Liver Function Tests

Major Metabolic Functions of the Liver

Synthetic Function	Detoxification and excretion	Storage Function	Production of bile salts
1- Plasma proteins (albumin, globulins) 2- Cholesterol 3- Triglycerides 4- lipoproteins	1- Ammonia to urea (urea cycle) 2- Bilirubin 3- Cholesterol 4- drug metabolites	Vitamins A, D, E, K and B12	Helps in digestion

Some example of liver dysfunction	Liver Function Tests (LFTs)
• Hepatocellular disease • Cholestasis (obstruction of bile flow) • Cirrhosis • Hepatitis • Jaundice • Liver cancer • Steatosis (fatty liver) • Genetic Disorders ○ Hemochromatosis (iron storage)	• Noninvasive methods for screening of liver dysfunction • Help in identifying general types of disorder • Assess severity and allow prediction of outcome • Disease and treatment follow up

Liver Function Tests (LFTs)

Broadly classified as:	Limitations of LFTs

1. Tests to detect hepatic injury:
• Mild or severe; acute or chronic
• Nature of liver injury (hepatocellular or cholestasis)
2. Tests to assess hepatic function
	• **Normal LFT values <u>do not always</u> indicate absence of liver disease**
	  ○ Liver a has very large reserve capacity
	• **Asymptomatic people may have abnormal LFT results**
	  ○ Diagnosis should be based on clinical examination

Classification of LFTs

Group I: Markers of liver dysfunction	Group II: Markers of hepatocellular injury	Group III: Markers of cholestasis
▫ **Serum bilirubin**: total and conjugated ▫ Urine: bile salts and urobilinogen ▫ **Total protein**, serum albumin and albumin/globulin ratio ▫ **Prothrombin Time**	▫ **Alanine aminotransferase (ALT)** ▫ **Aspartate aminotransferase (AST)**	▫ **Alkaline phosphatase (ALP)** ▫ **γ-glutamyltransferase (GGT)**

Common serum liver chemistry tests

Liver chemistry test	Clinical implication of abnormality
Alanine aminotransferase	Hepatocellular damage
Aspartate aminotransferase	Hepatocellular damage
Bilirubin	Cholestasis, impaired conjugation, or biliary obstruction
Alkaline phosphatase	Cholestasis, infiltrative disease, or biliary obstruction
Prothrombin time	Synthetic function
Albumin	Synthetic function
γ-glutamyltransferase	Cholestasis or biliary obstruction
Bile acids	Cholestasis or biliary obstruction

Markers of liver dysfunction

Bilirubin

- A byproduct of red blood cell breakdown
- It is the yellowish pigment observed in jaundice
- **High bilirubin levels are observed in:**
  - Gallstones, acute and chronic hepatitis

Metabolism of bilirubin

1. Hemoglobin form the RBCs breakdown into a heme and a globin.
2. The heme group is taken up by macrophages of the reticuloendothelial system (including tissue macrophages and that of the liver & spleen) into bilirubin.
3. Bilirubin is insoluble in the blood so it attaches & is carried to the liver by albumin.
4. Bilirubin is derived from the albumin, enters the hepatocytes & conjugates with glucoronic acid by the enzyme UDP-glucourinile.
5. This soluble conjugated form is excreted via the bile duct into the intestine where the bacteria removes the glucoronic acid & coverts bilirubin into urobilinogen.
6. Some of the urobilinogen is reabsorbed from the gut and enters the portal circulation.
7. Some is recycled in the enterohepatic cells.
8. The remainder is transported along with the blood to the kidneys where it is converted into urobilin that is excreted in the urine giving it it's characteristic yellow color.
9. Mainly urobilinogen in the gut is oxidized by the bacteria into strecobilin which is excreted in the feces giving it it's brown appearance

Serum bilirubin levels

- Normal (0.2 – 0.8 mg/dL)
- Unconjugated (indirect) (0.2 – 0.7 mg/dL)
- Conjugated (direct) (0.1 – 0.4 mg/dL)
- Latent jaundice: (Above 1 mg/dL)
- Jaundice: (Above 2 mg/dL)

Bilirubin levels and jaundice

Classes of Jaundice

Pre-hepatic or hemolytic	Hepatic or Hepatocellular	Post-hepatic
Abnormal red cells; antibodies; drugs and toxins; thalessemia Hemoglobinopathies, Gilbert's, Crigler-Najjar syndrome	1- Viral hepatitis 2- toxic hepatitis 3- intrahepatic cholestasis	Extrahepatic cholestasis; gallstones; tumors of the bile duct, carcinoma of pancreas

Urobilinogen (UBG) and bile salts

- Most UBG is metabolized in the large intestine but a fraction is excreted in urine (less than 4 mg/day)
- Normally bile salts are NOT present in urine
- **Obstruction in the biliary passages causes:**
  - Leakage of bile salts into circulation
  - Excretion in urine

Serum Albumin

- **The most abundant protein** synthesized by the liver
- **Normal serum levels**: 3.5 – 5 g/dL
- Synthesis depends on the extent of functioning liver cell mass
- Longer half-life: 20 days
- **Its levels decrease in all chronic liver diseases**

Serum Globulin

- **Normal serum levels**: 2.5 – 3.5g/dL
- α and β-globulins mainly synthesized by the liver
- They constitute immunoglobulins (antibodies)
- **High serum γ-globulins are observed in chronic hepatitis and cirrhosis:**
  - IgG in autoimmune hepatitis
  - IgA in alcoholic liver disease

Albumin to globulin (A/G) ratio

- Normal A/G ratio: 1.2/1 – 1.5/1
- **Globulin levels increase in hypoalbuminemia as a compensation**

Prothrombin Time (PT)

- **Prothrombin**: synthesized by the liver, a marker of liver function
- Half-life: 6 hrs. (indicates the present function of the liver)
- **PT is prolonged only when liver loses more than 80% of its reserve capacity**
- **Vitamin K deficiency also causes prolonged PT**
- Intake of vitamin K does not affect PT in liver disease

Group II: Markers of hepatocellular injury

Aspartate aminotransferase (AST)

- Normal range: 8 – 20 U/L
- A marker of hepatocellular damage
- **High serum levels are observed in:**
  - Chronic hepatitis, cirrhosis and liver cancer

Alanine aminotransferase (ALT)

- More liver-specific than AST
- Normal range (U/L):
  - Male: 13-35
  - Female: 10-30
- **Appears in plasma many days before clinical signs appear**
- A normal value does not always indicate absence of liver damage
- **Obese but otherwise normal individuals may have elevated ALT levels**

High serum levels	Moderate elevation	Minor elevation
in acute hepatitis (300-1000U/L)	in alcoholic hepatitis (100-300U/L)	cirrhosis, hepatitis C and non-alcoholic steatohepatitis (NASH) (50-100U/L)

Group III: Markers of cholestasis

Alkaline phosphatase (ALP)

- A **non-specific** marker of liver disease
- Produced by **bone osteoblasts (for bone calcification)**
- Present on hepatocyte membrane
- Normal range: 40 – 125 U/L

Modearte elevation observed in:	High levels are observed in:	Very high levels are observed in:
○ Infective hepatitis, ○ alcoholic hepatitis ○ hepatocellular carcinoma	○ Extrahepatic obstruction (obstructive jaundice) ○ intrahepatic cholestasis	Bone diseases

γ-glutamyltransferase (GGT)

- Used for **glutathione synthesis**
- Normal range: 10 – 30U/L
- **Moderate elevation observed in:**
  - Infective hepatitis and prostate cancers
- **GGT is increased in alcoholics despite normal liver function tests**
  - **Highly sensitive to detecting alcohol abuse**