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LIVER DISEASES-AN OVERVIEW

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ABSTRACT

Liver disease is the major cause of death every year. Approximately 29 million people suffer from a chronic liver condition (Blachier M, *et al*, 2013[1]) and more than 30 million Americans have liver diseases (American liver foundation, 2017[2]). Liver diseases is the fifth big killer in England after cancer, stroke and respiratory disease. The most common causes of liver disease worldwide are chronic hepatitis B and C, alcohol and non alcoholic steatohepatitis associated with obesity and metabolic syndrome (HEPAMAP, 2007[3]). Around 10 lakh patients of liver cirrhosis are newly diagnosed every year in India. Liver disease is the tenth most common cause of death in India as per the World Health Organization. Liver disease affect every one in five Indians. Liver disease kills more people than diabetes and road deaths. Liver diseases does not usually cause any obvious signs or symptoms until it's fairly advanced and the liver is damaged. A number of liver function test are available to test the proper function of the liver.

KEYWORDS: Liver, Hepatitis, Liver Cirrhosis.

INTRODUCTION

Liver is the second largest organ in human body, more than 5,000 separate bodily functions including helping blood to clot, cleansing the blood of toxins to converting food into nutrients to control hormone levels, fighting infections and illness, regenerating back after injury and metabolizing cholesterol, glucose, iron and controlling their levels. Most people never give their liver a thought until something goes wrong, yet, liver diseases on rise, affecting one in ten. Liver diseases can be inherited or caused by a variety of factors that damage the liver**.** In fact, there are many types of liver diseases that can be caused by a virus, damage from drugs or chemicals, obesity, diabetes or an attack from own immune system, when the condition is

left untreated, it can become life threatening and can permanently damage the liver or the bile duct. This damage leads to malignancy and cause liver cancer.

Liver Diseases

Numerous liver diseases are accompanied by jaundice caused by augmented levels of bilirubin in the body. Bilirubin is the result of degradation of hemoglobin of dead red blood cells which are normally removed by the liver and excreted via bile. In hepatitis, inflammation of the liver, is caused by different viruses, but also some toxic substances, autoimmune diseases and inherited conditions; Liver cirrhosis is the formation of fibrous tissue in the liver to kill hepatocytes, respectively. Liver cell death can be caused by viral hepatitis, alcohol poisoning or other toxic substances; Hemochromatosis is an inherited disorder that causes iron accumulation in the body, leading to long-term liver damage; Benign tumors such as adenoma, "angioma" focal nodular hyperplasia. Liver cancer as the primary tumor or carcinoma cholangiocarcinoma or metastasis of cancer to other parts of the digestive system; Wilson disease is an inherited disorder that causes copper accumulation in the body; Primary sclerosing cholangitis, an inflammatory autoimmune disease carries bile; Primary biliary cirrhosis, autoimmune disease of minute rage ducts; Budd-Chiari syndrome or hepatic vein obstruction; Gilbert's syndrome, a genetic disorder of bilirubin metabolism. There are also many pediatric liver diseases. Proper liver function can be verified by a number of specialized clinical studies, which measure the presence or absence of typical enzymes, metabolites or substances associated with the regular activities.

Acute Liver Failure (Julie Polson *et al*., 2005[4])

Acute liver failure occurs when your liver rapidly loses its ability to function. More commonly, liver failure develops slowly over the course of years. But acute liver failure, develops in a matter of days. Acute liver failure can cause many complications, including excessive bleeding and increasing pressure in the brain. Another term for acute liver failure is fulminant hepatic failure. Acute liver failure is a medical emergency that requires hospitalization. Some causes of acute liver failure can be reversed with treatment. But in other situations, a liver transplant may be the only cure for acute liver failure.

Hepatitis (Dienstag JL, 2008[5])

Hepatitis is swelling and inflammation of the liver. The term is often used to refer to a viral infection of the liver. Hepatitis can be caused by immune cells in the body attacking the liver and causing autoimmune hepatitis, infections from viruses (such as Hepatitis A, B,C, D and

E), bacteria or parasites, liver damage from alcohol, poisonous mushrooms or other poisons, medications such as an overdose of acetaminophen, which can be deadly, Liver disease can also be caused by inherited disorders such as cystic fibrosis or hemochromatosis, a condition that involves having too much iron in our body (the excess iron deposits in the liver). Other causes include Wilson's disease (excess copper deposits in the body). The symptoms of hepatitis include: Abdominal pain or distention, breast development in males, dark urine, pale or clay colored stools, fatigue, usually low-grade fever, general itching, jaundice (yellowing of the skin and eyes), loss of appetite, nausea, vomiting and weight loss.

Hepatitis A

Hepatitis A is an inflammation (irritation and swelling) of the liver from the hepatitis A virus. The hepatitis A virus is found mostly in the stools and blood of an infected person about 15 - 45 days before symptoms occur and during the first week of illness. Symptoms will usually show up 2 - 6 weeks after being exposed to the hepatitis A virus. They are usually mild, but may last for up to several months, especially in adults. Dark urine, fatigue, itching, loss of appetite, low-grade fever, nausea, vomiting, anorexia, malaise(Koff RS,1998[6] & Elisabetta Franco, Cristina Meleleo *et al*, 2012[7]), pale or clay-colored stools and yellow skin.

Hepatitis B

Hepatitis B is an irritation and swelling (inflammation) of the liver due to infection with the hepatitis B virus (HBV). Hepatitis B spread by contact with the blood or body fluids (such as semen, vaginal fluids, and saliva) of a person who has the virus. Symptoms of hepatitis B may not appear for up to 6 months after the time of infection. Early symptoms include loss of appetite, fatigue, low fever, muscle and joint aches, nausea and vomiting, jaundice, dark urine right upper quadrant pain and hepatomegaly (Lee W, 1997[8]).

Hepatitis C

Hepatitis C is a viral disease that leads to swelling (inflammation) of the liver. Hepatitis C infection is caused by the hepatitis C virus (HCV). Hepatitis C spreads by contact with the blood of someone who has hepatitis C. The following symptoms may occur with hepatitis C infection like pain in the right upper abdomen, abdominal swelling due to fluid (ascites), clay-colored or pale stools, dark urine, fatigue, fever, itching, jaundice, loss of appetite, nausea and vomiting.

Delta Agent (Hepatitis D)

Delta agent is a type of virus called hepatitis D. It causes symptoms only in people who also have a hepatitis B infection. Hepatitis D virus (HDV) is found only in people who carry the hepatitis B virus. HDV may make a recent (acute) hepatitis B infection or an existing long-term (chronic) hepatitis B liver disease which is worse. It can even cause symptoms in people who carry hepatitis B virus but who never had symptoms. Risk factors include abusing intravenous (IV) or injection drugs, being infected while pregnant (the mother can pass the virus to the baby), carrying the hepatitis B virus, men having sexual intercourse with other men, receiving many blood transfusions. Symptoms may include abdominal pain, dark-colored urine, fatigue, jaundice, joint pain, loss of appetite, nausea and vomiting.

Hepatitis E

Hepatitis E is inflammation of the liver caused by infection with hepatitis E virus. It is one of five known human hepatitis viruses. A,B,C,D and E. Heapatitis E Virus is a positive –sense, single stranded non enveloped RNA icosahedral virus. HEV is predominantly transmitted by faecal contamination of drinking water as a result of poor sanitation.(WHO. Hep. E Fact Sheet. 2017[9] & Khuroo MS & Khuroo NS *et al*, 2016[10]) other routes of transmission include consumption of contaminated food, such as raw or undercooked meat (eg: pork and shellfish) derived from infected animals (Coloson P, Borentain P *et al*. 2010[11], Lewis Hc, Wichmann O et al, 2010[12], Li TC, Chijiwa K *et al*. 2005[13] & Berto A, Martelli F *et al*, 2012[14]). and through transfusion of infected blood products which is more common in highly endemic areas. (Khuro MS, Kamili S *et al*, 2004[15]). Symptoms may include jaundice, malaise, anorexia nausea, vomiting, abdominal pain, hepatomegaly, pruritis and arthralgia.

Alagille Syndrome (Kamath BM *et al*., 2007[16])

Alagille syndrome is sometimes an autosomal dominant disorder, meaning a person inherits it from one parent who has the disorder. In other cases, a gene mutation develops spontaneously, meaning neither parent carries a copy of the mutated gene. A child who has a parent with Alagille syndrome has a 50 percent chance of developing the disorder. Most people with Alagille syndrome have a mutation or defect, in the *Jagged1 (JAG1)* gene. Mutations in the NOTCH2 gene are seen in less than 1 percent of people with Alagille syndrome. Infants with Alagille syndrome may have symptoms of liver disease and poor bile drainage from the liver in the first few weeks. These symptoms can also occur in children and adults with Alagille syndrome.

Alcohol-Related Liver Disease (O'Shea RS *et al*., 2010[17] & Choi G *et al*., 2012[18])

Alcohol can damage or destroy liver cells. The liver breaks down alcohol so it can be removed from body. Liver can become injured or seriously damaged if drink more alcohol than it can process. There are three main types of alcohol-related liver disease: fatty liver disease, alcoholic hepatitis and alcoholic cirrhosis. Many heavy drinkers will progress from fatty liver disease to alcoholic hepatitis to alcoholic cirrhosis over time. However, some heavy drinkers may develop cirrhosis without having alcoholic hepatitis first. Others may have alcoholic hepatitis but never have symptoms.

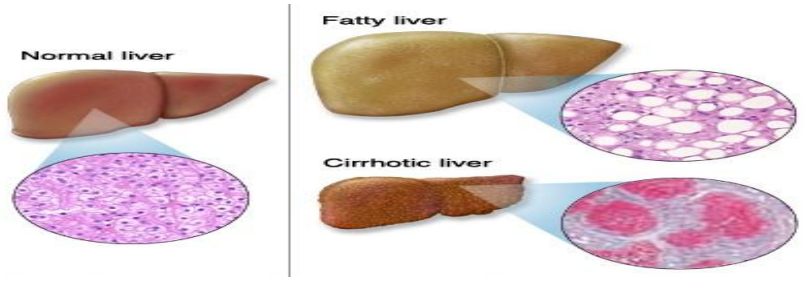

Figure. 1: Normal liver and Alcohol affected liver.

Fatty Liver

Fatty liver disease is the build up of extra fat in liver cells. It is the earliest stage of alcohol-related liver disease. There are usually no symptoms. If symptoms do occur, they may include fatigue, weakness, and weight loss. Almost all heavy drinkers have fatty liver disease. However, if they stop drinking, fatty liver disease will usually go away.

Alcoholic Hepatitis

Alcoholic hepatitis causes the liver to swell and become damaged. Symptoms may include loss of appetite, nausea, vomiting, abdominal pain, fever and jaundice. Up to 35 percent of heavy drinkers develop alcoholic hepatitis. Alcoholic hepatitis can be mild or severe. If it is mild, liver damage may be reversed. If it is severe, it may occur suddenly and quickly lead to serious complications including liver failure and death.

Alcoholic Cirrhosis

Alcoholic cirrhosis is the scarring of the liver (hard scar tissue replaces soft healthy tissue). It is the most serious type of alcohol-related liver disease. Symptoms of cirrhosis are similar to those of alcoholic hepatitis. Between 10 to 20 percent of heavy drinkers affect by cirrhosis. The damage from cirrhosis cannot be reversed and can cause liver failure. Stoping alcohol consumption can help to prevent further damage.

Enlarged Liver (Ferri FF, 2012[19] & Goldman L *et al*., 2012[20])

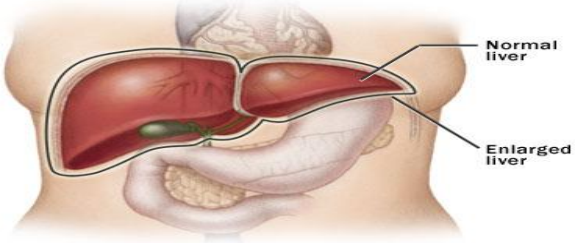

Figure. 2: Enlarged liver.

An enlarged liver is one that's bigger than normal. The liver is a large, football-shaped organ found in the upper right portion of abdomen. The medical term for enlarged liver is hepatomegaly (hep-uh-to-MEG-uh-le). Enlarged liver isn't a disease. It's a sign of an underlying problem, such as liver disease, congestive heart failure or cancer. Treatment for enlarged liver involves identifying and controlling the underlying cause of the condition. Many diseases and conditions can cause an enlarged liver, including: Liver diseases, Cirrhosis, Hepatitis caused by a virus (including hepatitis A, B and C) or caused by infectious mononucleosis, Non alcoholic fatty liver disease, Alcoholic fatty liver disease, amyloidosis (a disorder that causes abnormal protein to accumulate in liver), Wilson's disease (a disorder that causes copper to accumulate in liver), hemochromatosis (a disorder that causes iron to accumulate in liver), Gaucher's disease (a disorder that causes fatty substances to accumulate in liver), liver cysts (Fluid-filled pockets in the liver), Noncancerous liver tumors, including hemangioma and adenoma, Obstruction of the gallbladder or bile ducts and toxic hepatitis.

Alpha-1 Antitrypsin Deficiency (Czaja AJ, 1998[21])

Alpha-1 antitrypsin deficiency (Alpha-1) is a hereditary genetic disorder which may lead to the development of lung and/or liver disease. It is the most common genetic cause of liver disease in children. Adults can also be affected by Alpha-1 and may develop lung conditions such as emphysema as well as liver problems. Fortunately, many persons diagnosed with Alpha-1 never develop any of the associated diseases.

Budd-Chiari Syndrome (Eldon A. Shaffer, 2007[22])

Budd-Chiari syndrome is caused by blood clots that completely or partially block the large veins that carry blood from the liver (hepatic veins) into the inferior venacava. Usually, the cause is a disorder that makes blood more likely to clot, such as excess red cells (polycythemia), sickle cell disease, inflammatory bowel disease and connective tissue disorders.

Gilbert's Syndrome (Claridge LC *et al*., 2011[23]): Gilbert's syndrome is a common, mild liver condition in which the liver doesn't properly process a substance called bilirubin. Bilirubin is produced by the breakdown of red blood cells. Gilbert's (zheel-BAYRZ) syndrome typically is harmless and doesn't require treatment. Gilbert's syndrome is caused by an inherited gene mutation. Person born with Gilbert's syndrome, may often goes undiscovered for many years. Gilbert's syndrome is often discovered by accident, such as a person have a blood test that shows elevated bilirubin levels. Gilbert's syndrome is also known as constitutional hepatic dysfunction and familiar non hemolytic jaundice.

Liver-Hemangioma (Assy N *et al*., 2009[24])

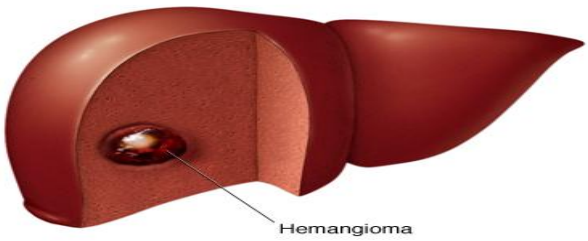

Figure. 3: Liver Hemangioma.

Liver hemangioma (he-man-jee-O-muh) is a noncancerous (benign) mass that occurs in the liver. Liver hemangioma is made up of a tangle of blood vessels. Most cases of liver hemangioma are discovered during a test or procedure for some other condition. Most people who have a liver hemangioma never experience signs and symptoms and don't need treatment. There's no evidence that an untreated liver hemangioma can lead to liver cancer.

Nonalcoholic Steatohepatitis (American Liver Foundation, 2006[25])

Nonalcoholic steatohepatitis or NASH is a common, often “silent” liver disease. It resembles alcoholic liver disease, but occurs in people who drink little or no alcohol. The major feature of NASH is fat in the liver, along with inflammation and damage. Most people with NASH feel well and are not aware that they have a liver problem. Nevertheless, NASH can be severe and can lead to cirrhosis, in which the liver is permanently damaged and scarred and no longer able to work properly. Although having fat in the liver is not normal, by itself it probably causes little harm or permanent damage. If fat is suspected based on blood test results or scans of the liver, this problem is called nonalcoholic fatty liver disease (NAFLD). If liver biopsy is performed in this case reports will show that some people have NASH while others have simple fatty liver.

Portal Hypertension (Steven K. Herrine, 2012[26])

Portal hypertension is abnormally high blood pressure in the portal vein (the large vein that brings blood from the intestine to the liver) and its branches. Cirrhosis (scarring that distorts the structure of the liver and impairs its function) is the most common cause in Western countries. Portal hypertension can lead to a swollen abdomen, abdominal discomfort, confusion, and bleeding in the digestive tract.

Hepatic Encephalopathy: Hepatic encephalopathy (portosystemic encephalopathy, liver encephalopathy or hepatic coma) is deterioration of brain function that occurs because toxic substances normally removed by the liver build up in the blood and reach the brain. Hepatic encephalopathy may be triggered by bleeding in the digestive tract, an infection, failure to take drugs as prescribed, or another stress in people who have a long-standing (chronic) liver disorder. People become confused, disoriented, drowsy with changes in personality, behavior, and mood.

Ascites: Ascites is the accumulation of protein-containing (ascitic) fluid within the abdomen. Many disorders can cause ascites, but cirrhosis is the most common. If large amount of fluid accumulates, the abdomen becomes very large, sometimes making people lose their appetite and feel short of breath and uncomfortable. Analysis of the fluid can help to determine the cause. Usually, a low-sodium diet and diuretics can help to eliminate excess fluid. The symptoms may include sudden weight gain, distended abdomen, abdominal pain, heart burn, nausea and vomiting.

Cholestasis: Cholestasis is reduction or stoppage of bile flow. Disorders of the liver, bile duct or pancreas can cause cholestasis. The symptoms of cholestatis is like skin and sclera of the eyes look yellow, itching of skin, dark coloured urine, light-coloured and foul smelling stool. With cholestasis, the flow of bile (the digestive fluid produced by the liver) is impaired at some point between the liver cells (which produce bile) and the duodenum (the first segment of the small intestine). When bile flow is stopped, the pigment bilirubin (a waste product formed when old or damaged red blood cells are broken down) escapes into the bloodstream and accumulates. Normally, bilirubin binds with bile in the liver, moves through the bile ducts into the digestive tract and it is eliminated from the body via stool.

Jaundice: In jaundice, the skin and sclera of the eyes look yellow. Jaundice occurs when there is too much bilirubin (a yellow pigment) in the blood (a condition called

hyperbilirubinemia). Bilirubin is formed when hemoglobin (the part of red blood cells that carries oxygen) is broken down as part of the normal process of recycling old or damaged red blood cells. These symptoms may include nausea, vomiting, abdominal pain, and small spider like blood vessels that are visible in the skin (spider angiomas). Men may have enlarged breasts, shrunken testes, and pubic hair that grows as it does in women.

Primary Sclerosing Cholangitis (PSC): PSC is a disease that damages and blocks bile ducts inside and outside the liver. Bile is a liquid secreted by liver. Bile ducts are tubes that carry bile out of the liver to the gallbladder and small intestine. In the intestine, bile helps in break down of fat in food. In PSC, inflammation of the bile ducts leads to scar formation and narrowing of the ducts over time. As scarring increases, the ducts become blocked. As a result, bile builds up in the liver and damages liver cells. Eventually, scar tissue can spread throughout the liver, causing cirrhosis and liver failure.

Biliary Atresia (Hartley JL *et al*., 2009[27])

Biliary atresia is a life-threatening condition in infants in which the bile ducts inside or outside the liver do not have normal openings. The two types of biliary atresia are, fetal and perinatal. Fetal biliary atresia appears while the baby is in the womb. Perinatal biliary atresia is much more common and does not become evident until 2 to 4 weeks after birth. Some infants, particularly those with the fetal form, also have birth defects in the heart, spleen or intestines. Symptoms may include weight loss, irritability, jaundice, liver may become harden and distended abdomen, pale grey stools and dark urine.

Test For Liver Diseases: A number of liver function test are available to test the proper function of the liver, (serum proteins, serum albumin, bilirubin (direct and indirect), ALT, AST, GGT, ALP, PT and PTT). Imaging tests such as transient elastography, ultrasound and magnetic resonance imaging can be used to examine the liver tissue and bile ducts. Liver biopsy can be performed to examine liver tissue to distinguish between various conditions; tests such as elastography may reduce the need for biopsy in some situations (Tapper EB, Lok AS, 2017.[28]). Liver Biomarkers as well as the related in vitro diagnostic antibodies used for diagnosis being provided.

CONCLUSION

Liver diseases can be inherited or caused by a variety of factors that damage the liver (virus, drugs or chemicals, obesity, diabetes or an attack from own immune system), when the

condition is left untreated, it can become life threatening and can permanently damage the liver or the bile duct. This damage can then become malignant. The liver disease prognosis depends on how quickly the condition was diagnosed and treated. In beginning stages, liver disease usually responds to treatment, but in advanced liver disease, the damage done by fibrosis, cirrhosis and liver failure cannot be reversed. This advanced stage leads to eventual death. While diagnosing liver disease, the condition causing the disease must be treated. If caught early, and are treated correctly, the damage to the liver may heal. In the middle stages of disease, treatment may work to help heal the damage, but as the disease progresses, treatments focus on managing the disease and prolonging the diagnosis.

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