

# *Clinical Enzymology*

## **Plasma enzymes**

Blood plasma contains many enzymes , which are classified into functional and non functional enzymes :

**Functional enzymes** present at all times in the circulation and perform a physiologic function in the blood , examples of these functional enzymes include lipoprotein lipase , pseudocholinestrerase and enzymes of blood coagulation .

These enzymes are synthesized and secreted by the liver .

**Non functional enzymes** : plasma also contains numerous other enzymes that perform unknown physiologic function in blood . These non functional plasma enzymes arise from the routine normal destruction of erythrocytes , leukocytes , and other cells . Tissue damage or necrosis resulting from injury or disease is generally accompanied by increasing in the levels of several non functional plasma enzymes . Therefore several enzymes are used in the diagnosis .

## **Medical importance of non functional plasma enzymes .**

Measurement of non functional enzymes is important for :

- 1- Diagnosis of diseases as diseases of different organs cause elevation of different plasma enzymes .
- 2- Prognosis of the diseases : we can follow up the effect of treatment by measuring plasma enzymes before and after treatment .

	Functional plasma enzymes	Non Functional plasma enzymes
Concentration in plasma enzymes	Present in plasma in higher concentration in comparison to tissues	Normally , present in plasma in very low concentrations in comparison to tissues
Function	Have known functions	No known functions
Substrate	Their substrates are always present in the blood .	Their substrate are absent from the blood .
Site of synthesis	Liver	Different organs e.g. liver , heart , brain , and skeletal muscles .
Effect of diseases	Decrease in liver diseases	Different enzymes increase in different organ diseases .
Examples	Clotting factors e.g. prothrombin , lipoprotein lipase , and pseudocholine esterase .	ALT, AST , CK , LDH , alkaline phosphatase , acid phosphatase , and amylase .

## **Lactate Dehydrogenase ( LDH ) ( LD )**

### **1 – Normal values**

Lactate dehydrogenase will convert pyruvate to lactate . The normal value of LDH in serum is 100 – 200 U/L . Values in upper range are generally seen in children . Strenuous exercise will slightly increase the value . LDH level is 100 times more inside the RBC than in plasma , and therefore minor amount of hemolysis will result in a false positive test .

### **2 – LDH and heart attack**

In myocardial infarction , total LDH activity is increased . The time course of LDH level after a heart attack is given in the following figure . The magnitude of the peak value as well as the area under the graph will be roughly proportional to the size of myocardial infarction .

## **Creatine kinase ( CK )**

### **1 – Normal values**

It is used to convert creatine to creatine phosphate , therefore it was called creatine phosphokinase in old literature . Normal serum value for CK is 15 – 100 U/L for males and 10 – 80 U/L for females .

### **2 – CK and heart attack**

- CK values in serum is increased in myocardial infarction , the time course is shown in the former figure . The CK level starts to rise within 3 – 6 hours of infarction .
- Therefore CK estimation is very useful to detect early cases , where ECG changes is ambiguous .
- The CK level is not increased in hemolysis or in congestive cardiac failure , and therefore CK has an advantage over LDH . The area

under the peak and slope of initial rise are proportional to the rise of infarction .

### 3 – CK and muscle diseases

- The level of CK in serum is very much elevated in muscular dystrophies ( 500 – 1500 IU/L )
- CK level is highly elevated in crush injury , fracture and acute cerebrovascular accidents .

### **Aspartate amino transferase ( AST )**

- In old literature it was called as serum glutamate oxaloacetate transaminase ( SGOT ) . AST needs pyridoxal phosphate ( vit. B6 ) as coenzyme .
- Normal serum level of AST is 8 – 20 U/L . The level is significantly elevated in myocardial infarction . The time course of AST is shown in in the former figure .
- It is moderately elevated in liver diseases .

### **Alanine amino transferase ( ALT )**

- In old literature it was called as serum glutamate pyruvate transaminase ( SGPT ) . The enzyme needs pyridoxal phosphate as coenzyme .
- Normal serum level of ALT for male is 13 – 35 U/L . Very high values ( 300 – 1000 U/L ) in acute hepatitis , either toxic or viral in origin .
- Both ALT and AST levels are increased in liver diseases , but ALT > AST .

## **Alkaline phosphatase ( ALP )**

- This enzyme is produced by osteoblasts of bone , and is associated with the calcification process . It is activated by magnesium and manganese . Zinc is a constituent ion of ALP .
- Normal serum value of ALP is 40 – 125 U/L . In children the upper level of normal value may be more , because of the increased osteoblastic activity in children .
- Moderate increase ( 2-3 times ) in ALP level is seen in hepatic diseases such as infective hepatitis , alcoholic hepatitis or hepatocellular carcinoma .
- Very high level ( 10 – 12 times of upper limit ) may be noticed in extrahepatic obstruction ( obstructive jaundice ) caused by gallstone or by pressure on bile duct by carcinoma of head of pancreas .
- ALP is produced by epithelial cells of biliary canaliculi and obstruction of bile with consequent irritation of epithelial cells leads to secretion of ALP into serum .
- Drastically high levels of ALP ( 10 – 25 times of upper limit ) are seen also in bone diseases where osteoblastic activity is enhanced such as Paget's disease , rickets osteomalacia , osteoblastoma , metastatic carcinoma of bone and hyperparathyroidism .

## **Nucleotide phosphate ( NTP )**

- It is also known as 5 nucleotidase , this enzyme hydrolyses 5 nucleotides to corresponding nucleosides at an optimum pH of 7.5 . Nickel ions inhibit NTP .
- Normal NTP level in serum is 2 – 10 IU/L . It is moderately elevated in hepatitis and highly elevated in biliary obstruction .

## **Gamma Glutamyl Transferase ( GGT )**

- In the body it is used in the synthesis of glutathione . It is seen in liver , kidney , pancreas , intestinal cells and prostate gland .
- Normal serum value of GGT is 10 – 30 U/L . It is moderately increased in infective hepatitis and prostate cancer .
- GGT is clinically important because of its sensitivity to detect alcohol abuse . GGT is increased in alcoholics even where other liver function tests are within normal limits .
- GGT level is rapidly decreased within a few days when the person stops to take alcohol . Increase in GGT level is generally proportional to the amount of alcohol intake .

## **Enzyme Profile in Liver Diseases .**

Enzymes commonly studied for diagnosis of liver diseases are :

1. ALT
2. ALP
3. NTP
4. GGT

## **Acid Phosphatase ( ACP )**

- Normal serum value of ACP is 2.5 – 12 U/L .
- ACP is secreted by prostate cells , RBC , platelets and WBC .
- ACP total value is increased in prostate cancer and highly elevated in bone metastasis of prostate cancer
- ACP is an important tumor marker
- Since blood cells contains excess quantity of ACP , care must be taken to prevent hemolysis while taking blood from the patient . prostate massage may also increase the value . So blood may be collected for ACP estimation before rectal examination of patient .

## **Amylase**

- This splits starch to maltose . It is activated by calcium and chloride ions . It is produced by pancreas and salivary glands .
- Normal serum value is 50 – 120 IU/L the value is increased 1000 times in acute pancreatitis which is a life threatening conditions . The peak values are seen between 5 – 12 hours after the onset of disease and returns to normal levels within 2 – 4 days after the acute phase .
- Moderate increase in serum levels are seen in chronic pancreatitis , mumps ( parotitis ) and obstruction of pancreatic duct .

## **Lipase**

- It will hydrolyse triglycerides to beta monoglyceride and fatty acid . The enzyme is present in the pancreatic secretion .
- The level in blood is highly elevated in acute pancreatitis and this persists for 7 – 14 days . Thus lipase remains elevated longer than amylase .
- Moreover , lipase is not increased in mumps . Therefore , lipase estimation has advantage over amylase . It is moderately increased in carcinoma of pancreas , biliary diseases , perforating peptic ulcer .