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Diseases of the liver: A basic review

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Abstract
Liver diseases (basic review) are to understand very easily for graduate, post graduate and post doctoral ayush, dental, medical etc., students. I am explaining main and important diseases in liver in day to day practical life for medical students and professionals. Diseases are jaundice, ascities, hepatitis, acute hepatic failure and cirrhosis of liver.

Keywords: Liver diseases, causes, clinical features, investigation

Introduction
We have lot of diseases to explain in liver. But only main/few diseases are reviewing for under graduate, post graduate and post doctoral Ayush, dental, medical, nursing etc., for entrance and main examination purpose.

Jaundice
Jaundice/Hyperbilirubinemia define as "the yellow discoloration appearance of the sclera, skin and mucous membranes resulting from an increased bilirubin concentration in the body fluids". It is a multifactorial disorder with many symptoms. Generally, the physiological jaundice is the most prevalent type however in some regions pathological jaundice is also common. This review article focuses on a brief introduction to jaundice, its types and causes, measuring the bilirubin level, clinical approaches towards hyperbilirubinemia, different precautionary measures for the parents of babies suffering from hyperbilirubinemia. Acute jaundice is often an indicator of significant underlying disease and occurs secondary to intra and extra hepatic etiologies. A retrospective study of more than 700 individuals found that most cases (55%) of acute jaundice in adults are caused by intra hepatic disorders, including viral hepatitis, alcoholic liver disease, and drug induced liver injury. The remaining 45% of acute jaundice cases are extra hepatic and include gallstone disease, hemolysis, and malignancy. My article provides a systematic approach to the diagnosis of jaundice in adults and reviews common etiologies of hyperbilirubinemia. It is detectable clinically when the plasma bilirubin exceeds 3 mg/dl. Internal tissues and body fluids are coloured yellow but not the brain [1].
Unconjugated bilirubin is produced (250 – 300 mg daily) from the catabolism of haem after removal of its iron component. Uconjugated bilirubin is conjugated by the endoplasmic reticulum enzyme. Glucuronyl transfers, in to bilirubin mono and diglucuronide.

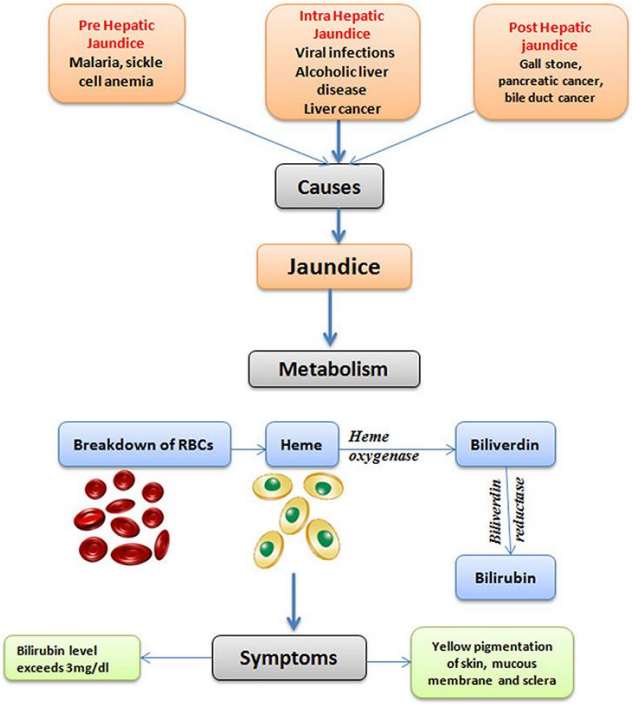

Fig 1: Pathophysiology of jaundice

Causes
Causes of cholestatic jaundice is Primary biliary cirrhosis, primry sclerosing cholangitis, alcohol, drugs, viral heptatitis, autoimmune hepatitis, severe bacterial infections, post operative, hodgkin's lymphoma, pregnancy, idiopathic recurrent cholestasis and extrahepatic is carcinoma of ampullary pancreatic, bile dut, cystic fibrosis, parasitic infection and traumatic biliary structures [2, 3].

Clinical features
In cholestasis early symptoms are dark urine, pale stools,

pruritus. Cholangitis are fever, rigors, pain and hepartic abscess. Late features are xanthelasma and xanthomata, malabsorption are weight loss, steatorrhoea, osteomalacia and bleeding tendency.

Investigations
In portal/hepatic venous obstruction can do angiography. Ultrasound in cases of dilated bile duts and abnormal parenchyma/no dilated ducts. PTC, ERCP in case of dilated bile ducts and liver biopsy for abnormal parenchyma. Focal liver lesions (tumor, cyst, abscess) are fine needle aspiration/FNA.

Ascites
It is free fluid in the peritoneal cavity [4, 5].

Causes
Common causes of ascites are malignant disease (hepatic, peritoneal), cardiac failure, hepatic cirrhosis and other causes are hypoproteinaemia- nephritic syndrome, protein – losing enteropathy, mainutrition, hepatic venous occlusion llike budd chiari syndrome, veno occlusive disease, infection – tuberculosis, spontaneous bacterial, peritonitis, pancreatitis, lymphatic obstruction, rare – meigs syndrome, vasculitis, hypothyroidism, renal dialysis.

Pathogenesis
Liver failure and portal hypertension in cirrhosis cause sodium and water retention in the body. Because of this cause localization of fluid collection in the peritoneum due to the high venous pressure in the mesenteric circulation. The means where by Na+ and water retention occurs are unknown [6, 7].

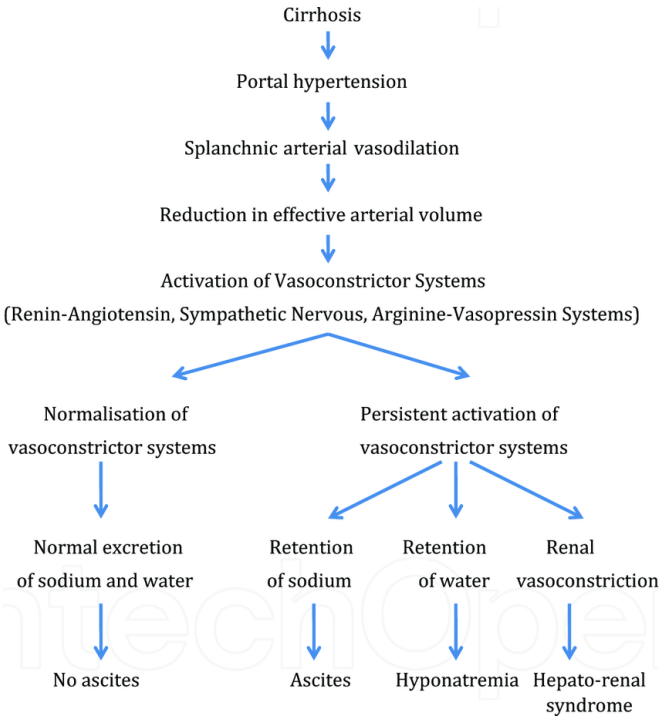

Fig 2: Pathophysiology of Ascites

The mechanisms for renal sodium retention remain poorly understood but include activitation of the rennin angiotensin system with secondary aldosteronism, increased sympathetic nervous activity, alteration of atrial natriuretic hormone secretion and altered activity of the kallikrein kinin system.

Clinical features
It causes abdominal distension with fullness in the flanks, shifting dullness on percussion, divarication of the umbilicus, hernia, abdominal striae, meralgia paraesthetica, scrotal oedema. Pleural effusion can be found in some cases, usually on the right side.

Investigation
Ultrasonography can confirm ascites. Abdominal radiographs can show ascites, but they are insensitive and non specific. Ascites protein concentrations below 25 g/l or serum ascites albumin gradients above 1.5 are usually found in ascites due to cirrhosis. Cytological examination can reveal malignant cells and polymorphonuclear leucocyte counts above.

Diagnosis
In the great majority of patients ascites is caused by malignant disease, cirrhosis or cardiac failure. However the presence of cirrhosis does not necessarily mean that this is the cause of the ascities. Ascities with a protein concentration above 25 g/l raises the possibility of infection (especially tuberculosis), malignancy, hepatic venous obstruction, pancreatic ascites or rarely, hypothyroidism.

Management
Restriction of dietary sodium intake is essential to achieving negative Na balance in patients with ascities. Ascities can be mange with anti diuretic drugs.

Acute hepatic failure
Acute failure is rare syndrome in which hepatic encephalopathy, characterized by mental changes progressing from confusion to stupor and coma [8, 9].

Causes
Acute liver failure (ALF) is the culmination of severe liver cell injury from a variety of causes including viral hepatitis, toxins, metabolic disorders, and vascular insults. In India, viral hepatitis A and E are the most common cause for ALF. About 15-22% of ALF occur without any identifiable cause [10].

Wilson's disease accounts for 6-12% of cases of ALF. ALF due to Wilson disease occurs mainly in young females. It should be suspected when patient has very high serum bilirubin and low alkaline phosphatase at presentation. Hemolysis, elevated liver enzymes, low platelet syndrome, and acute fatty liver of pregnancy are two overlapping syndromes occurring in the second half of pregnancy.

Acute Budd-Chiari syndrome can rarely present as ALF [12]. Early recognition and prompt treatment can result in good recovery. Ischemic liver injury occurs in setting of cardiac arrest or intractable hypotension. Here, the aminotransferases will be markedly elevated and responds dramatically to stabilization of circulatory problem.

Acute liver failure occurs in <20% of autoimmune hepatitis. Presence of autoantibodies and a compatible picture on biopsy helps to make a diagnosis. Amanita Phalloides mushrooms, heat stroke, and malignant infiltration of the liver are rare causes of liver injury [11].

Pathology

Extensive parenchymal necrosis is the most common histological appearance. Severe fatty degeneration is characteristic of fulminant hepatic failure caused by drugs such as tetracycline, pregnancy and Reye's syndrome.

Clinical features: clinical features are reduced alertness and poor concentration, progressing through behavioral abnormalities such as restlessness, aggressive outbursts and mania, to drowsiness and coma.

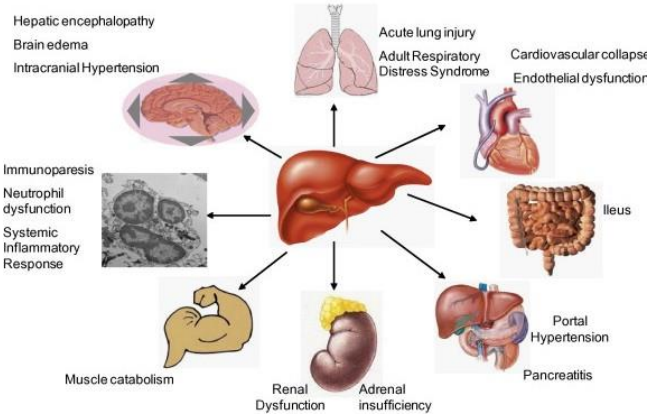

Fig 3: Systemic manifestation of acute liver failure

Investigation

Toxicology screen of blood and urine, IgM anti HBs, IgM anti HAV, anti HEV, cytomegalovirus, herpers simplex, Epstein barr virus, caeruloplasmin, serum copper, urinary copper, ultrasound of liver, Doppler of hepatic veins, chest radiograph, Auto antibodies like ANF, AMA, ASMA, LKM.

Complication

Complication of acute hepatic failure are encephalopathy, cerebral oedema, respiratory failure, hypotension, hypothermia, infection, bleeding, pancreatitis, renal failure, metabolic like hypoglycaemia, hypokalaemia, hypocalcaemia, hypomagnesaemia, acid base disturbance.

Management

Acute hepatic failure patients should be observed in ICU with clear observation like

1. Neurological – conscious level, pupils – size, equality, reactivity, fundi – papilloedema, plantar responses.
2. Cardiorespiratory – pulse, blood pressure, central venous pressure, respiratory rate.
3. Fluid balance – input – oral, intravenous and output are hourly urine out put, 24 hours sodium output vomiting, diarrhoea.
4. Blood analyses – peripheral blood count, Creatinine, blood urea, serum electrolytes, calcium, magnesium, glucose, prothrombin time.
5. Infection surveillance like cultures – blood, urine, throat, sputum, chest radiograph and temperature.

Hepatitis

It is inflammation of the liver which results in damage to hepatocytes with subsequent cell death [12-15].

Hepatitis A, B, and C cause acute infection of the liver that may manifest as an acute icteric illness or be detected incidentally as raised transaminase levels.

Hepatitis A virus

Hepatitis A virus (HAV) is transmitted faeco orally. There is evidence for sexual transmission between homosexual men with several outbreaks reported. The specific risk factors are not well defined but probably relate to oro anal or digital rectal contact, particularly in settings such as public saunas and dark rooms. Acute icteric hepatitis appears after an incubation period of 15–45 days, symptoms last for about 6 weeks, and it is only rarely fatal. Infectivity lasts from approximately 2 weeks before the onset of jaundice to 1 week after.

Hepatitis B virus

Hepatitis B virus (HBV) infection is transmitted vertically (mother to child), parenterally, and sexually. There is a much lower risk to household contacts of acute cases and high infectivity carriers. Of individuals seen in STD clinics, those at greatest risk of infection are homosexual men and injecting drug users. Acute hepatitis B has an incubation period of 40–160 days with symptoms lasting up to 12 weeks. Fulminant hepatitis occurs in about 1% and may be fatal [6]. About 5% of infected adults are asymptomatic. About 5–10% of immunocompetent patients and up to 40% of immunocompromised patients develop chronic infection. Symptomatic acute infection very rarely leads to chronicity. Infectivity lasts from approximately 2 weeks before the onset of jaundice until the loss of infection markers. Cirrhosis or liver cancer may develop in up to 20% of chronic carriers over 10–50 years.

Hepatitis C virus

Hepatitis C virus (HCV) is transmitted parenterally although there is a low rate of sexual and vertical transmission, which is more likely to occur within the setting of HIV/HCV co- infection. The majority (60–70%) develop chronic infection. As with HBV infection, cirrhosis and liver cancer ensue in 20% or more over the next 10–50 years.

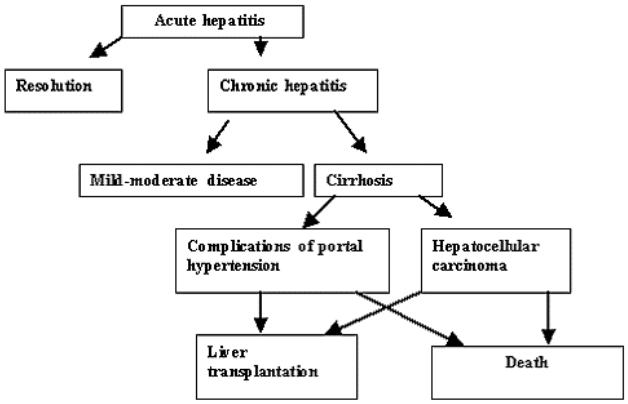

Fig 4: Flow chart of Hepatitis

Clinical features

Symptoms of hepatitis are fatigue, flu like symptoms, dark urine, pale stool, abdominal pain, loss of appetite, yellow skin and eyes, weight loss, anorexia and difficulty in concentration. Severe hepatitis may be associated with encephalopathy, increasing jaundice and prolongation of the prothrombin time.

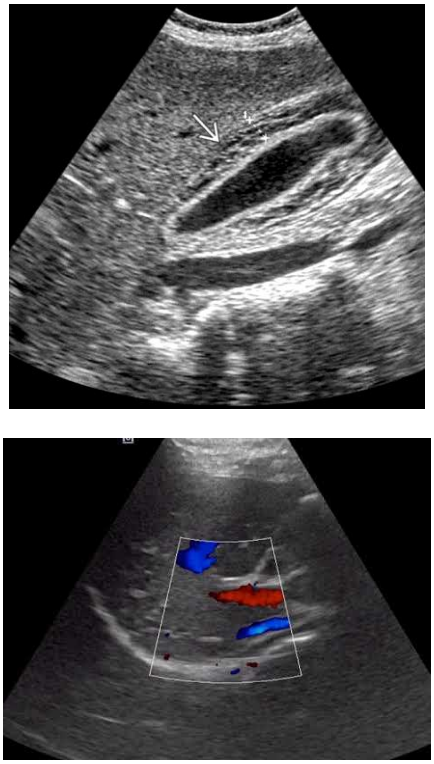

Fig 5: Ultrasound finding of hepatitis

Cirrhosis of the liver

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injur, that leads to portal hypertension and end stage liver disease. Recent advances in the understanding of the natural history and pathophysiology of cirrhosis, and in treatment of its complications, resulting in improved management, quality of life and life expectancy of cirrhotic patients [16, 17].

Etiology

Cirrhosis of the liver causes are any cause of chronic hepatitis, alcohol, primary biliary cirrhosis, primary sclerosing cholangitis, secondary biliary cirrhosis (stone, strictures), haemochromatosis, wilson's disease, alpha 1 antitrypsin deficiency.

Pathophysiology

Fibrosis describes encapsulation or replacement of injured tissue by a collagenous scar. Liver fibrosis results from the perpetuation of the normal wound healing response resulting in an abnormal continuation of fibrogenesis (connective tissue production and deposition). Fibrosis progresses at variable rates depending on the cause of liver disease, environmental and host factors. Cirrhosis is an advanced stage of liver fibrosis that is accompanied by distortion of the hepatic vasculature. It leads to shunting of the portal and arterial blood supply directly into the hepatic outflow (central veins), compromising exchange between hepatic sinusoids and the adjacent liver parenchyma, i.e., hepatocytes. The hepatic sinusoids are lined by fenestrated endothelia which rest on a sheet of permeable connective tissue (the space of Disse) which contains hepatic stellate cells (HSC) and some mononuclear cells. The other side of the space of Disse is lined by hepatocytes which execute most of the known liver functions. In cirrhosis the space of Disse is filled with scar tissue and endothelial fenestrations are lost, a process termed sinusoidal capillarization. Histologically, cirrhosis is characterized by vascularized fibrotic septa that link portal tracts with each other and with central veins, leading to hepatocyte islands that are surrounded by fibrotic septa and which are devoid of a central vein . The major clinical consequences of cirrhosis are impaired hepatocyte (liver) function, an increased intrahepatic resistance (portal hypertension) and the development of hepatocellular carcinoma (HCC). The general circulatory abnormalities in cirrhosis (splanchnic vasodilation, vasoconstriction and hypoperfusion of kidneys, water and salt retention, increased cardiac output) are intimately linked to the hepatic vascular alterations and the resulting portal hypertension. Cirrhosis and its associated vascular distortion are traditionally considered to be irreversible but recent data suggest that cirrhosis regression or even reversal is possible [18].

Clinical features

Cirrhosis of the liver symptoms are weakness, fatigue, muscle cramps, weight loss, anorexia, nausea, vomiting, upper abdominal discomfort, gaseous abdominal distension, hepatomegaly, jaundice, ascities, spider telangiectasia, palmar erythema, cyanosis, loss of llibido, hair loss, bruises, purpura, epistaxis, menorrhagia, splenomegaly, collateral vessels, variceal bleeding, fetor hepaticus, pigmentation, digital clubbing, low grade fever. In endocrine changes in men are gynaecomastia, testicular atrophy, impotence and for females are breast atrophy, irregular menses, amenorrhoea.

Investigation

Ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI) are not sensitive to detect cirrhosis, and final diagnosis still relies on histology. However, their specificity is high when an obvious cause is present and imaging reveals an inhomogeous hepatic texture or surface, rarefied hepatic central vein, an enlarged caudate lobe, splenomegaly or collateral veins. Ultrasonography and Doppler ultrasonography of portal and central vein diameters and velocities are useful screening tests for portal hypertension and vessel patency. *Contrast ultrasonography examines* the appearance of echogenic microbubbles in the hepatic vein. *Elasticity measurement* (Fibroscan) is a promising technique based on the velocity of an elastic wave via an intercostally placed transmitter. Liver biopsy is considered the gold standard for diagnosis of cirrhosis, and sequential histological *grading* of inflammation and *staging* of fibrosis can assess risk of progression. A liver biopsy is obtained by either a (radiographically guided) percutaneous, a transjugular or laparoscopical route. A greater risk of bleeding following a biopsy has been observed with larger diameter needles.

Complications

Cirrhosis of liver complications is variceal bleeding, ascities and renal failure.

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