

Liver Diseases: Epidemiology, Prevention, and Management Strategy

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Abstract

The liver is a highly complex many cell types largest internal solid organ in the body. The most common causes of liver disease are viral hepatitis; over alcohol, fat, and toxin chemicals consumption; autoimmunity; hepatocellular carcinoma (HCC); and hereditary problems and drug reactions. More than 844 million people worldwide suffer from a chronic liver disease and more than two million people die each year worldwide due to liver disease. About two-thirds of them are men, and most of them are related to complications of cirrhosis and hepatocellular carcinoma (HCC). The burden of liver disease is increasing due to unconscious lifestyle, consumption of unhygienic foods, poor available data, limitations of resources, hepatitis, inadequate and poorly national and global fund of liver treatment, insufficient hepatologists, use of traditional medicines and herbal supplements, poverty and malnutrition, etc. This review study tries to discuss the global and regional prevalence, incidence, fatality, mortality, diagnosis, and treatment of liver disease.

Keywords: liver disease, hepatitis, cirrhosis, mortality, treatment

1. Introduction

The liver is an essential organ in the human body that performs up to 5,000 different vital functions in combination with other organs and systems, such as supporting digestion, immunity, proteins synthesis, amino acid metabolism, blood coagulation, detoxification, vitamin storage, etc. (Hettiaratchi, 2022). It has many important roles within the body; such as it helps to break down food and convert into nutrients and energy, store carbohydrates and maintaining a good balance of glucose levels in the blood, develop proteins that support muscle and immune system, metabolize drugs, and store nutrients and energy. It metabolizes drugs, xenobiotic, and endogenous hormones and waste products; and produces bile to aid digestion and as route of excretion of liver waste (Ebrahimkhani et al., 2014). It also filters toxins from the blood and removes harmful substances from it before passing to the rest of the body. It helps in clotting blood; and controls some hormones and cholesterol levels, fights against infections and illness, and metabolizes vitamin A, B, D, E, and K, albumin, glucose, iron, and bile; and controls their proper levels. It has great regenerative powers to recover injury. It is the only organ in the body that can repair itself by creating new tissue (Sivakrishnan, 2019). It controls the availability of lipophilic hormones and regulates inflammation (Hofmann & Hagey, 2008).

At present the liver disease or hepatic disease becomes a major cause of morbidity and mortality worldwide. Most of the liver diseases are intrahepatic cholestasis, alcoholic liver disease, non-alcoholic fatty liver disease, viral hepatitis, and drug induced liver injury (Saigal et al., 2019). More than 844 million people worldwide suffer from a chronic liver disease, among them about 29 million are in the European region and about 30 million are in the USA (Blachier et al., 2013). About 4.5 million (1.8%) US adults have liver disease that causes about 57,000 deaths in a year. About 2 million people die each year worldwide due to liver disease: 1 million due to complications of cirrhosis, and 1 million due to viral hepatitis and hepatocellular carcinoma (HCC) (Chen & Yoon, 2022).

When liver is infected, bilirubin level increases in the blood. Bilirubin is a yellowish pigment that is created from the result of degradation of hemoglobin of dead red blood cells. It passes through the liver and is eventually excreted out of the body via bile (Bonnett et al., 1976). Bile ducts transport bile from the liver to the upper small intestine. The increasing impact of liver diseases have created greater problem in global economy and health care resources. It becomes a cause of premature death and disability (Turner et al., 2011).

2. Literature Review

The literature review section is an introductory region of research, which shows the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). It is a scholarly portion of theses, research papers or books. It deals with a secondary research source and does not report a new or a coming research work (Gibbs, 2008).

Sanjiv Saigal and his coworkers have analyzed the clinical use of ademetonine in various etiologies of liver disease. They have also studied the premature deaths from liver decompensation, cirrhosis, and hepatocellular carcinoma (HCC) (Saigal et al., 2019). Lukas Hettiaratchi has provided a review in-depth theory concerning liver transplantations along with the rehabilitation process that entails it. He has started the study with the analysis of the anatomy, physiology and pathophysiology of liver. Then he has the post-operative physiotherapy on a patient after liver transplantation (Hettiaratchi, 2022).

Yuan-Yao Zhang and his coworkers have shown that acute-on-chronic liver failure can be classified as type A; on the basis of chronic hepatitis, type B; on the basis of compensatory cirrhosis, and type C; on the basis of decompensated cirrhosis, and non-acute-on-chronic liver failure can be further classified as chronic hepatitis with acute exacerbation, the active phase of liver cirrhosis, and liver cirrhosis-acute decompensation (Zhang & Meng, 2022).

Elliot B. Tapper and Neehar D. Parikh have found that many symptoms of liver cirrhosis, such as muscle cramps, poor-quality sleep, pruritus, and sexual dysfunction are common and treatable. They have stressed that the first-line therapies, such as carvedilol or propranolol are used to prevent variceal bleeding, lactulose for hepatic encephalopathy, combination aldosterone antagonists and loop diuretics for ascites, and terlipressin for hepatorenal syndrome (Tapper & Parikh, 2023). Haradhan Kumar Mohajan has highlighted on various liver diseases that will be helpful for the patients (Mohajan, 2024b, c, e).

3. Research Methodology of the Study

Research is an essential device to the academicians for the leading in academic world (Pandey & Pandey, 2015). Methodology is a guideline for performing good research that helps the researchers to increase the trust of the readers (Kothari, 2008). Hence, research methodology is the collection of a set of principles for organizing, planning, designing and conducting good research (Legesse, 2014). In this study, I have tried our best to maintain the reliability and validity. I have tried to maintain the ethical credibility by citing references properly both in the text and reference list (Mohajan, 2017, 2020). To prepare this article, I have taken the help from the secondary data sources. I have analyzed the journal articles, conference papers, published books and handbooks, internet, websites, etc. to prepare this paper (Mohajan, 2018, 2020).

4. Objective of the Study

Main objective of this article is to review the aspects of liver diseases. The liver plays an important role through the digestion, the metabolism of carbohydrates, fats and proteins, storage of glycogen, vitamins, and minerals, etc. (Mohajan, 2024c). Other some minor objectives of the study are as follows:

- 1) to focus on causes and symptoms of liver diseases,
- 2) to highlight on types and stages of liver diseases, and
- 3) to show the diagnoses and treatment of liver diseases.

5. Common Liver Diseases

Liver disease is an inflammation of the liver usually with enlarged liver that is caused by various viruses, some liver toxins, alcoholism, autoimmunity, drug reactions or some hereditary conditions. The inflammation could be chronic or acute. Acute inflammation is characterized by sudden and massive death of hepatocytes over a short period of time (Zhang & Meng, 2022). An increased level of bilirubin in the body with jaundice is a common symptom of many liver diseases. Some other components of inflammation are liver enlargement and tenderness with coagulopathy. On the other hand, chronic inflammation is caused by slow but long-standing injury that leads to an ongoing process of cell death and healing, and gradually progresses from minimal fibrosis to cirrhosis in 10-20 years (Bonnett et al., 1976).

The most common liver diseases are chronic hepatitis B and C, alcoholic liver disease, non-alcoholic steatohepatitis, autoimmune disease, sclerosing cholangitis, primary biliary cirrhosis, hemochromatosis, and

Wilson's disease (Mincis, & Mincis, 2006). The intrahepatic cholestasis (IHC) is characterized by the presence of jaundice with elevated serum total bilirubin, alkaline phosphatase, and gamma-glutamyl transferase (GGT) levels (Dooley et al., 2018). One problem that can develop with liver disease is portal hypertension that is happened for the increased pressure in the vein that enters the liver. If it is not treated for a long-time it can permanently damage the liver and progress to cirrhosis, liver failure, and hepatoma that are life-threatening chronic liver diseases (Sivakrishnan, 2019).

Liver cirrhosis is the formation of fibrous tissue in the liver to kill hepatocytes. Liver cancer is the primary tumor or carcinoma cholangiocarcinoma or metastasis of cancer to other parts of the digestive system (Jokelainen, 2013). Liver diseases are extremely costly in terms of human suffering, doctor and hospital visits, and premature loss of productivity. More than two million deaths happen annually worldwide due to liver disease that is 4% of all deaths worldwide (Blachier et al., 2013).

5.1 Causes of Liver Disease

Hepatitis is a syndrome and not a disease by itself. It is a generic term for inflammation of the liver. Hepatitis viruses, such as hepatitis A, B, C, D and E can infect the liver that causes inflammation and reduces its functions. These viruses can be spread through infected blood, unprotected sex, contaminated food or water, or close contact with a person who is infected, and also who exercises tattoos or body piercings, and takes fluids with sharing needles. During viral infection reactive oxygen species (ROS) are produced up to 10,000-fold and damages DNA (Iida-Ueno et al., 2017).

Autoimmune can affect liver through the development of autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis. These can lead to liver scarring (cirrhosis) and permanent liver damage if not treated. Ischemia can reduce blood supply in liver to develop hepatitis. Various antitubercular drugs, such as INH, rifampicin, pyrazinamide; antiepileptic drugs, such as phenytoin; and paracetamol overdosing, etc. can develop liver diseases. An abnormal gene inherited from parents, such as hemochromatosis, Wilson's disease, Alpha-1 antitrypsin deficiency, etc. can cause genetic liver diseases (Lee et al., 2016). Over alcohol consumption causes a build-up of acetaldehyde that induces DNA damage and oxidative stress that lead to liver injury and ultimately hepatocellular carcinoma (Mohajan, 2024a, d).

Obesity is related to a higher risk of various liver diseases, such as liver cancer due to increase of pro-inflammatory cytokines and higher levels of deoxycholic acid that damage DNA (Aleksandrova et al., 2016; Mohajan & Mohajan, 2023a-d).

5.2 Symptoms of Liver Disease

Liver disease does not always show evident signs and symptoms. However, some common symptoms are nausea, jaundice, upper abdominal pain and swelling, fluid retention, itchy skin, easy bruising, tiredness and weakness at all the times, thrombocytopenia and coagulopathy, dark urine and pale stool color, fluid retention, poor or loss of appetite, weight loss, etc. (Tripodi & Mannucci, 2011). Blood vomiting, chronic fatigue, swelling in the legs and ankles, excess bleeding in the gastrointestinal, musty-smelling breath, mild brain impairment, loss of sex drive tract, etc. are some symptoms in advanced liver diseases (Rehm et al., 2013).

5.3 Types of Liver Diseases

At present there are more than a hundred different liver diseases. Some most common liver diseases are i) hepatitis which is caused by various viruses, autoimmunity, or liver toxins (Aghemo et al., 2015), ii) fascioliasis that is caused by *Fasciola hepatica* (Mas-Coma et al., 1999), iii) alcoholic liver disease that is caused by over consumption of alcohol (Aalto et al., 2011), iv) fatty liver disease that is caused for accumulation of large amount of triglyceride, which is reversible, v) drug-induced liver disease that is caused by various drugs, vi) non-alcoholic fatty liver disease is associated with obesity and metabolic syndrome (Amir & Czaja, 2011), vii) hereditary disease that is caused for the accumulation of iron in the body, viii) Wilson's disease is a genetic disorder in which excess copper builds up in the body (Pfeiffer, 2007), ix) cirrhosis is the formation of fibrosis that causes chronic liver failure, x) Gilbert's syndrome is a genetic disorder of bilirubin metabolism (Vítek & Tiribelli, 2023), xi) primary sclerosing cholangitis (PSC) is a serious chronic inflammatory disease of the bile duct due to autoimmune (Poupon et al., 1997), xii) primary biliary cirrhosis (PBC) is a serious autoimmune disease of the bile capillaries (Trivedi, 2014), xiii) secondary sclerosing cholangitis (SSC) is an inflammatory disease that is caused by misuse of drugs, etc. (Ludwig et al., 2023).

5.4 Stages of Liver Disease

Chronic liver disease progresses roughly in four stages: i) Stage 1: Hepatitis, ii) Stage 2: Fibrosis, iii) Stage 3: Cirrhosis, and iv) Stage 4: Liver failure (Wazir et al., 2023).

Stage 1: Hepatitis shows inflammation in the liver tissues due to injury or toxicity. It is the primary cause of liver disease that affects millions of people worldwide. Both infections and healing processes are happened in this

stage. But when the injury of liver continues, the inflammation is also increasing (Desmet, 1994). Common causes of this stage of liver disease are hepatitis B and C viruses, nonalcoholic steatohepatitis (NASH), alcohol-related liver disease, and autoimmune hepatitis. Chronic hepatitis causes hyperactive healing that eventually results in fibrosis (Murray et al., 2008).

Stage 2: Liver fibrosis is the excessive accumulation of extracellular matrix proteins. It is a pathological condition characterized by excessive production and accumulation of collagen, loss of tissue architecture, and organ failure in response to uncontrolled wound healing (Trautwein et al., 2015). When the liver is inflamed for a long-time, the cells try to repair themselves by producing collagen that makes the cells in the liver stiffer (Younossi et al., 2021). Finally, collagen and other proteins make scar tissue, such as fibrosis, which is a gradual stiffening of liver that reduces blood flow through the liver (Bataller & Brenner, 2005). **Fibrosis can be reversed if it is addressed early enough.** It can spread into the liver and stops it from working properly, and reduces its access to oxygen and nutrients, and gradually declines vitality of liver. Some amount of fibrosis is reversible, damage cells can regenerate, and damage slows down enough for it to recover. Advanced liver fibrosis results in cirrhosis, liver failure, and portal hypertension and often requires liver transplantation (Trautwein et al., 2015).

Stage 3: Cirrhosis is a severe permanent scarring in the liver. When fibrosis stage is no longer reversible, cirrhosis stage starts that is a severe scarring of the liver. It is the formation of fibrous tissue in the liver to kill hepatocytes (Alukal et al., 2020). It is the end-stage of every chronic liver disease, is not only the major risk factor for the development of hepatocellular carcinoma but also a limiting factor for anticancer therapy of liver and non-hepatic malignancies (Asrani et al., 2019). It is a global health concern. It is the result of persistent liver damage over many years. Even at this stage of liver disease, **fixing the underlying condition can reverse cirrhosis** and prevent complications like liver failure (Geong et al., 2019). It is a progressive condition that worsens as more and more scar tissue develops. Too much scarring blocks the flow of blood and oxygen through the liver tissues and slows the activities of liver. In this situation there is no longer enough healthy cells left to work for regenerating. But, at this stage the damage still can be slowed or stopped (Pinter et al., 2016).

Stage 4: Liver failure begins when the liver can no longer function adequately for needs of the body. Actually, liver failure develops slowly over the course of years. This situation is called “decompensated cirrhosis” i.e., the body can no longer compensate for the losses. Acute liver failure can cause many complications, including excessive bleeding and increasing pressure in the brain (Larson et al., 2005). Chronic liver failure is a gradual process, but it eventually needs a liver transplant for the best chance of living with a good quality life. Liver cancer and liver failure can be treated through the various modern attempts, such as radiation, medication, surgery, etc. (Livingston & Durkalski-Mauldin, 2022).

5.5 Diagnoses of Liver Disease

Appropriate liver activities can be identified by a number of clinical diagnoses by the measurement of typical enzymes, metabolites, and other substances that run its activities smoothly (Singal & Mathurin, 2021). Blood tests can usually confirm the presence of liver disease. At present there are a number of liver function tests (LFTs) for the confirmation of presence of enzymes in blood, such as serum bilirubin (direct and indirect), serum proteins, serum albumin, serum globulin, alanine transaminase, aspartate transaminase, prothrombin time, partial thromboplastin time, etc. (Tapper, 2023).

Some imaging tests, such as transient elastography (TE), abdominal ultrasonography (USG) show the size and texture of the liver and other organs, such as the gall bladder, bile ducts, spleen and kidneys. Pelvic computed tomography (CT) and magnetic resonance imaging (MRI) can be used to show the condition of liver tissue and the bile ducts. These show the size, shape and texture of the infected liver. Endoscopic examination of the bile ducts (ERCP) may be necessary to confirm the diagnosis. A liver biopsy is done if there is a problem with the liver and to examine various conditions of the liver tissue (Tapper & Lok, 2017).

5.6 Treatment of Liver Disease

Liver diseases are associated with multiple common physical and psychological symptoms that can be improved with proper treatment (Tapper & Parikh, 2023). Some of the most common types of liver diseases are treatable with diet and lifestyle changes, while others may require lifelong medication to manage. Early treatment can often prevent permanent damage. Last-stage liver disease is a more complicated stage to treat (Wazir et al., 2023). At present there are effective treatments to control and support the liver. Treatment depends on the specific liver disease, and the age and condition of the patient. Treatments are medicines, special diets, surgery, exercise or lifestyle change, and liver transplantation (Ginès et al., 2021).

Anti-viral medications are available to treat some liver infections, such as hepatitis B and C (De Clercq et al., 2010). Steroid-based drugs are used to treat autoimmune hepatitis (Hirschfield & Heathcote, 2011). Wilson's disease can be managed with drugs that bind copper. Medication ursodeoxycholic acid may be given to a patient

of cholestatic liver disease (Cheng et al., 2017). If iron is overload in the blood a quantity of blood is removed regularly through the vein (Yu et al., 2021).

6. Global Health Burden

The global health sector is heavily burdened for creating the awareness, recognition and management of various liver diseases, such as acute liver failure, viral hepatitis, and alcoholic and nonalcoholic fatty liver disease (NAFLD) (Louvet & Mathurin, 2015). Every nation has stressed on reaching in the three goals: i) viral hepatitis B and C elimination, ii) increasing awareness of alcohol-associated liver disease (ALD) and non-alcoholic steatohepatitis (NASH), and iii) early screening for cirrhosis through the 90% reduction in incidence, treatment of 80% of eligible people and a 65% reduction in mortality (Sidhu et al., 2018). The WHO has stressed on the preventive policies and measures to reduce alcohol consumption, and unhealthy eating and damage (Blachier et al., 2013).

7. Conclusions

In this study, I have observed that liver diseases can be caused by viruses, toxin chemicals, drugs, over alcohol and fat consumption, etc.; and sometimes inherited that damage liver temporarily or permanently. It may happen due to autoimmune, obesity, or uncontrolled diabetes. In the early stages the disease usually responds to treatment and may be recovered completely. If it is left untreated, can permanently damage the liver, and can become life threatening. In advanced stages of liver disease, such as fibrosis, cirrhosis, and cancer; the liver damage may not be reversed. Liver diseases are very high costly in terms of human suffering, doctor and hospital visits, and premature loss of productivity. Therefore, quick and proper diagnosis and treatment may recover the damage to the liver in most of the cases.

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