Liver Function Tests

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Liver

Liver is vital organ it's one of the largest organ in human body
Weighing 1.5kg, (2- 3 % of the body mass),
Oxygen consumption (25 – 30 %)
The liver is of vital importance in the intermediary metabolism and in the detoxification and elimination of toxic substance.

Anatomical Structure of Liver
The organ is made up of hexagonal lobules of cells
Row of hepatocytes radiate from the central hepatic vein and and seperated by sinosoidal spaces
Along the wall interspread the the kupffer cells

Portal tract consist of

- hepatic artery
- portal vein
- bile ducts

The main blood supply is from the portal vein and hepatic artery

the blood flow from the portal tracts toword the central hepatic vein

Major Functions of Liver

General metabolic function

Carbohydrate metabolism
Gluconeogenesis
Glycogen synthesis and breakdown
Lipid metabolism
Fatty acid synthesis
Cholesterol synthesis and excretion
Lipoprotein synthesis

Synthetic function

Plasma protein (Except immunoglobulin and complements)
Coagulation factors (**1972**)
Primary bile acids

Excretory and detoxification function
Metabolism and excretion of bilirubin
Deamination of amino acid and ammonia produced are converted into urea
Many drug metabolized and inactivated by enzymes of the endoplasmic reticulum and excreted in the bile
Toxin extracted by kupffer cells

Liver Function Test

Various Biochemical test that provide a quantitative assessment of functional hepatic cell activity
They are cheap, noninvasive and widely available

Liver Function Test

They are valuable in:

- Detecting the presence of liver disease
- Placing disease into the appropriate broad category
- Following progress

Biochemical Test for Liver Disease
Excretory function (hepatic anion excretory function)
TSB (Total Serum Bilirubin) DB(direct bilirubin)
Synthetic Funciton
albumin
Prothrombin time
Cell Damage
transaminases (ALT, AST)
inflammatory ALT>AST
infilterative AST>ALT
Alkaline phosphatase : related to biliary tract and regurgitated into plasma
Gamma glutamyl transferase

Bilirubin Metabolism

80% of bilirubin is produced from the breakdown of haem in reticuloendothelial system
After the protein part (globin) has been removed, the tetrapyrrole ring cleaved between rings A and B by *heme oxygenase.* Produce **Green Biliverdin,**
biliverdin is reduced by *biliverdin reductase to the orangecolored* **bilirubin.**
Bilirubin transported to liver bound to albumin (**Unconjugated bilirubin (**indirect) lipid soluble
In the liver, it transfer to ligandin (Y protein)
In SER it is conjugated with glucuronate by enzyme *uridyl diphosphate (UDP) glucuronyl transferase*

Conjugated bilirubin enter the gut lumen is boken down by bacterial acition into stercobilinogen
Some is absorbed into the portal circulation by enterhepatic circulation and excreted in urine in the form of urobilinogen which then oxidized to urobilin

Urobilin and stercobilin are coloured compound and called **Bile Pigments**
Urobilinogen in contrast to bilirubin normally present in the urine

Jaundice

Is yellowish discoloration of skin, sclera and mucus membrane beocmes clinically apperant when the plasma bilirubin concentration reaches about 50 μmol (3 mg).

Jaundice

- Prehepatic : bilirubin excretion exceed the normal capacity
- Hepatic : normal bilirubin load can not conjuageted
- Post hepatic: biliary flow is obstructed

Hyperbilirubinemia is not always present in patients with liver disease nor is it exclusively associated with liver disease
E.g
Well compensated cirrhosis **NO JAUNDICE**
Advance pancreatic carcinoma **JAUNDICE**

Types of Hyperbilirubinemia

- Unconjugated Hyperbilirubinemia
  (**retention hyperbilirubinemia)**
  acholuric jaundice
- Conjugated Hyperbilirubinemia
  (**regurgitation hyperbilirubinemia)**
  choluric jaundice

Unconjugated hyperbilirubinemia

Occur if there is
Increase in bilirubin load e.g hemolysis or hemorrhage
Impaired binding of bilirubin to ligandin or impaired conjugation with glucuronate in the liver

- Hemolytic anemia
- Neonatal jaundice
- Gilbert syndrome
- Criglar Najjar syndrome

Hemolytic anemias

unconjugated hyperbilirubinemia is usually only slight (< 4 mg/dL; < 68.4 mol/L) even in the event of extensive hemolysis because of the healthy liver's large capacity for handling bilirubin.

Physiologic Jaundice

common cause of unconjugated hyperbilirubinemia
accelerated hemolysis around the time of **birth**
immature hepatic system for the uptake, conjugation, and secretion of bilirubin
kernicterus
hyperbilirubinemic toxic encephalopathy amount of bilirubin is unconjugated, it is capable of penetrating the blood-brain barrier when its concentration in plasma exceeds that which can be tightly bound by albumin (20–25 mg/dL).
Crigler-Najjar Syndrome

Type I Crigler-Najjar syndrome

rare autosomal recessive disorder
severe congenital jaundice exceeds 20 mg/dL
fatal within the first 15 months
mutations in the gene encoding bilirubin-UGT activity in hepatic tissues

Crigler-Najjar Syndrome, Type II

some activity of the enzyme is retained
Serum bilirubin concentrations usually do not exceed 20 mg/dL
Patients with this condition can respond to treatment with large doses of phenobarbital

Gilbert Syndrome

Present in second decade
Bilirubin between 20 – 40 µmol/L (1.2 -2.5 mg/dl)
Precipitate by fasting and intercurrent illnesses
Causes include
Shortened red cell survival
Impaired uptake and conjugation
30% of the enzyme's activity is preserved

Conjugated hyperbilirubinemia

results from blockage of the hepatic or common bile ducts
bilirubin diglucuronide cannot be excreted

Cholestatic Jaundice

all cases of extrahepatic obstructive jaundice. It also covers those cases of jaundice that exhibit conjugated hyperbilirubinemia due to micro-obstruction of intrahepatic biliary ductules by swollen, damaged hepatocytes

Dubin-Johnson Syndrome
benign autosomal recessive disorder
childhood or during adult life
Defect in the excretion of bilirubin but not bile acid
Alkaline phosphatase normal
Hepatomagaly with dark brown pigment

cholestasis

Intrahepatic: bile secretion from the hepatocyte into the canaliculi is impaired
viral hepatitis
drugs cholangitis

Extrahepatic: obstruction to the flow through biliary tract
biliary stones Biliary atresia , carcinoma of head of pancreas

Biochemical features

BILIRUBIN may be normal in intrahepatic cholestasis or increased
ALKALINE PHOSPHATASE activity is most sensitive and its level is usually increased
Dark urine and Pale stool
prolong **prothrombin** time due to deficiency of vitamin k

Plasma Enzyme

- Aspartate aminotransferase
- Alanine aminotransferase
- Alkaline phosphatase
- Gama glutamyl transferase

Increase in aminotransferase > 10 times ULN In patients with hepatitis
Increase in Alkaline phosphatase In cholestasis because increase synthesis and and enzyme in the biliary tract regurgitate
GGT derive from endoplasmic reticulum the increase in the activity of this enzyme is due to Intake of alcohol or induce by drug

Plasma Protein

Albumin: is synthesize in the liver
It reflect the functional reserve of organ
Normal in acute liver disease because of long half life (20 days)
Fall in Plasma albumin indicate significant deterioration in hepatic function
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Cirrhosis

End result of many inflammatory condition
In early stage no abnormal finding
Active stage : plasma AST↑ , Alt slight raised
Advance cases: reduced cell mass and and vascular shunting produce *β-γ fusion* on protein electrophoresis

Hepatocelluar Failure

Liver damage severe enough to cause obvious sign of impaired hepatocellular fucntion
Biochemical finding include
Jaundice progressive
Total amount of transaminases may be reduced
Hypovolumia and hypotension
hypoalbuminia
secondary hypoaldosteronism and hypokalemia
renal circulatory insufficiency with increased creatinine. **What about urea?!!**
impaired hepatic deamination of amino acid with overflow aminoaciduria
Impaired hepatic gluconeogenesis causes hypoglycemia

Bile acids & Gall Stones

Four Bile Acid
Primary : Cholic Acid and Chenodeoxycholic acid
Secondary : deoxycholic acid and lithocholic acid
Deficiency of bile acid lead to impaired micelle formation and malabsorption of fat

Gall Stones
Only 10 % radioopaque

Mixed stones
Found in chronic Hemolytic state
Small Hard dark green or black
Consist of Calcium, bilirubin