

Liver Cirrhosis: Causes, Severity, and Management Strategy

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Abstract

The liver is the largest internal organ of the body. It is a vital organ that performs various important physiological functions of the body. It is a unique organ that has the ability to regenerate itself. Liver cirrhosis is the end-stage of chronic liver disease (CLD) that is characterized by organ failures, increased levels of systemic inflammation and high short-term mortality. It is an awfully heterogeneous condition of the liver that spreads from an early asymptomatic to an advanced stage with various complications that continuously damages the liver and its functions. Some common causes of liver cirrhosis are over alcohol use, non-alcoholic fatty liver disease, hepatitis virus infections, with many patients having overlapping causes. These patients have experience of muscle cramps, pruritus, poor-quality sleep, and sexual dysfunction. Liver transplantation is the only life-saving option for cirrhosis patients. This study tries to discuss the causes, complications, severity, and management techniques of this fatal disease.

Keywords: liver cirrhosis, compensated and decompensated liver disease, liver transplantation

1. Introduction

The liver is the largest internal vital organ of the body. It is located within the peritoneal cavity, and is in the right upper quadrant of the abdomen. It is wedge shaped and dark pinkish-brown peritoneal organ, in an average adult human weighs about 2kg, with an average volume in healthy adult people is $1,225 (\pm 217) \text{ cm}^3$. It is divided into right and left lobes; the right lobe being larger than the left (Juza & Pauli, 2014). It is the powerhouse of the body for metabolism and a center for numerous physiological processes. It performs various functions, such as digestion, bile production, drug metabolism, bilirubin synthesis, etc. It removes or neutralizes poisons from the blood, produces immune agents to control infection, and removes germs and bacteria from the blood (Alamri, 2018).

The word “cirrhosis” means yellowish that refers to the damaging effects of inflammation, hepatocellular injury that result fibrosis and regeneration of the liver, which indicate the end-stage of chronic liver disease associated with variceal hemorrhage, ascites, encephalopathy, jaundice, and hepatocellular carcinoma (Peng et al., 2016). The medical term “cirrhosis” was coined in 1819 by French physician, musician, and inventor of the stethoscope Rene Laennec (1781-1826) (Barnett, 2018). Liver cirrhosis (LC) is defined as the fibrotic replacement of liver tissue that is created from any chronic liver disease (CLD). It shows elements of both progression and regression, the balance is determined by the severity and persistence of the underlying disease (Ivanova, 2016). It is scarring of the liver when healthy liver cells are died to form stiff scar tissue (fibrosis). When the entire liver is scarred, it shrinks and gets hard. In this situation it is called cirrhosis, and usually this damage cannot be reversed and happens very slowly (Bansal & Friedman, 2018). Gradually, the whole liver become harden and shrunken that make it very hard for blood to flow through the liver. The disease typically develops slowly over months or years, and may be decades. It is also an expensive disease (Tsochatzis et al., 2014).

At present more than 844 million people worldwide to have a CLD, and about two million of which die every

year (Byass, 2014). Also, the liver cirrhosis and its complications as a cause of mortality are increasing worldwide. It is the 11th most common cause of deaths in the world. Liver cirrhosis patients are at a higher risk of having liver cancer that is very serious (Magder et al., 2012). In 2019, the estimated number of deaths associated with cirrhosis worldwide was 1.5 million that was associated with 2.4% of global deaths (Huang et al., 2023).

In cirrhosis, the liver becomes lumpy and stiff, and it is harder for blood to flow into the liver, and causes increased pressure in the veins flowing into the liver. It is called portal hypertension (Boike et al., 2022). When the pressure in this vein is increased, it causes a backflow of blood up into the spleen and, some of the larger blood vessels in the oesophagus become swollen and enlarged and destroys more platelets than usual that results blood clotting (Asrani et al., 2019). Alcoholic liver disease, and non-alcoholic liver disease, and hepatitis B and C are probably the major contributors of cirrhosis and liver cancer-related mortality (Rogal et al., 2020). The development of cirrhosis is associated with related complications including portal hypertension, oesophageal varices, ascites, hepatic encephalopathy and hepatocellular carcinoma (Liu et al., 2019).

Cirrhosis has a major impact on global health due to the high amount of disability-adjusted life-years (DALYs) that it generates. It is more common in men than in women (Devarbhavi et al., 2023). The DALY rates have decreased from 1990 to 2017, with the decreased values from 656.4 to 510.7 years per 100,000 people (Sepanlou et al., 2020).

2. Literature Review

In any research area, the literature review is an introductory section of research, where the seminal works of previous researchers in the same field within the existing knowledge are highlighted (Polit & Hungler, 2013). It enhances the activities of researchers through the understanding the core idea of the subject area that has been carried out before (Creswell, 2007). Detlef Schuppan and Nezam H. Afdhal have focused on diagnosis, complications, and management of cirrhosis, and have proposed for new clinical and scientific developments. They have defined the cirrhosis as the development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end-stage liver disease (Schuppan & Afdhal, 2008). Elliot B. Tapper and Neehar D. Parikh have found that about 2.2 million US adults have cirrhosis. In 2021, the annual age-adjusted mortality of cirrhosis is 21.9 per 100,000 people. The most common causes of cirrhosis in the USA are alcohol use disorder (45%), non-alcoholic fatty liver disease (26%), and hepatitis C (41%) (Tapper & Parikh, 2023).

Jae Hyun Yoon and his coauthors have noticed that alcoholic liver disease is increasing worldwide. They have aimed to investigate the changes in liver cirrhosis etiology and severity in Korea, and the national policies and systematic approaches addressing the incidence, prevention, and treatment of alcoholic liver cirrhosis that are indispensable (Yoon et al., 2021). Baiq Nadya Putri Maharani and her coworkers have studied on liver cirrhosis, which is a fibrosis or nodule formation in the liver, and they have found that it is the 11th leading cause of death in the world, and caused 1.32 million deaths in 2017 (Maharani et al., 2023).

Chiang Jin Yu and his coauthors have highlighted that liver cirrhosis is one of common causes of mortality and morbidity worldwide and remains a burden to public health that is associated risk factors among adult patients. They have discussed the severity of the liver cirrhosis, together with the presence of complications and incidence of hepatocellular carcinoma (Yu et al., 2022). Irina Ivanova has shown the clinical manifestations of cirrhosis that are related to portal hypertension, hepatic dysfunction progressing to liver failure and development of hepatocellular carcinoma, conditions with unfavorable prognosis. She has also given the modern definition of liver cirrhosis that is heterogeneous, and multi-stage condition with variable prognosis, which is considered as a dynamic, biphasic process, based on numerous clinical reports indicating the reversal of advanced fibrosis and cirrhosis after cessation of perpetual injury (Ivanova, 2016).

3. Research Methodology of the Study

Research is a logical and systematic search for new useful information on a specific topic, which investigates to find solutions of scientific and social problems through systematic analysis (Rajasekar et al., 2013). In any research it is needed collection, interpretation and refinement of data, and ultimately prepares an acceptable article, working paper, book chapter or a thesis by the appropriate use of human knowledge (Pandey & Pandey, 2015). Methodology is a guideline to complete a familiar research that helps the researchers to grow the trust of a reader in the research findings (Kothari, 2008). It is influenced by a set of philosophical principles that influence research design and decision making during the research procedure (Birks & Mills, 2015). Therefore, research methodology is the collection of a set of principles for organizing, planning, designing and conducting a good research (Legesse, 2014).

The paper is prepared on the basis of secondary data sources (Mohajan, 2020a-s). The essential and necessary data are collected from previous research articles of reputed journals, published books of world famous authors,

handbooks of renowned scholars, conference papers on recent important topics, websites, etc. In the study we have tried to maintain the reliability and validity throughout the research (Mohajan, 2017, 2018, 2020).

4. Objective of the Study

The liver is an important organ in our body, and we cannot live without it that does a lot of different jobs for the body. Liver cirrhosis begins when healthy liver cells are inflamed and damaged due to scar tissue (fibrosis) (Ivanova, 2016). It increases the risk of liver cancer. There are two stages of liver cirrhosis: compensated and decompensated (D'Amico et al., 1986). The leading objective of this article is to discuss the aspects of liver cirrhosis. Other some trivial objectives of the study are as follows:

- to focus on the symptoms and causes of cirrhosis,
- to discuss the stages of cirrhosis, and
- to highlight on management of cirrhosis.

5. Causes of Cirrhosis

The damage of the liver due to cirrhosis progresses at variable rates depend on the cause of liver disease, environmental factors, and host factors (Sherlock & Dooley, 2002). There are many causes of liver cirrhosis that can usually be identified by the patient's history combined with serological and histological investigation (Wanless et al., 2000). Two main causes are chronic hepatitis B virus (HBV), and hepatitis C virus (HCV) infections in cases with long standing, e.g., more than six months (Perz et al., 2006); and alcoholic liver disease in cases with a long-term overconsumption of alcohol (Rogal et al., 2020).

Some other causes are over build-up of fat in the liver; non-alcoholic steatohepatitis (NASH) (Stickel et al., 2017); an aspartate aminotransferase (AST): alanine aminotransferase (ALT) ratio more than 1, and absence of other causes of liver injury; primary biliary cirrhosis in cases with elevated alkaline phosphatase (Lindor et al., 2019); primary sclerosing cholangitis in cases with elevated alkaline phosphatase and compatible radiological (Friedman, 2014); and positive anti-mitochondrial antibodies; autoimmune hepatitis, Wilson's disease, α 1-antitrypsin deficiency, and haemochromatosis (Chaurasia et al., 2013). Some more causes of cirrhosis are autoimmune hepatitis, certain medications and environmental chemicals, cystic fibrosis, biliary atresia and strictures, Budd-Chiari syndrome, lysosomal acid lipase deficiency, progressive familial intrahepatic cholestasis, tyrosinaemia type 1, and type IV glycogen storage disease (Lamers et al., 2010). Usually, cirrhosis is seen more frequently among people who are overweight or obese; who have hypertension and hyperlipidaemia; who have kidney problems, diabetes mellitus or metabolic syndrome, and takes more fats-, sugar- and starch- rich fast foods (Clària et al., 2016; Mohajan & Mohajan, 2023a-e, 2024).

6. Symptoms of Cirrhosis

In the early stages of the liver cirrhosis when compensated cirrhosis starts many people face no specific symptoms. Some people commonly complain of being lethargic and easily fatigued, may notice poor sleeping at night, reduced appetite and lack of libido, and periods of women usually stop (Vitale et al., 2024). The disease is often indolent, asymptomatic, and unsuspected until sever complications of liver disease are seen. Most of the patients never come to clinical attention, and remain undiagnosed (Conn & Atterbury, 1993).

When the decompensated cirrhosis develops specific symptoms are seen. The symptoms of cirrhosis may be emerged very slowly (Mohajan, 2024q). Some early symptoms of cirrhosis are exhaustion, fatigue, weakness, frequent heartburn, poor appetite, loss of appetite, white eye, weight loss, nausea and vomiting, changes in bowel function, dark urine, swollen belly, abdominal pain, increase in abdominal size, and non-obstructive jaundice. Muscle cramps and itchiness and pruritus are common in people with cirrhosis (Williams & Sidorov, 2024). At the end-stage of liver cirrhosis variceal bleeding, ascites, edema, portal hypertensive syndrome, hepatorenal syndrome, liver dysfunction, hepatic encephalopathy, and spontaneous bacterial peritonitis are some more complications of CLD (Bosch & Garcia-Pagan, 2000).

The cirrhosis can be asymptomatic or symptomatic. As the disease progresses, more complications are developed, such as bruising and bleeding, acute kidney injury, spider angiomas that develop on the skin, cachexia and muscle wasting, palmar erythema, hemochromatosis, gynecomastia, melena, hypogonadism, gallstones development, gastrointestinal bleeding, hair and nail loss, terry's nails, etc. (Friedman & Martin, 2018).

During cirrhosis a damaged liver is less able to filter toxins from the blood, such as elevated ammonia that can enter the brain and impair neuronal function and promote generalized brain edema that cause confusion, which is called encephalopathy (Rose et al., 2020). At the early stages of encephalopathy the patients have trouble of sleeping at night but feel very sleepy during the day. Ultimately, mental functioning can be dull that may cause personality changes, coma, and even death (Moon et al., 2023).

Brain non-functioning can unresponsiveness, forgetfulness, neglect of personal appearance, trouble concentrating, or changes in sleep habits. In fact, an individual can live many years with cirrhosis without being aware that their liver is scarred due to low pressure in the portal vein and there are still enough healthy liver cells to keep up with the need of body (KASL, 2020). The women may face various complications, such as amenorrhea or irregular menstrual bleeding, and the men may face development of hypogonadism, such as impotence, infertility, loss of sexual drive, and testicular atrophy (Jagdish et al., 2021).

7. Stages of Cirrhosis

There are two main different stages of cirrhosis: compensated and decompensated. The earliest stage of cirrhosis is called compensated cirrhosis that often have little or no symptoms due to availability of enough healthy cells in the liver to do its job because of a large reserve capacity in liver function, and a person may live many years with cirrhosis without knowing it (Abralde et al., 2016). In this stage the patients often are asymptomatic, and specific treatments aimed at the underlying cause of liver disease may improve or even reverse cirrhosis (Runyon et al., 2013).

If the liver continues to be damaged, the healthy liver cells will become stressed and no longer functions well and may progress from compensated to decompensated cirrhosis that causes a rapid decline in health and will experience signs and symptoms of portal hypertension and liver failure (Ginés et al., 1987). Decompensated cirrhosis is defined by the presence of clinical evidence of major complications, such as ascites, hepatic encephalopathy, jaundice, high total bilirubin, prolonged prothrombin time, variceal bleeding, spontaneous bacterial peritonitis, hepatorenal syndrome, and portal hypertensive gastrointestinal bleeding; and have the risk of death (Ivanova, 2016). It has a poor prognosis, and the mortality rate is much higher when cirrhotic patients require hospital admission due to recurrent episodes of liver decompensation and extra-hepatic complications in developing countries (Suraweera et al., 2016). The compensated stage can be divided into two sub-stages, and the decompensated stage can be divided into three sub-stages (Cholongitas et al., 2006).

Sub-stage 1: It is fully compensated cirrhosis, where varices and ascites are absent. In this stage, the liver is heavily scarred but still can perform most functions. Some people with compensated cirrhosis exhibit few or no symptoms. Extensive scar tissue formation impairs the flow of blood through the liver, causing more liver cell death and a loss of liver function (Asrani et al., 2022).

Sub-stage 2: It is partially compensated cirrhosis, where presence of esophageal varices and absence of ascites are happened. High pressure in the veins due to cirrhosis can store of fluid in the stomach, which is called ascites. In this situation transition to decompensation happens in 12.2% patients per year (Ivanova, 2016).

Sub-stage 3: It is related to portal hypertension where bleeding of the gastrointestinal tract is seen. Once the decompensation occurred, 20% died within one year. In this situation other decompensating events, such as ascites are developed among some patients (Abralde et al., 2016).

Sub-stage 4: In this situation ascites, jaundice, and encephalopathy are seen and mortality rate increases. It is a critical threshold beyond which the chronic liver disease becomes a definite systemic disorder (Serper et al., 2023). The belly becomes very large and sudden increases in weight. The patient feels quite uncomfortable and eating becomes difficult, also finds that breathing becomes difficult (Asrani et al., 2022). This stage is marked as a critical threshold beyond which the chronic liver disease becomes a definite systemic disorder (Ivanova, 2016).

Sub-stage 5: In this situation more than one complication, such as refractory ascites, intermittent encephalopathy, acute kidney injury, and advanced liver dysfunction are seen, and severity of decompensation with mortality increases (Caraceni et al., 2018). In this stage, the liver is extensively scarred and unable to function. Various complications are seen, such as high blood pressure in the vein that leads to the liver (portal hypertension), varices (stretched and weakened blood vessels) in the esophagus (swallowing tube) and stomach, internal bleeding, ascites (fluid accumulation), and other potentially life-threatening conditions (Ripoll et al., 2007). The cirrhosis may progress to liver failure and the patients may also experience encephalopathy, a complication related to portal hypertension, and hepatocellular carcinoma (Abralde et al., 2016).

The patient may face a spectrum of disturbances in consciousness, ranging from subtle behavioral abnormalities to deep coma and death. Sometimes the renal failure in individuals with severe chronic liver disease is seen (Ripoll et al., 2007). Acute decompensation (AD) of liver cirrhosis is the rapid development of overt ascites, hepatic encephalopathy, variceal bleeding, or any combination of them. It is seen particularly in patients with bacterial or fungal infection (de Franchis et al., 2022).

8. Diagnosis of Cirrhosis

Cirrhosis is diagnosed through the physical investigations, laboratory findings, medical history, radiologic and scans, such as ultrasonography (USG), magnetic resonance imaging (MRI), computed tomography (CT) scan, and sometimes with liver biopsy (Aach et al., 1981). Hematological and biochemical tests, such as complete

blood count, serum creatinine, blood urea nitrogen, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, albumin, and prothrombin time may be performed. Ascites can be diagnosed using ultrasonography (USG) and computed tomography (CT) (Yoon et al., 2021).

Laboratory abnormalities during cirrhosis are elevated serum bilirubin, AST, ALT, elevated alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), a prolonged prothrombin time, elevated international normalized ratio (INR), hyponatremia, hypoalbuminemia, and thrombocytopenia (DeRitis et al., 1972).

9. Management of Cirrhosis

The cirrhosis damages the liver permanently and cannot be reversed, but treatment can stop or delay further progression and reduce complications. Oral medications can reduce symptoms (Salerno et al., 2008). Cirrhosis increases the risk of a cancer developing in the liver, and ultimately the liver can become so scarred and shrunk that without a liver transplant the result is death. Liver transplantation (LT) is the only curative treatment option for patients in decompensated stages of liver cirrhosis (Bruix & Sherman, 2010). Nutrition therapy for cirrhosis consists of low sodium, high protein diet. Management of liver cirrhosis is a challenging task due to limitations of resources, hepatologists, and healthcare facilities; the differences in cultural beliefs; the dependence on untested and unproven traditional medicines and herbal supplements; a lack of universal education and the awareness of diseases and their modes of transmission; and increased prevalence of underlying poverty and malnutrition (Thuluvath, 2021).

Liver cirrhosis is preventable and treatable if the people are conscious of their ways of life. The cirrhosis patients are at risk for developing liver cancer and liver failure. The cirrhosis can be managed through the eating a healthy diet, reducing salt intake, avoiding alcohol (Amodio et al., 2013). The hepatitis A and B vaccines can reduce the viral hepatitis. Eating of a healthy, low in salt, and balanced diet and regular exercise are important for maintaining strength and achieving a healthy body weight. The balanced diet must include plenty of vegetables and fruit, high-fibred grain foods, unsaturated fats, milk and milk products, eggs, low fat and protein rich fish and meat, sufficient plain water, etc. (Mohajan, 2024c-e).

10. Conclusions

The cirrhosis is advanced hardening and scarring of the liver that is caused by a long-term liver damage. It is the final stage of chronic liver disease that results in distortion of the hepatic architecture by fibrosis, and the formation of regenerative nodules. It is an important cause of morbidity and mortality in people with CLD worldwide. The CLD patients not only remain hospitalized for a prolong period of time but also die due to liver damage related various complications with a miserable condition. The cost of cirrhosis in terms of human suffering, hospital costs, and the loss of productivity is very high. Global rising of alcohol consumption, continuous feeding of fast food, slow vaccination rate of hepatitis B and C viruses, unhealthy diets, and sedentary lifestyle are the causes of expanding of cirrhosis patients. The global burden of liver cirrhosis is also increasing due to the increasing of obesity and type 2 diabetes mellitus. Early detection of the liver complexities, primary prevention, proper treatment, efficient management, and improved care can reduce the cirrhosis worldwide.

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