemai in 110 of 167 (66%) patients of AVH. Tsianos et al., 1986 observed hyperamylasemai in 6 of 30 (20%) patients with CVH. Pezzilli et al. 1999 showed that 27 of 78 (35%) patients with CVH disease were complicated by hyperamylasemai. Where as in study conducted by Shrka et al. 1984 no significant changes were observed in AVH when compared with control subjects and same results were observed in study conducted by Yoffee B et al. 2003 however; our present study

shown that 21 of 50 (42%) patients with acute viral hepatitis B and C were complicated by hyperamylasemai. One reason for the discrepancy among studies may be the background liver disease.

The tissue source of the elevated serum amylase is not conclusive. Skrha et al. 1984 suggested that elevated amylase may be originated from salivary gland. Tsianos et al. 1986 reported that the origin of elevated amylase was pancreas. Pezzilli et al. 1999 reported that elevated amylase originated from pancreas in patients with cirrhotic changes. Our results have clearly shown that elevated serum amylase among patients with AVH originated from pancreas. The levels of serum amylase were higher in patients diagnosed with AVH at all stages of liver disease in comparison to those measured in healthy control subjects suggesting that AVH infection affects pancreatic enzyme secretions. In a study conducted by Shrka et al. 1984 levels of serum amylase were raised when compared to control group which suggest decreased clearance of pancreatic amylase by liver may be contributing to hyperamylasemia found in 42% (20 of 44) of patients with cirrhosis of liver. Whereas in study conducted by Pezzilli et al. 1999 serum amylase levels were abnormally elevated in 22 patients (35% cirrhosis of liver) while in the present study the mean level of serum amylase were significantly raised 36% of cirrhotic patients. During this study it is observed that the level of serum amylase increased with progression of liver disease, furthermore in patients with same clinical stage of hepatitis B or C the increased level of serum amylase was not significantly changed.

Therefore according to present study raised levels of serum amylase shows that pancreatic functions are derange in liver disease. It may be because of acute viral hepatitis or cirrhosis of liver as circulating pancreatic enzymes are removed by reticuloendothelial system in body and

liver is suspected to be the major organ for removal of serum amylase and liver is suspected to play major role in hyperamylasemia.

CONCLUSION:

In conclusion, this study demonstrate that elevated level of serum amylase can be found in acute viral hepatitis or cirrhosis of liver without any pancreatic disease. Therefore in the presence of hyperamylasemia, a careful evaluation of clinical history and symptoms are important in deciding the diagnostic workup.

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