



## DIAGNOSTIC VALUE OF SERUM ENZYMES-A REVIEW ON LABORATORY INVESTIGATIONS.

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### ABSTRACT

Enzymes are produced intracellularly, and released into the plasma and body fluids, where their activities can be measured by their abilities to accelerate the particular chemical reactions they catalyze. But different serum enzymes are raised when different tissues are damaged. So serum enzyme determination can be used both to detect cellular damage and to suggest its location in situ. Some of the biochemical markers such as alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma glutamyl transferase, nucleotidase, ceruloplasmin, alpha fetoprotein, amylase, lipase, creatine phosphokinase and lactate dehydrogenase are mentioned to evaluate diseases of liver, pancreas, skeletal muscle, bone, etc. Such enzyme test may assist the physician in diagnosis and treatment.

**KEYWORDS:** *Liver Function tests, Serum Amylase, Lipase, CPK and LDH.*

## INTRODUCTION

### DIAGNOSTIC SERUM ENZYME

Enzymes are very helpful in the diagnosis of cardiac, hepatic, pancreatic, muscular, skeletal and malignant disorders. Serum for all enzyme tests should be free from haemolysis and should be separated from the red cells within four hours of blood collection. The majority of serum enzymes remains stable for at least five days at 4°C.

### TRANSAMINASES

In human body tissue the predominant transaminases are glutamate – oxalacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT), both of which play an important role in the metabolism of amino acid. GOT catalyses the transfer of the amino group from the amino acid glutamate to the keto acid oxalacetate finally to pyruvate. These enzymes are referred to as aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Large amount of GOT are present in cardiac muscle compared with other tissues of the body such as liver, skeletal muscle and kidney<sup>1</sup>. However elevated

mitochondrial AST is seen in extensive tissue necrosis during myocardial infarction and also in chronic Liver diseases like liver tissue degeneration and necrosis<sup>2</sup>. But lesser amounts are found in brain, pancreas and lung. Although GPT is plentiful in the liver and occurs only in the small amount in the other tissues. In cellular injury to the cardiac muscle, GOT activity increases. In liver cell injury considerable increase in the serum level of both enzymes takes place. Transaminases in myocardial infarction SGOT is raised in 95% of the cases: maximum enzyme level rises during 6-8 hrs after infarction and reaches to peak level after 24 hrs. and returns to normal within 6 days. The SGPT usually remains normal, but may show an elevation slight in degrees compared with that of the SGOT if the infarct is normal. One of the studies has shown that coffee and caffeine consumption reduce the risk of elevated serum ALT activity in excessive alcohol consumption, viral hepatitis, iron overload, overweight and impaired glucose metabolism<sup>3</sup>.

### TRANSAMINASES IN LIVER DISEASE

Serum transaminase determination is useful in the detection of acute and chronic hepatocellular

disease, The differentiation of the jaundice of infective hepatitis from that of extra hepatic biliary obstruction and the detection of hepatic metastasis. Transaminase determination provides a most sensitive indicator of liver cell damage and may reveal liver disease at a time when conventional liver function tests are normal.

### ***VIRAL HEPATITIS***

In viral hepatitis level of both SGOT and SGPT increases markedly at the onset of disease. High values may also be encountered in the pre icteric phase. Enzyme level falls rapidly within a few days and in uncomplicated cases normal level are reached within 2 – 5 weeks from the onset of jaundice. Failure of viral hepatitis to resolve is associated with persistently raised transaminase activity.

### ***INFECTIOUS MONONUCLEOSIS***

SGOT and SGPT are almost invariably raised in infectious mononucleosis even in the absence of jaundice or any clinical evidence of hepatic involvement. Raised levels are found in the early course of the illness.

### ***TOXIC HEPATITIS***

The serum transaminases are elevated by a wide variety of the agents causing toxic damage to the liver. Raised values are observed in carbon tetrachloride poisoning, salicylate intoxication and chlorpromazine sensitivity. Mild elevation may also follow the administration of anovulatory compounds used as contraceptive agents, coumarin compounds and phenindione used in anticoagulant therapy of thrombotic disorders. Raised levels return to normal with the removal of the toxic agent.

### ***OBSTRUCTIVE JAUNDICE***

Both SGOT and SGPT are almost always raised in extra hepatic obstructive jaundice. The Transaminase level remain high until obstruction is relieved and returns to normal within a week.

### ***HEPATIC CIRRHOSIS***

Majority of the cases of cirrhosis show increased level of SGOT and one half of the cases of increased SGPT level may fluctuate widely.

### ***GAMMA GLUTAMYL TRANSFERASE (GGT)***

GGT is a microsomal enzyme present in hepatocytes and biliary epithelial cells, renal tubules, pancreas and intestine. In acute viral hepatitis the level of GGT will reach the peak

promptly. In other conditions like uncomplicated diabetes mellitus, acute pancreatitis, myocardial infarction, anorexia nervosa, Guillain Barre syndrome, hyperthyroidism, obesity and dystrophica myotonica, there are elevated levels of GGT<sup>4</sup>.

### ***HEPATIC METASTASIS***

In metastatic carcinoma of the liver SGOT is raised, whenever SGPT elevation is less frequent.

### ***CPK IN MUSCLE DISEASE***

Serum CPK activity is raised in all varieties of muscular dystrophy; the marked incidence and the highest values being noticed in the Duchenne type dystrophy. Levels are high in infancy and childhood also. Increased serum CPK values are also found in the myopathy which may accompany chronic alcoholism and with the muscular symptoms which may follow acute alcoholic intoxication.

### ***CREATINE PHOSPHOKINASE (CPK) IN MYOCARDIAL INFARCTION***

Majority of the patient with myocardial infarction show raised serum CPK value. Elevation commences some 4-5 hours following infarction, reaches a peak by 24 to 36 hrs, but returns to normal by the third day.

The sensitivity and early elevation of serum CPK following myocardial infarction may assist in the prompt selection of those patient with chest pain requiring the services of an intensive care unit.

CPK values are not altered in liver diseases. Therefore hepatic congestion and liver disorder, which may accompany cardiac disease are not a source of diagnostic confusion. Pericarditis also shows normal serum CPK activity, but raised values are found in myocarditis.

### ***CPK IN CEREBROVASCULAR AND OTHER DISEASES.***

The serum of patient with acute cerebrovascular disease may show raised CPK activity, which is maximal three days after the acute episode and return to normal by the fourteenth day. Slight elevation of CPK values are frequent in hypothyroidism and are occasionally found in peripheral arterial embolism.

### ***LACTATE DEHYDROGENASE (LDH)***

This enzyme catalyses the reversible oxidation of lactate to pyruvate and is important in anaerobic glycolysis, the process in which the body obtains its energy from carbohydrate breakdown. The enzyme

is abundant in renal, cardiac, Hepatic and muscular tissues.

### ***LDH IN MYOCARDIAL INFARCTION***

In myocardial infarction the incidence of LDH is higher than that of SGOT and CPK. The major advantage of LDH determination is that its elevation is much more prolonged, and is thus of special value. Initial blood samples cannot be obtained until some days after the infarctive episode. LDH starts to rise 12 hours after infarction, touches peak within 48 hrs. and stays elevated for another eleven days.

### ***LDH IN NON CARDIAC DISORDERS***

Raised LDH values are found in renal disease, liver disease, disseminated malignancy and certain hematological disorders. Renal infarction or trauma may be accompanied by raised LDH and some of cases of chronic hepatitis and nephritic syndrome may show increased LDH activity.

### ***HYDROLYSING ENZYME***

Hydrolytic reactions are catalyzed by many enzymes including the digestive enzymes, amylase, lipase and the phosphatase enzyme, 5'nucleotidase, amino peptidase and cholinesterase. Determination of amylase and lipase activity are used as aids to diagnose pancreatic disease. Alkaline phosphatase is useful in the study of disorders of bone and together with 5'nucleotidase and leucine aminopeptidase is used in the investigation of liver disease. Acid phosphatase is valuable in the diagnosis of prostatic malignancy. Cholinesterase determination is helpful in the detection of organo phosphorus insecticide toxicity.

### ***LIPASE***

Lipase is an enzyme that hydrolyses triglycerides to glycerol and free fatty acid is produced by the pancreas, and appears in the serum. Raised serum lipase values are found in acute pancreatitis and level may reach 10 times the upper limit of the normal. Serum lipase activity remains elevated longer than does amylase and may thus permit confirmation of the diagnosis of suspected acute pancreatitis when amylase activity has returned to normal. Serum lipase levels may be elevated following hormone stimulation of the pancreas in subjects with carcinoma of the pancreas or chronic pancreatitis.

### ***AMYLASE***

The starch splitting serum enzyme amylase is principally derived from the pancreas and salivary

glands. In acute pancreatitis, the serum enzyme starts to rise within a few hours and remains elevated for three to four days. For amylase many commercial assay's are not yet traceable to the IFCC reference measurement procedure<sup>5</sup>. In other acute abdominal conditions, e.g. perforated peptic ulcer, cholecystitis, common bile duct and intestinal obstruction, raised serum amylase values are also found, but the levels are seldom as high as those found in acute pancreatitis.

### ***THE PHOSPHATASE***

Several enzymes in serum hydrolyse phosphate monoesters. Two of these are relatively non specific in their substrate requirements and are optimally active at alkaline and acid pH and hence are known as alkaline and acid phosphates respectively. A third which hydrolyses nucleotide pentose 5 phosphates as specific substrate is known as 5 nucleotidase.

### ***ALKALINE PHOSPHATASE***

The phosphate is most active between pH values of 8 and 9. Normal range is different according to the use of substrate. Alkaline phosphatase is formed in bone intracellularly by osteoblast and is also present in liver, kidney, intestine and placenta. Increased serum level of alkaline phosphatase are found both in skeletal and hepatic disorders.

### ***ALKALINE PHOSPHATASE IN BONE DISEASE***

Raised serum alkaline phosphatase is found in Paget disease, Hyperparathyroidism, in healing fractures, and in presence of osteoblastic carcinoma metastases. Increased serum alkaline phosphate activity accompanied by raised serum calcium suggests hyperparathyroidism. Healing fracture may show very slight alkaline phosphatase elevation.

### ***ALKALINE PHOSPHATE IN LIVER DISORDERS***

Determination of serum alkaline phosphatase is of great value in the differential diagnosis of jaundice.

### ***ACID PHOSPHATASE***

An enzyme that acts to liberate phosphate under acidic conditions and is made in the liver, spleen, bone marrow, and prostate gland. High serum levels of acid phosphatase may indicate infection, injury, or cancer of the prostate.

### ***ALPHA FETOPROTEIN (AFP)***

AFP is the major serum protein in the developing

mammalian foetus produced at a high level by the foetal liver and visceral endoderm of the yolk sac and at low levels by foetal gut and kidney. AFP is required for female fertility during embryonic development by protecting the developing female brain from prenatal exposure to estrogen<sup>6</sup>. The normal level of AFP is 0 – 7 IU/ml. A high value more than 500 IU/ml has been considered to be diagnostic of hepatocellular carcinoma in patient with cirrhosis.

### **CERULOPLASMIN**

Ceruloplasmin is synthesized in the liver and is an acute phase protein. It binds with the copper and serves as a major carrier for copper in the blood<sup>1</sup>. The level is elevated in infections, rheumatoid arthritis, pregnancy, non - Wilson liver disease and obstructive jaundice. Decreased rate of synthesis of the ceruloplasmin is responsible for copper

accumulation in liver because of copper transport defect in Golgi apparatus, since ATP 7B is affected<sup>4</sup>, serum ceruloplasmin levels are increased in the chronic active liver disease but lowered in the Wilson's disease. Hence it is a more reliable screening test to differentiate between chronic Liver Disease and Wilson's disease<sup>7</sup>.

### **5'NUCLEOTIDASE**

5'nucleotidase is a protein produced by the liver and the test can be measured in the laboratory to know the activities in patient with obstructive jaundice, parenchymal liver disease, hepatic metastases and bone disease<sup>8</sup>. Elevation of 5'nucleotidase is found in both acute infective hepatitis and in chronic hepatitis<sup>9</sup>; however increased activity is higher in acute hepatitis as compared to that in chronic hepatitis.

## **DIAGNOSTIC VALUE OF SERUM ENZYMES-A REVIEW ON LABORATORY INVESTIGATIONS.**

Sr. No.	ENZYMES	METHOD	NORMAL VALUE
1.	SGOT	ENZYMATIC	5 – 50 U/L
2.	SGPT	ENZYMATIC	5 – 50 U/L
3.	GGT	ENZYMATIC	5-35 U/ML
4.	CPK	ENZYMATIC	24– 105 U/L
5.	LDH	ENZYMATIC	230 – 400 U/L
6.	LIPASE	ENZYMATIC	0 – 190 U/L
7.	AMYLASE	ENZYMATIC	60 – 160 SU
8.	ALKALINE PHOSPHATASE	ENZYMATIC	70 – 230 U/L
9.	ACID PHOSPHATASE	KING ARMSTRONG	1.5 – 3.5 KA
10.	ALPHA FETO PROTEIN	AUTOMATIC SYSTEM	0 – 7 IU/ML
11.	CERUOPLASMIN	MANUAL	24– 36 mg/dl
12.	5' NUCLEOTIDASE	MANUAL	2-17 IU/L

*Reference values of serum enzymes.*

## **REFERENCES**

- Panteghini M, Bias R, Van Solinge WW. Enzymes. In: Burtis CA, Ashwood ER, Brun DE, editors. Tietz textbook of Clinical Chemistry and molecular Diagnostics. Philadelphia, PA: Elsevier Saunders; 2006. pp 597-643.
- Thapa BR, Anuj W. Liver Function tests and their interpretation. Indian J. Padiatr. 2007; 74: 663- 671.
- Everhart JE, Ruhl CE. Coffee and caffeine consumption reduce the risk of elevated serum alanine aminotransferase activity in the United States. Gastroenterology. 2005; 128: 24-32.
- Rosalki SB, McIntyre N. 2<sup>nd</sup> ed. New York: Oxford university press; 1999. biochemical investigation in the management of Liver disease; pp. 503-521. Oxford test book of clinical hepatology.
- Schumman G, Aoki R, Ferrero CA, Ehlers G, Ferad G, Gella FJ et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degree C. Clin Chem Lab Med. 2006; 44: 1146-55.
- Zhifang Xie, Hai Zhang, Wenwei Tsai. Zinc finger protein ZBTB20 is a key repressor of alpha Fetoprotein gene transcription in liver. PNAS. 2008; 105: 10859-10864.

7. LaRusso NF, Summerskill WH, McCall JT. et al. Abnormalities of chemical tests for copper metabolism in chronic active liver disease: differentiation from wilson's disease. *Gastroenterology*. 1976;70:653-655.
8. Daniel SP, Marshal MP. In Schiff's diseases of the liver. 10<sup>th</sup> edition. Eugene RS, Michel FS, Willis CM, editors. Vol. 1. lippincot Williams and Wilkins; 2007. Laboratory test; pp. 19-54.
9. Pratibha K, Usha A, Rajni A, Serum adenosine deaminase, 5' nucleotidase and malondialdehyde in acute infective hepatitis. *Ind J Clin Biochem*. 2004;19:128-131.