**Liver Function Tests**

is large , bilobed, complex organ that receiving large amount of blood and nutrients from gastro-intestinal system by portal vein.

The structural unit of liver is lobule that consist of clusters of hepatocytes around central liver.

It is of vital importance in intermediary metabolism and detoxification and elimination of toxic substances. Damage to the organ may not obviously affect its activity because Liver has considerable functional reserve .

**Major functions of the liver**

\* Carbohydrate metabolism such as Gluconeogenesis and glycogenolysis

\* Fat metabolism such as Lipoprotein synthesis , Ketogenesis and Bile acid synthesis

\*Protein synthesis such as Urea synthesis from ammonia Coagulation factors synthesis

\* Metabolism and excretion such as Bile 3L/day ,Steroid hormones

And Drugs(detoxification by either bind drug to inactivate compound, or chemically modify compound to be excreted)

\*Storage such as Glycogen and Vitamin A

**Bile**/is compose of bile acid, bile salt, and bile pigment(bilirubin).

**BILIRUBIN METABOLISM**

The hemoglobin molecule consist of haem and globin ,and when red cells are removed from circulation by reticuloendothelial system mainly spleen, so the haem is liberated and degraded to porphyrin then to biliverdin then to bilirubin pigment. About 80% of bilirubin is derived from haem within reticuloendothelial system but other sources of compounds chemically related to haemoglobin such as myoglobin and cytochromes. Bilirubin is unconjugated bilirubin that is transport in bloodstream bound to albumin bec. It is water insoluble, it is lipid soluble so it can cross cell membrane include blood-brain barrier.

It is taken up by hepatocytes to undergo conjugation with glucuronic acid to form diglucuronides by enzyme uridine diphosphate glucuronyl transferase (UDPGT).

The resulting conjugated bilirubin is water soluble that is secreted into biliary canaliculi(as bile) to reach distal ileum and colon where is broken down by bacterial action to urobilinogen(stercobilinogen)(colourless pigment) . Most of urobilinogen in gut is oxidized in colon to a brown pigment called stercobilin (coloured pigment) which is excreted in stool.

Some urobilinogen is absorbed from gut into portal blood and systemic circulation to be excreted in urine. 80% of bilirubin comes from Hb and 20% from heme containing protein like myoglobin.

The measurement of plasma bilirubin is insensitive test of liver function because It is frequently normal in early mild liver disease. In health bilirubin is not detected in urine. Conjugated bilirubin in urine is always pathological.

**Causes of jaundice**

-Pre-hepatic such as Hemolysis and Rhesus incompatibility

-Hepatic such as Hepatits,Cirrhosis and Prematurity and Physiological (low activity or deficiency of hepatic conjugating enzyme because of immature liver so indirect bilirubin is deposited in brain causing cell damage).

-Post-hepatic such as Gall stone and Carcinoma of head of pancreas

**PREHEPATIC /HEMOLYTIC LABORATORY FINDINGS**

\* Increase plasma unconjugated bilirubin ,LDH , reticulocyte count and urine urobilinogen.

\* Decrease plasma haptoglobin and haemoglobin

Juandice may be due to increament of un-conjugated bilirubin or conjugated bilirubin Or both.

-In unconjugated hyperbilirubinemia result from increase production of bilirubin at a rate that exceeds capacity of liver to conjugate the pigment (hemolysis) or lack of conjugating enzyme activity(prematurity).

there is no bilirubin in urine.

-In conjugated hyperbilirubinemia is due to leakage of conjugated bilirubin from either hepatocytes or biliary system into blood

stream,so excreted in kidney so urine develops a deep orange –brown colour.

In complete biliary obstruction no bilirubin reach the gut so no stercobilin is formed and stool is pale

**Plasma aminotransferase (transaminases)**

1- ALT(alanine aminotransferase) is more specific to liver dysfunction.

2- AST(aspartate aminotransferase)

Both AST and ALT increased in cell damage like hepattis.

3- ALP(alkaline phosphatase) this enzyme is increased (enzyme induction) stimulated by cholestasis.

4- Gama glutamyl transferase(¥GT)

It is sensitive indicator but non specific for hepatobiliary disease.

In practice increament of all liver enzymes presents in both hepatocellular disease and cholestatic disease.

In fact falling aminotransferase activity suggest decrease hepatocellular damage, and falling ALP activity suggest resolution of cholestasis.

**Plasma albumin**

its concentration represent liver functional capacity in chronic liver disease .So normal plasma albumin concentration in chronic liver disease means adequate synthesis and fall concentration mean deterioration.

**INR**

IT is international normalized ratio which is ratio of prothrombin time to control value. It is a test of plasma clotting factors activity which are vit.K dependent factors that synthesize by liver. So prolong prothrombin time often early feature of acute liver disease.

**Inherited abnormalities of bilirubin metabolism**

1-Gilbert syndrome: is autosomal dominant dis. That leads to decreased enzyme activity(UDP) to 20%-30% so decrease conjugation of bilirubin . This disease presents intermittently, often noticed during infection, or fasting .

There may be mild malaise and abdominal discomfort with no abnormal physical signs .The liver is histologically normal .

It is diagnosed by exclusion of other causes of hyperbilirubinemia like hemolysis.

2-Crigler-Najjar/absence of conjugating enzyme

3-Dubin-Johnson/decrease hepatic excretion of conjugated bilirubin.

4-Rotor syndrome

**Liver diseases**

1.Acute hepatitis

Is usually caused by viral infection like A,B,C,D,E and drugs like paracetamol.

There are two stages:

\* pre-icteric stage /with non-specific symptoms like anorexia and malaise, which improved when jaundice appear, here plasma aminotransferases are very high, urine bilirubin is high, but plasma bilirubin and plasma alkaline phosphatase are normal.

\* Icteric stage / jaundice appear, here plasma bilirubin, and plasma alkaline phosphatase are increased , but aminotransferase begun to decrease.

Hepatitis A and E recover completely and aminotransferase activities falling to normal in 10-2 weeks.

In some patients with hepatitis B and C infection, aminotransferase activities remain elevated and chronic liver disease ensues.

2.chronic hepatitis

Is hepatic inflammation more than 6 months.

Causes:

\* Autoimmune hepatitis

\* Chronic infection by B,C viruses

\* Alcoholic hepatitis

Hepatitis A(infectious hepatitis)-

Transmitted by feco-oral route as food born infection. It diagnosed by hepatitis A viral antibodies of IgM class detectable in plasma of patients at onset of symptoms.The presence of an IgG anti-HAV antibody is suggestive of previous infection.

-Hepatitis B (serum hepatitis)

Transmitted by blood products and other body fluids. It is diagnosed by presence of viral surface Ag (HBs Ag) and core antigen(HBc Ag), then after 8 weeks the anti-HBc antibody appear then after anti-HBs antibody will appear.

-Autoimmune hepatitis(primary biliary cirrhosis)

It occur three times more frequently in middle –aged women than men characterized by destruction of intra-hepatic bile ducts . The atiology is unknown although there is strong association with other autoimmune diseases.

-Autoantibodies ( anti-mitochondrial antibodies) are frequently present in serum in high titer . Plasma aminotransferase activities are elevated, and the natural history of autoimmune hepatitis is of progression to cirrhosis which is preventable if immunosuppressive treatment is started early.

-Cirrhosis

Is a process in which death of liver cells with regeneration lead to fibrosis ,scarring and destruction of normal liver architecture. Causes of cirrhosis include chronic alcohol intake, autoimmune hepatitis ,chronic infection with hepatitis B or C ,Wilson disease, hemochromatosis. Consequences include impaired hepatic function progression to liver failure. Hypoalbumenemia and ascites is complications of liver cirrhosis.