
Liver Function Test
Triglyceride
Liver Function Test
Total Protein
Albumin
Globulin
Total Bilirubin
Direct Bilirubin
AST (SGOT)
ALT (SGPT)
Alkaline Phosphatase
Enzyme

LIVER FUNCTON TESTS

COMPETENCY NO: BI-11.17

GROUP D

ELINA PAUL(56)

FAIHA FIROS(57)

GATHA K S(58)

GIJS JENNY(59)

GOPIKA AIPPU(60)

SPECIFIC LEARNING OBJECTIVE

- Define liver function tests and explain their clinical importance.
- List the common components of liver function tests:
- Explain the physiological roles of the liver in metabolism, synthesis, detoxification, and excretion.
- Interpret abnormal LFT results in relation to liver pathology (e.g., hepatocellular injury, cholestasis, synthetic dysfunction).

1. FUNCTIONS OF LIVER

Major Functions of the Liver:

- Synthesis of plasma proteins (e.g., albumin, coagulation factors).
- Synthesis of cholesterol and triglycerides.
- Lipoprotein synthesis.
- Carbohydrate metabolism (glycogen synthesis, breakdown, gluconeogenesis).
- Protein metabolism (amino acid synthesis, breakdown of ATP).
- Bilirubin metabolism (conjugation of bilirubin for excretion).
- Drug metabolism (detoxification).
- Excretory functions (bile production, excretion of bile acids, cholesterol, etc.).
- Role in vitamin A, D, K, and B12 storage and bile production for digestion
- Bile Acids and Digestion:
- Bile acids, synthesized from cholesterol, help in the digestion and absorption of lipids and fat-soluble vitamins (A, D, E, K).

- Fluid Distribution:

The liver plays a role in fluid distribution between intravascular and tissue spaces by synthesizing albumin, which maintains oncotic pressure.

- Bilirubin Metabolism:

The liver conjugates bilirubin (a breakdown product of heme) to make it water-soluble for excretion in bile.

- Detoxification:

The liver detoxifies harmful substances (e.g., ammonia, drugs) and excretes them via bile or urine

- Excretory Functions:

The liver produces about 3 liters of bile daily, which is excreted into the gut.

2. CLINICAL MANIFESTATIONS OF LIVER DYSFUNCTION

JAUNDICE

- Jaundice is the yellowish discoloration of skin and mucous membranes due to elevated bilirubin levels.
- It occurs when the rate of hemolysis (red blood cell breakdown) increases or when bilirubin excretion is impaired, leading to a rise in serum bilirubin levels

PORTAL HYPERTENSION

- This occurs when there's increased pressure in the portal vein system (which drains blood from the gastrointestinal tract, spleen, and pancreas).

CAUSES

- Pre-sinusoidal: e.g., portal vein thrombosis.
- Sinusoidal: e.g., cirrhosis.
- Post-sinusoidal: e.g., hepatic vein thrombosis.

EFFECTS

- Increased pressure in the portal system leads to varices (dilated veins), which can rupture and cause bleeding

- Portosystemic shunting (bypassing the liver) leads to metabolic dysfunction, such as **hyperestrogenism** (causing testicular atrophy, gynecomastia, and palmar erythema) and failure to detoxify ammonia (leading to hyperammonemia and hepatic encephalopathy).
- Decreased albumin synthesis leads to **hypoalbuminemia**, causing fluid to leak into the peritoneal cavity (ascites).
- Diminished synthesis of clotting factors predisposes to bleeding.
- Loss of thrombolytic factors can lead to thrombosis

ASCITES

- Ascites is the accumulation of fluid in the abdominal cavity, often due to portal hypertension and hypoalbuminemia.

3. LIVER FUNCTION TESTS(LFTs)

LFTs are used to assess the function of the liver, kidney, thyroid, and adrenal glands.

- They help diagnose and monitor liver diseases.
- **Serum Bilirubin**: Elevated in liver disease (total and conjugated).
- Hepatic Enzymes:

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST): Indicate liver cell damage.

Alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT): Indicate cholestasis (bile flow obstruction).

- **Serum Total Proteins and A/G Ratio**: Assess synthetic function (albumin/globulin ratio).
- **Prothrombin Time**: Measures clotting factor synthesis (prolonged in liver dysfunction).
- **Urine Analysis**: Checks for bile pigments and salts, which are elevated in liver diseases

4. PATHOGENESIS OF ASCITES

Hypertension and Ascites:

- Increased liver scarring leads to resistance to blood flow, causing portal hypertension.
- Hypoalbuminemia (low albumin) reduces oncotic pressure, leading to fluid leakage into the peritoneal cavity.
- Decreased blood pressure triggers the renin-angiotensin system, causing sodium and water retention, which worsens ascites.
- Fluid escapes into the peritoneal cavity, further exacerbating the condition.

MARKERS OF EXCRETORY FUNCTION OF LIVER

- Bilirubin,the product of heme catabolism is taken up , conjugated and excreted by liver. Normal level of total bilirubin is less than 1 mg/dl, but clinical jaundice is manifested only when bilirubin level reaches more than 2.5mg/dl

VAN DEN BERGH REACTION

- It is a chemical test used to detect the presence of bilirubin in a sample and also helps in determining different types of jaundice
- The van den bergh reagent contains sulfanilic acid and sodium nitrite
- When diazotized sulfanilic acid reacts with bilirubin , a purple colored azobilirubin is produced
- This reaction is used to distinguish between conjugated bilirubin(direct)and unconjugated bilirubin(indirect)

1.A Direct positive reaction is indicated by immediate development of a purple color which is given by conjugated bilirubin

2.An indirect positive reaction is given when color develops after addition of alcohol which is given by unconjugated bilirubin

3.A biphasic reaction is given when color develops immediately , but intensifies on addition of alcohol

. Normal serum will not give a positive reaction

. Hyperbilirubinemia and its nature is identified by van den bergh reaction

UNCONJUGATED HYPERBILIRUBINEMIA

- This results from defective conjugation or from increased production.
- Hemolysis of any cause leads to excessive production of bilirubin causing HEMOLYTIC JAUNDICE OR PREHEPATIC JAUNDICE (problem arises before bilirubin reaches the liver)
- Bilirubin level rises more than 3mg/dl

TABLE 21.1 Laboratory findings in serum in jaundice cases.

	Hemolytic jaundice	*Obstructive jaundice*	*Hepatocellular jaundice*
Total bilirubin	Elevated	Elevated	Elevated
Conjugated bilirubin	Normal	Elevated	Elevated
Unconjugated	Elevated	Normal	Elevated
Van den Bergh reaction	Indirect +ve	Direct +ve	Biphasic

CONJUGATED HYPERBILIRUBINEMIA

- When there is obstruction to flow of bile after bilirubin has been conjugated in liver,conjugated hyperbilirubinemia occurs and results in OBSTRUCTIVE JAUNDICE or POSTHEPATIC JAUNDICE
- It is commonly seen in conditions like gallbladder stones , carcinoma of head of pancreas .
- It is also seen in DUBIN JOHNSON SYNDROME(a rare inherited disorder where excretion of conjugated bilirubin into bile is impaired)

URINARY BILIRUBIN

- Only conjugated bilirubin is soluble in water and is excreted in urine
- In prehepatic jaundice , when unconjugated bilirubin is increased in blood ,it does not appear in urine ,hence called **acholuric jaundice**
- But in obstructive jaundice urine contains bilirubin ,hence it is called **choluric jaundice** .

TABLE 21.2 Laboratory findings in urine in jaundice cases.

	Hemolytic jaundice	*Obstructive jaundice*	*Hepatocellular jaundice*
Bile pigments	Absent	+++	++
Bile salts	Absent	++	+
Urobilinogen	Elevated	Absent	Normal or decreased
Positive test	Ehrlich's +ve	Fouchet's +ve	Hay's test +ve

URINARY UROBILINOGEN

- In case of obstruction , bile is not reaching the intestine so urobilinogen may be decreased or absent in urine (since it is formed from bilirubin in gut by bacterial action)
- The first indication of recovery from obstructive jaundice is the reappearance of urobilinogen in urine indicating the bile is once again entering the intestine
- Bilirubin is detected by **Fouchet's test** and urobilinogen by **Ehrlich's test**

URINE BILE SALTS

- Normally bile salts are present in bile, but are not seen in urine
- Bile salts in urine are detected by Hay's test
- Positive Hay's test indicates the obstruction in the biliary passages causing regurgitation of bile salts into the systemic circulation leading to its excretion in urine

SERUM BILE ACIDS

- Serum bile acids are normally secreted into bile and reabsorbed in enterohepatic circulation
- Estimation of serum bile acids has proved to be of value in diagnosis of cholestasis(impaired bile flow)where bile acid accumulate in blood leading to elevated serum levels
- The test is useful in the diagnosis of intrahepatic cholestasis of pregnancy

ENZYME MARKERS OF LIVER INJURY

- The aminotransferase enzymes, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the markers of liver injury.

- Normal reference range is **15–35 u/l**, but depending on the method used, values can vary.
- Raised levels of one or both indicate hepatocellular injury, ALT being a more liver specific enzyme.

- Even a mild injury to liver tissue like infection or inflammation (hepatitis) will lead to release of enzymes into circulation leading to elevated levels. When there is necrosis, large fractions are released to bloodstream.
- In cases of infective hepatitis, the values may increase very high, greater than 1,000 u/l with alt greater than AST.

- High levels are seen in drug toxicity and ischemic liver injury.

- Moderate elevation of 100–300 U/L may be seen in alcoholic hepatitis, autoimmune hepatitis and chronic active hepatitis (nonalcoholic).

- Mild elevation in levels (lower than 100 U/L) is seen in chronic hepatitis C and B, NASH, hemochromatosis and intake of drugs like metformin and statins.

- The AST/ALT ratio is known as De Ritis Ratio.
- Ratio greater than 2:1 is suggestive of alcoholic liver disease particularly in the setting of an elevated gamma-glutamyl transferase.

Box 21.4 Clinical significance of AST/ALT ratio.

Normal AST: ALT ratio is 0.8. A ratio >2 is seen in:

- Alcoholic hepatitis
- Hepatitis with cirrhosis
- Nonalcoholic steatohepatitis (NASH)
- Liver metastases
- Myocardial infarction
- Erythromycin treatment

ALT higher than AST is seen in:

- Acute hepatocellular injury
- Toxic exposure
- Extrahepatic obstruction (cholestasis)

MARKERS OF CHOLESTASIS

- In cholestasis, ALP and GGT rise several times above the reference value.

- Elevation of GGT accompanied by ALP marks cholestasis, but isolated GGT may be due to intake of alcohol or enzyme induction by drugs (barbiturates, dilantin).

- There is marked elevation of ALP in rickets and in Paget's disease.
- ALT + GGT + ALP to confirm liver disease and biliary obstruction.

- Hepatitis B and C can be diagnosed only by immunological tests for specific antibodies or detection of viral nucleic acids by polymerase chain reaction (PCR) amplification.

- Since all types of hepatitis can exist in acute and chronic states, chances of progression to cirrhosis and HCC are high, especially in hepatitis B and C.

- conventional markers may not show any variation, new markers and marker panels are to be used to detect early progression and response or nonresponse to treatment.

Markers of Chronic Liver Disease – Synthetic Function

- Most common test of synthetic function of liver is the **estimation of total proteins and albumin** in serum and calculation of A/G ratio.
- All serum proteins , except gamma globulins are synthesized by the liver.

1. **Serum Albumin Level**

- Serum albumin is quantitatively the most important protein synthesized by the liver, and reflects the extent of functioning liver cell mass.
- It has a half-life of about 20-25 days ,so it is a good marker to assess chronic liver damage.

- **Low serum albumin** is commonly observed in **patients with severe liver damage**. Note that the serum albumin concentration is also **decreased in non-hepatic causes like malnutrition**.

2. Prothrombin time

- Liver synthesizes all the blood clotting factors. A decrease in concentration of plasma clotting factors is found in the impairment of liver function. So, in chronic liver disease, prothrombin time is **prolonged**.
- Vitamin K is required for the synthesis of factors II, VII, IX and X. So, vitamin K deficiency can also cause prolonged prothrombin time. Patients with cholestasis may have malabsorption of vitamin k.
- In obstructive jaundice, defective absorption of vitamin k is common. Hence prothrombin time must be measured before and after administration of vitamin k before drawing conclusions.

3. Alpha-1 Antitrypsin (AAT)

- It is an acute phase reactant and is synthesized and secreted by the liver.
- AAT inactivates serine proteases (elastase and collagenase)
- Low levels are associated with neonatal cholestasis , progressive juvenile cirrhosis in children and micronodular cirrhosis in adults.
- Low levels are also seen in panlobular **emphysema.** It is increased in acute trauma, infections or after estrogen therapy and in many malignancies.

4. Alpha- Fetoprotein (AFP)

- It is an important protein produced by yolk sac and liver during fetal development.
- Circulatory AFP levels decrease after birth and stabilize to normal range (<5 ng/ml serum) within 1 year.
- Elevated serum AFP is found in hepatocellular carcinoma and metastatic cancers of liver. Hence it is used as a **biomarker to detect tumors of liver, germ cells etc.**

5. Galactose tolerance

- Galactose is a monosaccharide, almost exclusively metabolized by the liver.
- Liver function can be **assessed by measuring the utilization of galactose.** This is referred to galactose tolerance test.
- The subject is given intravenous administration of galactose (about 300 mg/kg body weight). Blood is drawn at 10 minute intervals for the next 2 hours and galactose is estimated.
- In normal individuals, the **half-life of galactose** is about 10-15 minutes. This is markedly **elevated** in **hepatocellular damage** (**infective hepatitis, cirrhosis**).

6. Estimation of Blood Ammonia

- Ammonia levels are elevated in **hepatic failure and urea cycle disorders.**
- CNS disorders are also accompanied by high blood ammonia. It is a useful test in **hepatic encephalopathy**; but it has low diagnostic significance **.**

- The major source of ammonia in the blood is bacteria of gastrointestinal tract. It is produced by action of intestinal bacterial protease, urease and amino acid oxidase on the intestinal contents.
- The ammonia is later converted to urea by the liver, but this activity is considerably decreased in hepatic cell damage; or by the development of portocaval shunts causing portal blood to bypass the liver.
- Ammonia level is an indicator of the capacity of the liver to eliminate ammonia generated in intestine. Raised ammonia in the serum/plasma is suggestive of **cirrhosis** and/or development of collateral circulation. It may occur with **portocaval anastomosis.**
- Arterial blood is preferred to venous blood and estimation is to be done as early as possible to prevent elevations.
- Estimation is useful in excluding or diagnosing hepatic failure in a patient with unexplained stupor or coma and in urea cycle disorders.
- In neonates suspected to have urea cycle disorders, ammonia estimation is indicated.

Precautions: Stringent precautions are to be made. Blood is withdrawn until vacutainer is full. Partial filling allows entry of air. Enzymatic assay (with glutamate dehydrogenase) is done by photometry or by ammonia selective electrode.

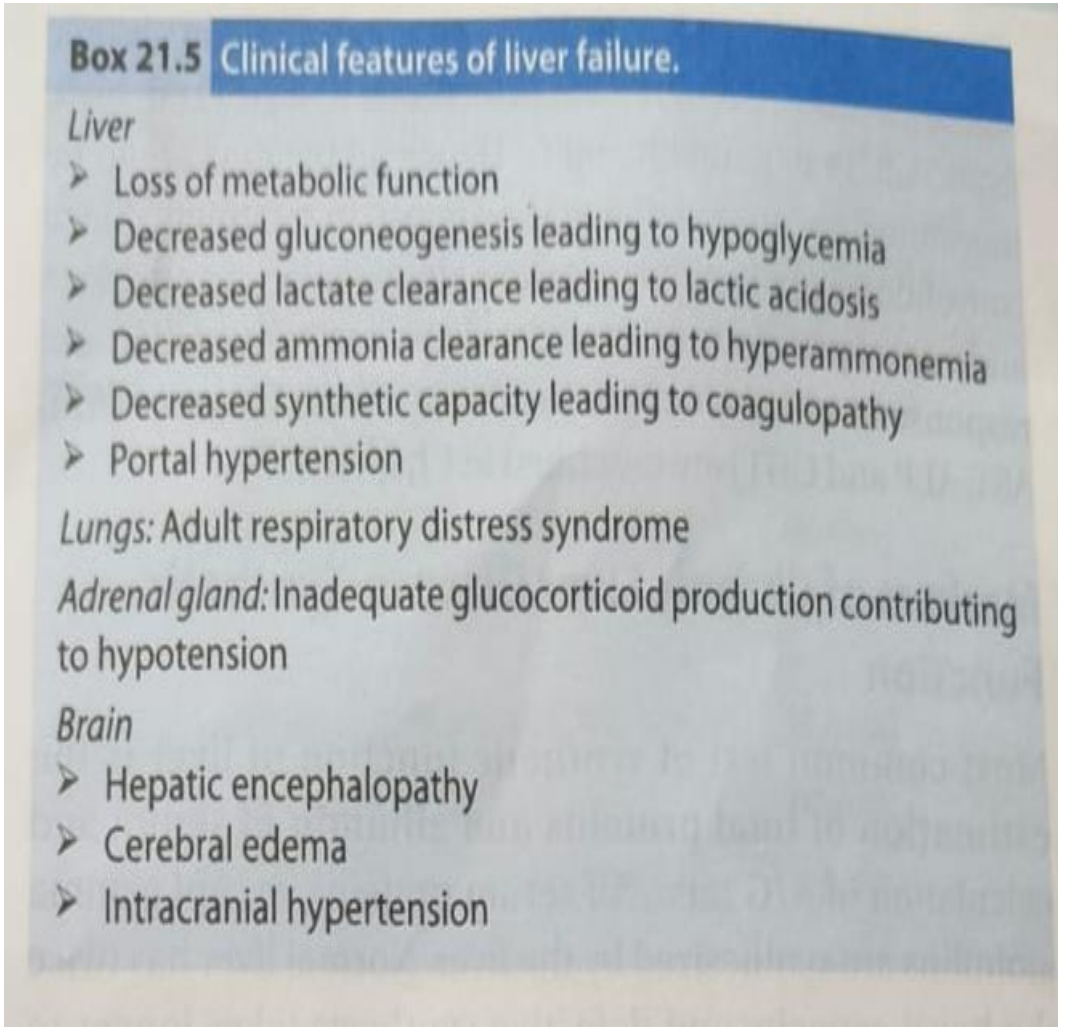
Tests of Metabolic Liver Disease

Estimation of serum ferritin and iron in hemochromatosis, serum ceruloplasmin and copper in Wilson's disease are often estimated. Autoantibodies, alpha-1 antitrypsin and beta-2 macroglobulin are estimated when indicated.

Tumor Marker – alpha fetoprotein

Lifestyle Diseases

Fatty liver disease and alcoholic liver disease have now reached epidemic proportions, which may be considered as lifestyle diseases and are amenable to lifestyle modifications.



Box 21.5 Clinical features of liver failure.

Liver

- Loss of metabolic function
- Decreased gluconeogenesis leading to hypoglycemia
- Decreased lactate clearance leading to lactic acidosis
- Decreased ammonia clearance leading to hyperammonemia
- Decreased synthetic capacity leading to coagulopathy
- Portal hypertension

Lungs: Adult respiratory distress syndrome

Adrenal gland: Inadequate glucocorticoid production contributing to hypotension

Brain

- Hepatic encephalopathy
- Cerebral edema
- Intracranial hypertension

NON ALCOHOLIC FATTY LIVER DISEASE

- Mostly seen in people between ages 40-50 years of age
- It often happens without signs and symptoms
- People with NAFLD are often;
  *over weight or obese
  *may have impaired glucose tolerance and signs of metabolic syndrome
- It can be detected by ultrasonography(USG)

NON ALCOHOLIC STEATOHEPATITIS :

- It is the serious form of NAFLD
- It involves inflammation and mild liver damage
- It can lead to **fibrosis** (liver scarring) and later to **cirrhosis**(permanent liver damage)

MARKERS FOR NAFLD

They are the specific signs present in the blood which helps to diagnose and track NAFLD

OUALITIES OF AN IDEAL MARKER

- Should be specific to liver
- No false positives
- Should be readily available and properly validated

Biomarkers(blood based indicators)

They have indeterminate results in patients with F1-F2 stages of fibrosis

So their levels have to be correlated with fibroscan to decide on the feasibility of transplantation

MARKERS OF HEPATIC FIBROSIS

It is the scarring of the liver caused by chronic liver injury

- **DIRECT MARKERS**

They are produced from **hepatic stellate cells(HSC)**which is released in to blood during extracellular matrix remodelling as a result of chronic liver injury.

These markers helps

*to distinguish stages of fibrosis

*to distinguish fibrosis from cirrhosis

- Serum hyaluronic acid (SHA)

  Normal – less than 50 mg/l
- Procollagen type caboxy terminal peptide(PICP)
- Procollagen type III aminoterminal peptide(PIIINP)
- Matrix metalloproteinases
- Transforming growth factor beta-1

➢INDIRECT MARKERS

- These are used to assess the extent of fibrosis,predict progression and utility of liver transplantation
- These can be detected by a blood test or an enzyme test
- Platelet count,apolipoprotein A1, alpha-2 macroglobulin,AST/ALT ratio are often used

AST/ALT ratio can be determined(**NORMAL – 0.8**)

AST/ALT>1 : NAFLD,chronic viral hepatitis,primary biliary cirrhosis

AST/ALT>2 : alcoholic hepatitis

CAUSES FOR LIVER DISEASE

- Hepatitis virus – It is the most common cause for **hepatocellular jaundice**
  - ➢Hepatitis A virus (HAV)
    It is transmitted through contaminated food and water
  - ➢Hepatitis B virus(HBV)
    It is transmitted mainly through parenteral contamination
    It is a DNA virus which destroys hepatic cells
    HBV is called as an **oncogenic virus**
- Alcohol
- Toxins – chloroform , carbon tetrachloride etc
- Bacterial infections – TB , leptospirosis etc
- Drugs – salicylate , tetracyclines , halothane etc

IMMUNOLOGICAL TESTS IN LIVER DISEASE

AUTOANTIBODIES

Due to the defective suppressor T cells leads to the production of autoantibodies against hepatocyte surface antigens which causes **autoimmune chronic hepatitis**

LIVER FUNCTION TESTS IN GENERAL

Most commonly employed LFTs are;

- Serum bilirubin
- A/G ratio
- ALP,AST,ALT

LIVER FUNCTION IN COVID 19

- Elevated ALT and LDH
- A rise in **Ferritin and D-Dimer** follows which are indicators of inflammation and a procoagulant state

ASPIRIN TOXICITY

It produces mixed acid base disturbances,inhibits the TCA cycle, producing lactic acidosis and ketosis

TREATMENT – Normalising pH and correcting electrolyte imbalance

PREVIOUS YEAR OUESTIONS

1)Enumerate liver function tests. Describe any two of them in detail (2024)

2)Urinary picture of different types of Jaundice (2024)

3) Van den Bergh test(2023)

4) What is post hepatic jaundice and how it is diagnosed biochemically (2013)

5)What is the most common cause of hepato cellular Jaundice (2023)

OUR REFERENCES

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- Textbook of Biochemistry U. Satyanarayanan 6th Edition

THANK YOU