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Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network

REVIEW ARTICLE BIOSCIENCE RESEARCH, 2021 18(3): 2460-2467. **OPEN ACCESS**

Liver Ailments and its Consequences: A review

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Liver illness is considered a big death cause in the world 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 (Jepsen and Younossi 2021). 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 affects every one in five Indians(Rawat et al. 2021). Liver disease kills more people than diabetes and road deaths. Liver diseases do 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. Liver Biomarkers as well as the related in vitro diagnostic antibodies used for diagnosis 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,

Keywords: Liver, Vital, Diseases , Syndrome

INTRODUCTION

Liver is the largest organ in human body, performing various vital functions such as 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(Qamar and Mukherjee 2021). 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(Bartneck 2021). Liver Diseases Numerous liver diseases are accompanied by jaundice caused by augmented levels of bilirubin in the body. Inflammation of the liver, is caused by different viruses, but also some toxic substances, autoimmune diseases and inherited conditions; Liver cirrhosis is the leading cause of hepatic cell death as a result of the formation of fibrotic tissue in the liver (Dong et al. 2020). Hepatocyte death can be caused due to viral hepatitis, alcohol

poisoning or other toxic agent. Hemochromatosis is a genetic disorder that results the accumulation of iron in the body, causing a long-term liver injury, initiate tumor like adenoma, "angioma" focal nodular hyperplasia(Sergi 2020).Liver cancer as the principal tumor or carcinoma cholangiocarcinoma or metastasis of cancer to other parts of the digestive system. 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(Vlăduţ et al. 2020). There are also several pediatric hepatic disorders. Normal liver function can be confirmed by a number of particular clinical trials, which measure the existence or lack of characteristic enzymes, metabolites or substances associated with the regular activities. Acute Liver Failure (Bernal et al. 2010).

Acute liver failure arises when your liver quickly loses its power to function properly. More frequently, liver failure develops gradually over the period of ages. But acute liver failure can happen in a matter of days. Acute liver failure is associated with many problems, including excessive haemorrhage and increasing pressure in the brain (Thawley 2017) ; (Anand et al. 2020). Acute liver failure is a clinically emergency that needs hospitalization(Tittarelli et al. 2017). Specific reasons of acute liver failure can be treated with treatment. But in other circumstances, a liver transplant might be the only remedy for acute liver failure(Cardoso et al. 2018).

Hepatitis

Hepatitis is inflammation and swelling of the liver. The term is mostly used to mention a viral poisoning of the liver(Nakhleh 2021). Hepatitis can be triggered by immune cells in the body attacking the liver and producing autoimmune hepatitis, (Mieli-Vergani et al. 2018), infections from viruses (such as Hepatitis A, B,C, D and E , bacteria or parasites(Calder et al. 2020), liver damage from alcohol, poisonous mushrooms or other poisons(Kamar et al. 2017) ;(Ganne-Carrié and Nahon 2019), medications such as an overdose of acetaminophen(Rotundo and Pyrsopoulos 2020), which can be lethal, Liver illness can also be initiated by inborn disorders such as cystic fibrosis or hemochromatosis, a condition that includes having high quantity of iron in the body (the excess iron deposits in the liver) (Sivakrishnan and Pharm 2019). Other reasons include Wilson's disease (excess copper deposits in the body(Gerosa et al. 2019).

The indications of hepatitis are: Abdominal pain, growth of breast in males, dark urine, pale or grey colored stools, weakness, usually low-level temperature, general itching, jaundice (yellowing of the skin and eyes), loss of appetite, nausea, vomiting and weight loss(Pikul et al. 2019) ; (Murray et al. 2018).

Hepatitis A Hepatitis A is an inflammation of the liver from the hepatitis A virus(Control and Prevention 2017). 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(Nelson et al. 2020). They are typically minor, but may proceed for up to numerous months, especially in adults(Lemon et al. 2018). 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 half an year after the time of infection. Early symptoms include fatigue, loss of appetite, low fever, muscle and joint aches, nausea and vomiting, jaundice, dark urine right upper quadrant pain and hepatomegaly (Rengabashyam 2020). 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 (Ferreira et al. 2020). Similarly in hepatitis C the above mentioned symptoms are appeared following.. 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 chronic hepatitis B liver disease which is worse(Rengabashyam 2020). It can even produce symptoms in people who carry hepatitis B virus but who never had symptoms. Risk factors consist disturbing 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 (Pajovic 2020). 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(Lhomme et al. 2020). Heapatitis E Virus is a positive –sense, single stranded non-enveloped RNA icosahedral virus. Symptoms may include jaundice, malaise, anorexia nausea,

vomiting, abdominal pain, hepatomegaly, pruritis and arthralgia. Alagille Syndrome (Sherman et al. 2020). 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 (Sadagopan 2021). 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 (Hankeova et al. 2021). 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(Ayoub and Kamath 2020).

Alcohol-Associated Liver disorder

Disease can damage or destroy liver cells. The liver breaks down alcohol so it can be removed from body (Xu et al. 2020). There are three main types of alcohol-related liver disease: fatty liver disease, alcoholic hepatitis and alcoholic cirrhosis (Gao et al. 2021). 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(Buchanan and Sinclair 2021).

Fatty liver syndrome

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 (Prasun et al. 2021). 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.

Liver enlarged

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 (Sivakrishnan and Pharm 2019). Enlarged liver is not 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 (Burra 2013) 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 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(Yeo 2015). 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 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(Ruigrok et al. 2021). 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 (Sivakrishnan and Pharm 2019)

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(Sivakrishnan and Pharm 2019). 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 (Tucker et al. 2019). 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 non-alcoholic fatty liver disease (NAFLD) (Noakes and Sboros 2021). If liver biopsy is performed in this case reports will show that some people have NASH while others have simple fatty liver.

Portal Hypertension

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(Ramirez et al. 2019); (Northrop 2017). Portal hypertension can lead to a swollen abdomen, abdominal discomfort, confusion, and bleeding in the digestive tract. Hepatic Encephalopathy:

Hepatic encephalopathy

Hepatic 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(Goh et al. 2017). 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(Fontana and Bari 2017). People become confused, disoriented, and drowsy with changes in personality, behaviour, and mood with hepatic encephalopathy (Stefanacci 2020).

Ascites

Ascites is the accumulation of protein-containing (ascitic) fluid within the abdomen. Many disorders can cause ascites, but cirrhosis is the most common(Goh et al. 2017). 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(Sivakrishnan and Pharm 2019). 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(Van Campenhout et al. 2019). 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)(Gijbels et al. 2021). 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 breakdown 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(McDaniel Kelly Marie 2017). Eventually, scar tissue can spread throughout the liver, causing cirrhosis and liver failure(Waters et al. 2017).

Biliary Atresia

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(Archer and Davies 2021). 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(Mysore et al. 2019). Symptoms may include weight loss, irritability, jaundice, liver may become harden and distended abdomen, pale grey stools and dark urine(Glöckler et al. 2018). 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)(McDaniel M Jane 2019). 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 (Silva-Sepulveda et al. 2019). Liver Biomarkers as well as the related in vitro diagnostic antibodies used for diagnosis being provided(Musaddaq et al. 2019).

CONCLUSION

Liver diseases can be hereditary or caused by a variety of other factors that harm the liver (virus, drugs or chemicals, obesity, diabetes or an attack from own immune system), when condition is left untreated, it can become life threatening and can permanently impair the liver or the bile duct. This impairment can then become malignant. The liver illness prognosis depends on how rapidly the condition was analysed and treated. During initial stages, hepatic illness generally reacts to treatment, but in advanced liver disease, the damage resulted by fibrosis, cirrhosis and liver failure cannot be recovered. Finally this advanced stage can caused 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.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEGEMENT

Present research work was supported and facilitated by, Department of Zoology, University of Malakand, Khyber Pakhtunkhwa Pakistan

AUTHOR CONTRIBUTIONS

B.A, D.NZ and THQ designed A.A, A U H performleed the experiments I.K ,IU and M I wrote the manuscript. SA, IAS and AK performed animal treatments, flow cytometry experiments, tissue collection, and data analysis. All authors read and approved the final version.

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