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Liver Cirrhosis: Understanding the Causes and Symptoms and Management

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ABSTRACT

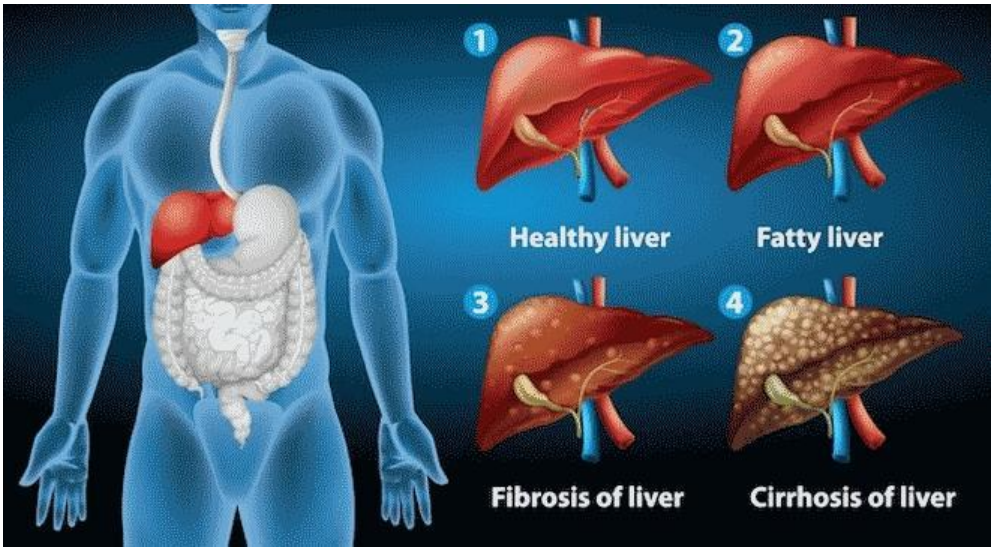
Liver cirrhosis is very common and can occur due to various causes like weight gain, metabolic dysfunction-associated steatotic liver disease, high intake of alcohol, hepatitis, immunological disease etc. Liver is a very important organ in our body, it is responsible for various function like, detoxification, bile production and metabolic regulations due to which sometimes it gets affected and that continuous damage leads to liver cirrhosis. The pathophysiology of cirrhosis include occurring of cirrhosis after a long time of inflammation which leads to development of dense connective tissue and hepatic regenerative nodules resulting in cirrhosis, as condition worsens fatigue, jaundice and abdominal swellings become evident as the stage of liver cirrhosis advances. Diagnosis of liver cirrhosis includes various test like physical test, laboratory tests, imaging studies and liver biopsy, in case the patient is in advance stage, it also include study of combination of medical history of the patient. It often leads to high mortality rate. Therapy is mainly focused on the root cause an symptoms. Management of Liver cirrhosis can be done by changing ones lifestyle, taking medication to reduce symptoms ,and in worse conditions a liver transplantation can be done. Prevention can be done by, low alcohol intake, proper vaccination hepatitis, preventing overweighting, and taking proper care of our body. In most of the cases liver cirrhosis is early detected leading to increase survival and better life. This review aims to explorer about liver cirrhosis and understanding its causes symptoms and also reviewing its prevalence and global impact by studying about its risk factor pathophysiology and how it is diagnosed and also about its management.

Key Words: *liver cirrhosis, Non alcoholic fatty liver disease(NAFLD), Hepatitis infections, Pathophysiology.*

INTRODUCTION

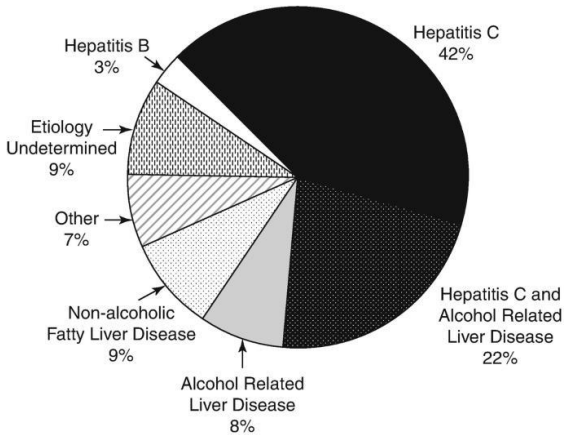
Definition of liver cirrhosis

Liver Cirrhosis or hepatic cirrhosis or end stage liver disease is a very common and can cause you to various causes like obesity non alcoholic fatty liver disease high alcohol consumption hepatitis b or C infection autoimmune disease . Cirrhosis occurs after a long time of inflammation which leads to development of fibrotic tissue and regenerative nodules resulting in portal hypertension it often leads to high mortality rate its therapy is mainly focused on the root cause and symptoms relevant transplant can be done in some cases. Fatigue, Jaundice and abdominal swelling becomes evident as the stage of liver cirrhosis advances. in extreme cases liver cirrhosis can also lead to death.



Epidemiology and prevalence of liver cirrhosis

Cirrhosis is an effective reason for the illness and death in people who are suffering from a long time liver disease globally. 2.4% of worldwide deaths in 2019 occurred because of cirrhosis. Due to increase in prevalence of corpulence and high alcohol intake from one point of view and betterment in the treatment of hepatitis B&C virus from another point of view the case controls studies and cost of illness are changing globally. The main cause for cirrhosis is the viral hepatitis infection but in many places Non alcoholic fatty liver disease and alcohol associated cirrhosis are also increasing . between 2012 to 2017 the number of death from cirrhosis increased worldwide but ASDRS decreased. However the age standardised death rate from other causes has decreased for cirrhosis but the H standardised death rate form non alcoholic Fatty liver disease has increased. It is expected that the number of deaths will increase in next century. Due to all these causes higher attempts are required to simplify upstream prevention and premature identification and prompt therapy of liver disease and to increase approach to care.[2]



Importance of understanding cirrhosis in clinical practice

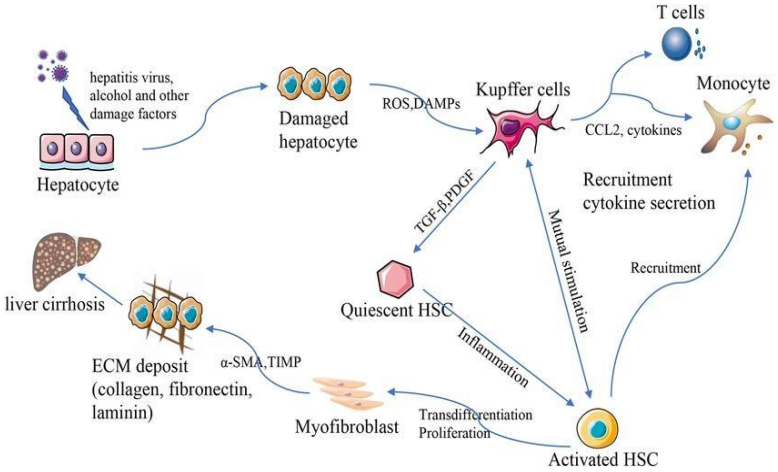
Even after development in understanding and treatment of liver cirrhosis its difficulty remain a notable worldwide health problem. Premature identification and treatment might decrease the effect of cirrhosis. On the other hand it can be very hard task for the medical professions to recognise and risk for people who are suffering from cirrhosis if they don't have enough knowledge and resources. Patients who are suffering from cirrhosis should be examined and the primary causing factors of the liver disease should be taken care of properly. Primary care provider should know all the indications and illness of cirrhosis so they could recommend medical care to the patients when required a balance between specialist and medical professionals can increase the chances of premature identification and proper treatment and management of disease. [3]

PATHOPHYSIOLOGY

Overview of liver structure and function

The liver is a very important organ in our human body and it plays an important role in many functions in our body like metabolism, vitamin storage, digestion and detoxification. In adults body weight liver contributes 2% part. The portal vein blood flow and the hepatic artery blood flow makes liver off very different organ., The various functions of liver are bile production, fat soluble vitamin storage, drug metabolism, bilirubin metabolism and other function include it's major Participation in functioning of thyroid hormone as it helps in deiodination of T4 &T3.[4]

MECHANISM OF LIVER INJURY LEADING TO CIRRHOSIS



Various cell which are involved in cirrhosis are hepatocytes and sinusoidal lining cells which include cells such as Hepatic Stellate cells(HSCs), Sinusoidal endothelial cells(SECs), &Kupffer cells (KCs). HSCs play an important role in storage of vitamin A. All these cells when open to inflammatory cytokinins, these cells get triggered and then they get converted to myofibroblasts and starts accumulating collagen on liver surface, Leading to fibrosis. Endothelial lining formed by sinusoidal endothelial cells are described by the pores they form in the wall that leads to the interchange of fluid and nutrients into cynosure voids and hepatocytes. Deportation of the sinusoidal wall can occur due to long term alcohol use and causes perisinusoidal fibrosis. . Cirrhosis pathogenesis is also caused by hepatocytes as the inflammatory mediators and reactive oxygen species released by defective hepatocytes which further leads to triggering hepatic stellate cells(HSCs) and liver fibrosis. The main cause of death and illness in people who are suffering from liver cirrhosis is occurring of portal hypertension and hyperdynamic circulation. After fibrosis, portal hypertension occurs leading to vasoregulatory changes ,Systematically and intra hepatically causing formation of collateral circulation and hyperdynamic circulation.Due to high endothelin-1(ET-1)Production and low nitric oxide production with sensitivity of its receptors cirrhosis patients it leads to high intrahepatic vasoconstriction and hindrance causing portal hypertension. **[5]**

CLINICAL MANIFESTATIONS

Common symptoms of liver cirrhosis

Most number of patients who are suffering from cirrhosis does not show any symptoms until the most critical stage, but in patients whom symptoms are visible including weakness, fatigue , low appetite leading to low food intake, frequent weight loss, jaundice, portal hypertension with ascites and peripheral edema & hepatic encephalopathy (confusion and insomnia). [6]

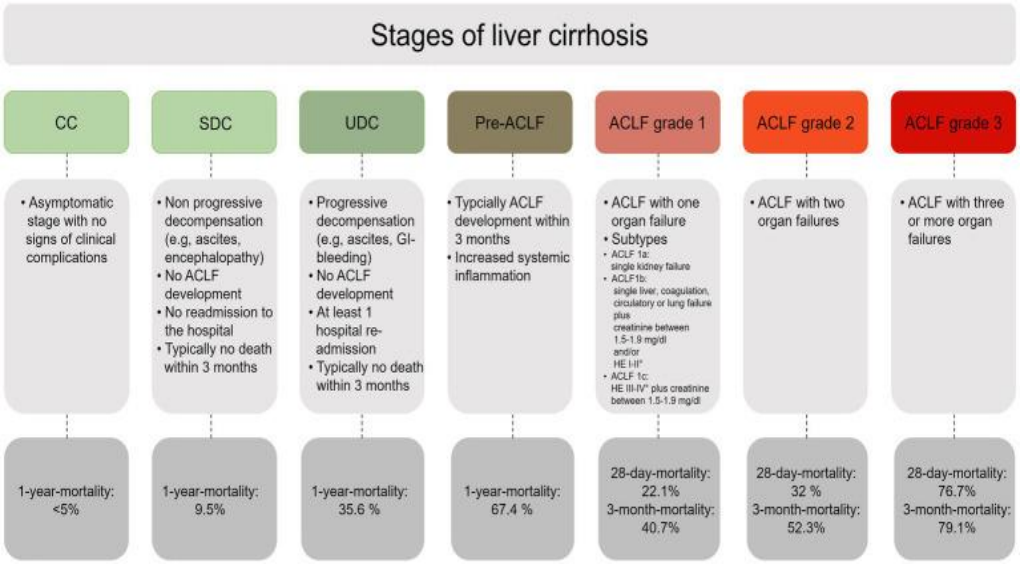
Complications of liver cirrhosis

The complications which occur mostly in cirrhosis are enlarged veins in oesophagus which can rupture or bleed, accumulation of fluid in the peritoneal cavity that leads to abdominal swelling, hepatic encephalopathy, hepatocellular carcinoma, coagulation disorder nohepatopulmonary hypertension and spontaneous bacterial peritonitis. These generally occur after portal hypertension or abnormal synthetic function, but in some cases these complications occur along with portal hypertension and abnormal synthetic function.[7]

Staging of liver cirrhosis

The different stages of liver cirrhosis include:

1. Compensated cirrhosis(CC)
2. Stable decompensated cirrhosis(SDC)
3. Unstable decompensated cirrhosis(UDC)
4. Pre-acute-on-chronic liver failure(PACLF)
5. Acute-on-chronic liver failure(ACLF) [8]



Diagnostic Approach in liver cirrhosis

Laboratory tests

1. **Liver enzyme tests-** Increased levels of Aspartate amino transferase and analine aminotransferase is checked.[9]
2. **International normalized ratio(INR) -**The ability of blood to clot is checked in this test and if it comes to be abnormal then it indicates defective liver. Studies show that if INR is done for a person who's suffering from cirrhosis then his early treatment can be done.[10]

Imaging technique

- **Ultrasound –** size, shape, abnormal tissue growth or lumps can be detected by ultrasound of liver.
- **CT scan-** C. t scan can show the fibres or blockages in biliary channels.
- **MRI –** It is done for verifying the biliary system which is part of liver.[11]

Liver biopsy

An endoscopy method that can confirm the presence of cirrhosis in a person by laparoscope, transjugular or percutaneous. [11]

MANAGEMENT STRATEGY OF LIVER CIRRHOSIS

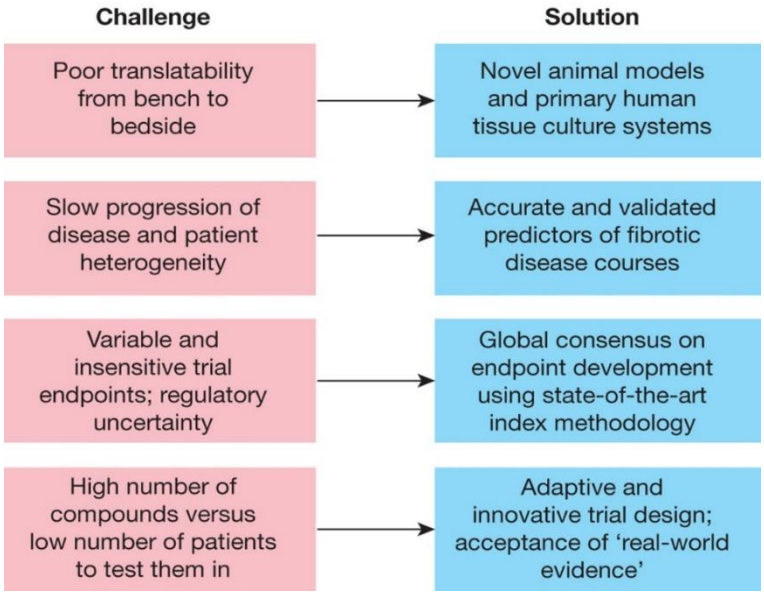
LIFESTYLE CHANGES- lifestyle changes that can reduce the risk of cirrhosis are low alcohol intake, avoid intake of drugs that can damage liver like paracetamol and if a person is suffering from obesity then he or she should reduce his or her weight to avoid liver cirrhosis . Changes in diet can also prevent cirrhosis by intake of high protein diet with calorie control and low sodium intake.[12]

Pharmacological treatment- The medications that can be used to reduce the symptoms of liver cirrhosis are diuretics and beta blockers for sleep disorders and alcohol withdrawal. For pain relief and for endoscopy surgery sedatives and aesthetics are used. Acid suppressing medications and different antimicrobial agents are also used for concomitant medical condition. Herbal and other alternative medicines are used by advanced liver cirrhosis patients and it can cause unpredicted adverse effects.[13]

Liver transplantation indication contraindication and outcomes- The 9th leading cause of liver death in world is liver cirrhosis or decompensated liver disease, so to prevent these deaths we can use liver transplant technique as it restores the normal life of a person by 15 years. It is indicated in 2 situation first the person should be suffering from acute or chronic liver disease where medical medications are of no use.

Some important indications for liver transplant are:

1. **Graft failure –** It is one of the most important indications in liver transplantation, in this hyper acute rejection occurs leading to hepatic artery thrombosis and it occurs just after post operative phase.
2. **Chronic hepatitis C-** to stop infection from occurring again because of hepatitis C after liver transplantation it is a very important to first remove hepatitis C virus from body.
3. Cystic fibrosis and glycogen storage disease are more indications for liver transplantation.



Contra indications for liver transplantation – There are 2 types of Contra indications for liver failure are :

Absolute contraindications

1. Advanced cardiac disease
2. Active use of alcohol or drug
3. Intrahepatic cholangiocarcinoma
4. Hemangiosarcoma

Relative Contraindications

1. General debility
2. Advanced age
3. Extensive portal thrombosis
4. Persistent non compilance

Recent advances and future directions in liver cirrhosis

Emerging therapies – In most of the cases usually liver transplant is seen as the most effective technique for the treatment of liver cirrhosis, But for better results and convenience of patients many emerging therapies and management strategies are being evolved.[15]Most of the problems caused in services are result of portal hypertension due to which more depths are occurring. In new healing techniques better predictions have been seen but this is a still not better. New medicines and techniques either taken or used alone or in combination, show positive action leaving a deep impact on portal hypertension and reducing effect and growth of disease, and also by decreasing fibrosis leading to reduction of cirrhosis[16].

Role of personalised medicines in treatment of liver cirrhosis

Personalised medicines play an important role in healing a patient who has liver cirrhosis by treating patient on the basis of their unique genetic an internal body features so the drug used has reduced adverse effect. Use of personalised medicines in treatment of liver cirrhosis also include all the causes that are mainly involved in causing long term liver disease worldwide[17]Like high alcohol intake ,hepatitis virus (B&C), Autoimmune disease. However the spreading of these causes may vary from country to country[18]Due to change in pharmacokinetics Drugs are often recommended in lower doses to reduce their hepatotoxic effect. Drugs that are avoided in liver cirrhosis are drugs that cause precipitated renal failure , gastrointestinal bleeding encephalopathy.

Ongoing clinical trials and research directions in liver cirrhosis

In recent times single cell genomics method has made various new achievements in treatment of cirrhosis still the priority of these researches are to find some better anti fibrotic medicines and therapies so that the treatment of cirrhosis can prevent cirrhosis at an early stage by treating fibrosis of liver. This field is going forward day by day by discovering new therapies and medicines and by calculating multiple genomes in single cells[20-22].Novel drugs used for one disease can be used for other fibrotic disease 2 due to same pathways. g rearrangement attempts can also be affected by these studies.[23]Anti fibrotic drug cocktail will mark different type of impertinent apparatus, along with a group of receptors, signalling pathways and cell types that are involved in fibrosis. These various approaches will show us a better way to the delivery of an productive antibiotic medicine and therapy in future.

Conclusion - we should not treat cirrhosis as an irreversible process of end stage liver disease like before because it is curable now due to various emerging therapies new personalized medications. By using these new medications and therapies we can early diagnosis of liver cirrhosis patients and this method can help us to reduce the morbidity and mortality caused by liver cirrhosis.

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