Liver Diseases

The liver is the largest organ in the body. It plays a central role in digestion and in the regulation of protein, carbohydrate and lipid metabolism, and is responsible for the metabolism of drugs and environmental toxins. In view of this, it is not surprising that diseases of the liver are a major cause of morbidity and mortality; worldwide, 1 in 40 deaths are due to liver disease or primary liver cell cancer.

The liver is one of the heaviest organs in the body, weighing 1.2–1.5 kg, its functional unit is the hepatic acinus. Hepatocytes comprise 80% of liver cells and the remainder is made up of sinusoidal endothelial cells (10%), bile duct endothelial cells (1%) and cells of the immune system (9%).

In developed countries, the most common cause of liver disease is alcohol abuse, while in the developing world, infections caused by hepatitis viruses, often complicated by hepatobiliary cancer, and those caused by parasites, are responsible for most chronic liver disease.



**Investigation of Hepatobiliary Disease**

**Liver function tests**

Liver function tests (LFTs) include the measurement of:

1- serum bilirubin (total, direct, and indirect)

2- aminotransferases (ALT & AST) >>> high levels indicate hepatocytes damage.

3- alkaline phosphatase (ALP) >>> high levels indicate hepatic obstruction.

4- gamma-glutamyl transferase (GGT) >>> high levels indicate hepatic obstruction.

5- albumin.

Most analytes measured by LFTs are not truly ‘function’ tests, but rather provide biochemical markers of liver cell damage. Liver function is best assessed by the serum albumin, prothrombin time and bilirubin.

**Hepatitis**

Hepatitis is defined as inﬂammation of the liver tissue. It is classically divided into:

**1- Acute hepatitis**

Which could be due:

A- infectious (viral and bacterial)

B- non-infectious causes (drugs, poisons, and autoimmune diseases).

**2- Chronic hepatitis**

This type represents inﬂammation of liver that persists for > 6 months which may follow acute hepatitis and may progress to cirrhosis (liver ﬁbrosis). Chronic liver disease includes chronic hepatitis, and cirrhosis.

Causes of chronic liver disease:

A- alcohol

B- viruses (HBV, HCV)

C- drugs (methotrexate)

D- autoimmune hepatitis

E- metabolic (hemochromatosis)

**Clinical features**

Clinical features of liver disease vary according to the type, onset, and severity.

A patient with acute hepatitis may be asymptomatic or may complain from malaise, anorexia, fatigue, low grade fever (< 38 °C), upper abdominal discomfort, and jaundice or icterus (yellow skin and sclera caused by raised serum bilirubin > 3 mg/dl).

Jaundice is caused by liver inability to metabolize bilirubin (product of hemoglobin breakdown) either due to:

1- poor conjugation of high amount of bilirubin as in hemolytic anemia.

2- impaired function of liver as in hepatitis.

3- inability to excrete bile as in cholestatic jaundice which in turn may be intrahepatic or extrahepatic:

A. Intrahepatic cholestasis from hepatocyte damage which is detected by increased alanine transaminase (AST).

B. Extrahepatic cholestasis from obstructed common bile duct by gallstone, tumor, or adjacent lymph nodes.

Obstructive liver disease can present with:

1- steatorrhea (pale fatty stool)

2- weight loss, nausea, anorexia, vomiting

3- itching

4-bleeding tendency (malabsorption of vitamin K)

The most striking laboratory findings of obstructive liver disease is the elevated levels of: ALP, GGT, and direct bilirubin.

For hepatocellular liver disease (hepatitis), the most important laboratory finding is the extremely high level of ALT which is present even in the prodromal symptoms before the onset of jaundice. **Infectious causes of hepatitis include:**

1- viral (A, B, C, D, E, G, CMV, EBV, congenital rubella, and yellow fever)

2- parasitic (toxoplasmosis, Amebiasis).

**Hepatitis A (infectious hepatitis)**

RNA virus is common and endemic among children and overcrowded community of poor socioeconomic status. Spread by feco-oral route through consumption of contaminated water.

**Clinical features**

After incubation period of 15-50 days, the patient has:

1- asymptomatic

2- has typical features of acute hepatitis: (fatigue, nausea, vomiting, abdominal pain or discomfort, loss of appetite, low grade fever (< 38 °C), jaundice and itching) and rarely muscle pain, rash and arthralgia.

Blood and feces become non-infective during or shortly after the acute illness. Complete recovery is usual without carrier state or chronicity. Mortality rate < 0.1%.

**Investigation**

Positive Anti-HAV IgM within 10 days and IgG after old infection or vaccination.

LFT: raised ALT, AST and bilirubin.

**Treatment**: self-limiting disease without treatment

Prevention: infection with HAV gives long-lasting immunity.

HAV vaccine for travelers and health care providers in endemic areas and immunoglobulin to prevent the disease during outbreak.

**Dental aspects**: It is unlikely that the patient seeks dental treatment during acute phase and there is no risk of transmitting HAV during proper dental care.

**Hepatitis B virus (serum hepatitis)**

HBV is a DNA virus causes acute hepatitis that can lead to chronic hepatitis, cirrhosis, and hepatoma

**Mode of transmission**

HBV is transmitted mainly through parenteral route; examples include:

 1- blood or blood products

 2 -intravenous drug abuse

 3- hemodialysis

 4- tattoos

 5- sexual contact

 6- perinatal.

HBV virus can survive more than week in dried blood, and has been transmitted to patients and health care staff, hemophiliacs, traveler to endemic areas, and non-parenteral route through bite and close contact (virus in gingival exudate and not in saliva).

**Clinical features**

After incubation period of 50 -180 days, 30% are asymptomatic (anicteric hepatitis) or show 2 weeks of prodromal feature of anorexia, malaise and nausea followed by period with jaundice, pale stool, dark urine, enlarged and tender liver, pruritus, muscle pains, arthralgia, rash, and fever.

**Complications**

1- carrier state 2- chronic infection (10%) 3- cirrhosis 4- liver cancer

Carrier state is considered when HBV persists for > 6 months in asymptomatic healthy subject, while chronic infection is considered when there is persistent abnormal LFT.

**Investigation**

1- Serology: HBV surface antigen (HBsAg), envelop antigen (HBeAg), core antigen (HBcAg),

surface antibody (Anti-HBs), core antibody (Anti-HBc), envelop antibody (Anti-HBc).

+ve HBsAg: acute infection and carrier state.

+ve HBeAg: chronic active hepatitis with high infectivity.

+ve Anti-HBs: previous infection or vaccination.

+ve Anti-HBc — IgM: acute recent infection.

+ve Anti-HBc — IgG: carrier or chronic states.

+ve Anti-HBe: chronic inactive hepatitis and low infectivity

2- HBV DNA - PCR: blood viral count by polymerase chain reaction: sensitive and speciﬁc test.

LFT: raised AST, ALT, ALP, and bilirubin.

**Treatment**

Acute hepatitis B: resolve spontaneously

Chronic hepatitis B: interferon-alpha for 6 months with or without antiviral (Lamivudine) for 1-3 years.

**Dental aspects**

**1.** Active HBV vaccine (recombinant HBsAg) or combined HAV and HBV vaccine for clinical staff especially those who undertake exposure prone procedure (EPP) like dentist, people work with high risk group (travelers, injecting drug users, and hemophiliac who receives therapeutic blood products) and baby of infected mother (given vaccine with HB immunoglobulin).

**2.** Post-exposure prophylaxis (PEP): after needle stick injury with HBV infected person, the health care provider needs HB Ig &/ or HBV vaccine after evaluation of HBsAg status of the source and vaccination and the vaccine response status of the exposed person within 24 hours of contact with follow up for antibody level after 6 months.

**3.** Universal precautions should be applied against transmission through blood, blood products, body ﬂuids and contaminated instruments (syringe, needle, razor, tattoo piercer, and toothbrush) among risky people.

**4.** Barrier precautions (mask and glove) and safety handling of sharp instrument (disposal). It requires 0.0000001 ml of HBsAg positive serum for transmitting the disease. Also, saliva may contain HBV (gingival exudate) is risky in close contact, as in human bite.

**5.** Practitioners who have hepatitis should stop dental practice until recovered.

6.Dentists and dental students with +ve HBeAg or -ve HBeAg & >l000 HBV particle/ml should avoid EPP.

**6.** Avoid hepatotoxic drugs.

**7.** To avoid risk of bleeding tendency, conﬁrm the hemostatic state by testing platelet count and prothrombin time (INR).

**8.** Avoid blood, organs, or tissue donation if HBV or HCV positive.

**Hepatitis C**

HCV is an RNA virus which spreads through blood and tissue donors infected with HCV, illegal drug abusers, long term renal dialysis, accidental needle stick injury, sexual contact, and bite of infected patient.

**Clinical features**

After an incubation period of (14 - 150 days), most patients are asymptomatic and 80% of them have persistent abnormal LFTs (carrier), of those: 60-70% develop chronic liver disease, 5-20% develops cirrhosis, 1-5% develops cancer.

**Investigation**

1- Serology (Anti-HCV antibodies)

2- HCV - RNA by PCR

3- LFT (raised liver enzymes),

4- Liver biopsy.

**Treatment**

Interferon with ribavirin for 6 -12 months.

**Dental aspects**

- **HCV** RNA positive dentists and dental students are restricted from performing EPP should be

tested for HCV antibodies and, if positive to be tested for HCV RNA viral particle.

- **Post** HCV exposure prophylaxis (PEP): HCV status of the source and the exposed person, by follow-up HCV testing to determine if infection develops.

- **Treatment** is not recommended for PEP.

- **Early** treatment of acute hepatitis due to HCV may prevent chronicity.

**Prevention**

No vaccine available, so only avoidance of risk exposure.

HCV may be associated with oral features: sicca syndrome, non-Hodgkin lymphoma, and lichen planus.

**Hepatitis D virus (delta agent)**

HDV is incomplete virus (circular RNA) carried within HBV particle and will replicate only in the presence of HBV. HDV spreads parenterally by shared needles and blood products among drug abusers.

**Clinical features**

These are similar to HBV. 90% of cases are asymptomatic but 80% of super-infection HBV carriers with HDV can cause fulminant disease with mortality (30%), or chronic liver disease with cirrhosis.

**Investigation**: serology (HBsAg and delta antibody) indicate chronic hepatitis.

**Prevention**: vaccination against HBV protects indirectly against HDV.

**Treatment**: interferon.

Dental aspects: Same as for HBV.

**Hepatitis E virus (HEV)**

RNA virus spreads via feco-oral route and causes large epidemics. HEV causes a disease similar

to HAV, but in pregnant women cause high mortality (40%).

Investigation: serology (HEV antibodies).

Dental aspects: no transmission during dentistry.

**Hepatitis G virus (HGV)**

RNA virus may co-infect patients infected with HCV or HBV. It is highly prevalent in intravenous

drug users. HGV hepatitis is less severe than HCV but may be followed by persistent infection in

30%.

Treatment: interferon.

Dental aspects: no transmission, during dentistry.

**Cirrhosis**

A chronic liver damage characterized by hepatocellular necrosis and inﬂammation, followed by ﬁbrosis and regenerating nodules of hepatocytes, and vascular derangement, deterioration of liver function, blood ﬂow obstruction leading to blockade portal circulation leading to portal hypertension,

esophageal varices, gastrointestinal hemorrhage.

Hepatic encephalopathy might occur due to failure to detoxify normal metabolites leading to coma. Thrombocytopenia from splenomegaly, and low blood clotting factor levels, leads to a bleeding tendency.

**Complications**

- spontaneous bacterial peritonitis - peptic ulceration - renal dysfunction

- immune dysfunction - hepatoma.

**Clinical features**

- Finger-clubbing - opaque nails (leukonychia) - palmar erythema

- asterixis - spider naevi (angiomata) - scratch marks

- gynecomastia - hepato-splenomegaly - ascites

distended abdominal veins (caput medusa), - ankle edema.

**Investigation**

-Biochemistry: LFT (raised liver enzymes and low serum albumin).

-Serology: according to etiology (viral antibodies, auto-antibodies in autoimmune hepatitis and SLE).

-Hematology: thrombocytopenia, anemia, high MCV, and prolonged PT.

-Radiology: CT scan, ultrasound, or MRI.

-Liver biopsy for deﬁnitive diagnosis.

**Treatment**

**S**upportive (low salt, diuretic, BB, lactulose and neomycin for encephalopathy).

Speciﬁc treatment according to the etiology: corticosteroids for autoimmune hepatitis, interferon

and lamivudine for HBV and HCV.

Liver transplantation

**Dental aspects**

- Consider risks of bleeding tendency, infection, diabetes, anemia, drug therapy, poor wound healing, GIT bleeding, and alcoholism.

- Consider infection transmission (HBV, HCV, HIV)

- Clotting screen may be indicated and if PT is prolonged, need to consider:

 1- Parenteral vitamin K ,10 mg (phytomenadione) daily for several days preoperatively.

 2- Transfusion of fresh blood or plasma.

- Routine dental care can be done safely.

- Avoid hepatotoxic drugs, respiratory depressants (sedatives, hypnotics, and opioids) but reduced

doses of midazolam can be used and preferably inhalational sedation or nitrous oxide.

- LA is safe in normal doses (prilocaine is preferred to lidocaine).

- Isoﬂurane is preferable to halothane (halothane may cause hepatitis).

- Avoid suxamethonium (generalized muscle relaxant used in GA) from impaired cholinesterase.

- Avoid aspirin and most other NSAIDs (indomethacin) for the risk of gastric hemorrhage.

- For analgesia, use paracetamol or reduced doses of codeine.

- Antimicrobials are safe in normal doses: penicillin, cefalexin, cefazolin and imipenem.

- Avoid broad-spectrum antibiotics because of reduced vitamin K availability by destroying the gut

ﬂora.

- To prepare jaundiced patient with cirrhosis for major surgery: intravenous ﬂuids for hydration with

glucose 5% and mannitol diuresis to avoid acute renal failure which may complicate hepatic failure

(hepatorenal syndrome).

- Prophylactic antibiotic before invasive oral surgery (amoxicillin orally 2-3 g with metronidazole 1 hour preoperatively or intravenous imipenem) to protect the patient from spontaneous bacterial peritonitis.

- Some patients have sialosis (salivary gland swelling), or tooth erosion from gastric regurgitation.

-There is an association between liver cirrhosis and oral carcinoma.

**Alcoholic hepatitis**

Alcohol can be hepatotoxic as it blocks the metabolism of protein, fats and carbohydrates causing fatty change (alcoholic steatosis) leading to inflammation (alcoholic hepatitis) which is over long period may end with liver ﬁbrosis, which may be asymptomatic or may turn into cirrhosis and liver failure.

Other causes of fatty liver: obesity, diabetes, protein malnutrition, CAD, pregnancy, or corticosteroid.

**Drug induced hepatitis (DIH)**

Liver damage because of drug which is either dose related or immunologically mediated. Example

of drugs that may cause DIH:

Halothane, NSAIDs (paracetamol), tetracyclines, and erythromycin.

As antipyretic and analgesic in children < 16 years, aspirin is contraindicated and paracetamol is preferred otherwise if aspirin ingested by children during viral illness (e.g. chickenpox, inﬂuenza) may cause Reye's syndrome (fatty liver, encephalopathy & rising intracranial pressure) which presented with vomiting, nausea, tiredness, confusion, restlessness, lethargy, coma, convulsions and death.

**Post-operative jaundice**

After an operative intervention under general anesthesia, the patient may develop jaundice which could be due to the following causes:

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| --- | --- | --- |
| **Excessive bilirubin load** | **Hepatocellular damage** | **Others** |
| Hemolytic anemia | Gilbert's syndrome | Obstructive jaundice |
| Incompatible blood transfusion | Drug induced | Sepsis |
| RBC destruction of a hematoma | Viral hepatitis | Shock |
|  | Halothane toxicity | Pancreatitis |

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