INTERNATIONAL JOURNAL OF HEALTH & MEDICAL RESEARCH

ISSN(print): 2833-213X, ISSN(online): 2833-2148

Volume 03 Issue 10 October 2024

DOI : 10.58806/ijhmr.2024.v3i10n03

Page No. 715-723

An Extensive Analysis of Liver Cirrhosis's Genesis, Pathophysiology, Epidemiology, And Diagnosis

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ABSTRACT: Portal hypertension and liver failure can arise as a result of liver cirrhosis, a chronic illness characterized by the fibrosis and renewal of nodules in the liver. A number of long-term conditions can lead to cirrhosis, a progressive disease. after a few years or perhaps decades. Liver cirrhosis is one public health concern. Metabolic syndrome, autoimmune diseases, storage diseases, drug use, alcohol consumption, viral hepatitis, and toxic chemicals are the usual causes. Cirrhosis is the fourteenth most prevalent cause of death in adults. placing ninth overall and fourth in Europe and the US. Because this condition is symptomatic and often remains undiagnosed in its early stages, its frequency is underestimated. It typically progresses to the decompensated stage at a rate of 5 to 7% annually. Here, we discuss the pathophysiology, epidemiology, diagnosis, and etiology of liver cirrhosis.

KEYWORDS: Liver cirrhosis; epidemiology; etiology; risk factors; pathophysiology.

INTRODUCTION

Liver fibrosis and nodule regrowth, along with the development of portal hypertension and liver failure, are characteristic of the chronic condition known as liver cirrhosis (1). A number of long-term conditions can cause cirrhosis, a disease that progresses over years or decades. It may arise from an extrinsic toxic, viral, autoimmune, or vascular origin, or from an inherent metabolic error or deposition. When abnormalities in a patient's anatomy or liver function are found, the diagnosis is typically made by clinical examination, metabolic tests, imaging, and/or histological evidence (2). This global illness is associated with other chronic illnesses such as obesity, diabetes, and heart disease (3). It affects people of all ages, genders, and races and is the cause of a high prevalence of hospital admissions, doctor visits, health expenses, and morbidity. furthermore death (4). Liver cirrhosis is a public health concern (5). Generally, it is associated with infectious diseases including viral hepatitis, alcohol consumption, metabolic syndrome, autoimmune conditions, storage diseases, and drug and toxic substance usage (6). According to reports, up to 40% of patients go for extended times without showing any symptoms; nevertheless, if a liver transplant is the definitive course of therapy, the patient's condition steadily deteriorates and eventually leads to death as the complications intensify (7). Cirrhosis has a significant financial impact on the healthcare system. Data from the US indicates that this pathology results in 150,000 hospital admissions per year and $4 billion in costs. This condition may result in a monthly cost per patient in Europe of up to 664.77 euros (8,9). Cirrhosis is the fourteenth leading cause of death in the world for adults; in Europe, it ranks fourth, and in the US, it ranks ninth. It causes 1.3 million deaths worldwide each year (10,11). The most common causes of cirrhosis in the most industrialized nations are alcohol misuse, nonalcoholic steatohepatitis, and hepatitis C virus infection. Additional factors include autoimmune diseases, Hepatitis B, primary sclerosing cholangitis, primary biliary cirrhosis, prescription drugs, and hepatitis. After a When a cirrhosis-related problem arises, less than 20% of patients survive after five years (12, 13). Hepatorenal syndrome, hepatic encephalopathy, ascites, spontaneous bacterial peritonitis infection, hepatocellular cancer, and gastrointestinal variceal bleeding are among the primary complications (14). Ascites is one of the most common cirrhosis adverse effects and has a 20% yearly mortality risk (15–17). Thirty percent of deaths within a month are caused by infections, and thirty more percent within a year. The most frequent diagnosis include urinary tract infections, skin infections, pneumonia, and spontaneously developing bacterial peritonitis (18, 19). Esophageal varices affect between 30 to 70 percent of cirrhosis patients, with a 12% annual risk of bleeding (20). Bleeding is a potentially fatal condition that results in at least 20% of deaths within six weeks (21). The emergence of hepatic encephalopathy is a serious sign of cirrhosis since it might have a fatality rate of up to 64% within a year (22). Another complication is hepatocellular carcinoma. In about 70% of cases, it is determined to be an incurable cancer (23). Without treatment, 29% of patients survive each year (24).

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THE STUDY OF EPIDEMIOLOGY

Liver cirrhosis is a chronic illness that affects people all over the world and is dispersed unevenly across both sexes and ethnicities (25). In the world, it ranks as the 14th most prevalent cause of adult mortality; in Europe, it is fourth, and in the US, it ranks ninth. Globally, it results in 1.3 million fatalities annually (26, 27). In low- and middle-income nations, it ranks as the eighth cause of mortality in World Health Organization data from 2018 (28). Because this disease is symptomatic, it is not identified in its early stages, and its prevalence is underreported. usually progresses to the decompensated stage at a rate of 5 to 7% per year (29).

PATHOPHYSIOLOGY

There are multiple causes of liver cirrhosis, but they all culminate in hepatic fibrosis, which impairs function. Stimuli can cause damage to occur more quickly or more slowly; alcohol and viral hepatitis, for instance, cause damage to occur sooner. Hepatocytes undergo progressive deterioration that results in necrosis, and extracellular fibrotic scar tissue forms to replace the parenchyma with regeneration nodules (30). It has not been feasible to determine when the fibrosis process becomes irreversible or to develop a medication that halts its growth, despite the fact that the condition is dynamic and can be reversible in its early stages (31). The activation of the hepatic stellate cell, which happens in two phases, is regarded to be the main mechanism underlying the onset of fibrosis. The first kind, called initiation or pre-inflammatory, is produced by bodies that come from endothelial stimulation, hepatocytes, platelets, Kupffer cells, oxidative stress, and cellular apoptosis. Subsequently, the perpetuation phase begins, marked by fibrogenesis, cell proliferation, and a marked inflammatory response (32).

Metalloproteinases are responsible for the extracellular matrix's breakdown.

are mostly generated by stellate cells, and when there is an imbalance between the deterioration, after which fibrosis starts to replace the fabric. The search for new treatments is motivated by the theory that the reabsorption of this excess damaged matrix could correct the liver change (33, 34).

THE CAUSE CONSUMPTION OF ALCOHOL

The liver is the primary organ affected by ethanol damage because it is where the majority of metabolism occurs. Excessive alcohol consumption is linked to three types of chronic liver disease: fibrosis, cirrhosis, steatosis (fatty liver), and steatohepatitis (35, 36). Hepatic transplantation and liver cirrhosis are among the world's most common causes of alcoholism (37). Of all the patients with the condition in the United States, forty percent were alcoholics. 20% of the drinkers who take 40-80 g/day in males and 20-40 g/day in women will develop this condition within 10 to 12 years. In addition to alcoholism, other variables that affect liver damage include genetic predisposition, gender, hepatitis B or C virus infection, and malnourishment (38, 39).

HEPATITIS C

Acute or chronic hepatitis can be caused by the infectious disease known as hepatitis C virus (HCV), which mostly affects the liver (40). According to WHO estimates from 2018, there are 150 million instances of hepatitis C virus infection worldwide, with 4 million new cases this year. Additionally, reports indicate that HCV causes 500,000 fatalities annually in Europe, Africa, and the eastern Mediterranean. being the places with larger prevalence (1.5% to 2.3%) (41,42). The prevalence in the remainder of the world is roughly 1%. HCV is spread by direct contact with tainted blood, which can occur from blood transfusions, drug injection needle use, and the use of improperly sterilised medical supplies or equipment. The two least frequent kinds are sexual transmission and mother-to-child transfer during childbirth. During an acute infection, spontaneous recovery is uncommon; 75–85% of cases will develop to chronic illness. Between 50 percent and 85 percent of instances of the virus are asymptomatic patients. Persistent cirrhosis will develop in 20 to 30 years in 20% of hepatitis C patients due to the disease's progressive nature and chronic inflammation (43). Once evolution enters the cirrhotic phase, it might go years without manifesting clinically; this is why evolution is unpredictable (44). One to six percent of people will develop hepatocellular carcinoma in a given year, and three to six percent will experience hepatic decompensation (45). Despite the lack of a vaccination to prevent HCV, the illness can be treated with direct-acting antivirals, which have a greater than 95% cure rate. In developing countries, access to treatment is still either completely absent or highly restricted due to its high cost (46).

HEPATITIS B

Anicteric hepatitis, fulminant hepatitis, and chronic diseases characterized by chronic inflammation that might progress to cirrhosis or hepatocellular carcinoma are among the ailments that can be caused by the hepatitis B virus, or HBV (47). Globally, an estimated 250 million people have a persistent HBV infection. China, Brazil, Southeast Asia, and Africa have among of the highest incidence rates of HBV, at about 10% (48). According to WHO data from 2018, there are 4 million new cases of acute HBV hepatitis detected each year, and the virus is thought to be the cause of about 1 million hepatic cirrhosis fatalities (49). Seventy to ninety percent of individuals in countries where the virus is very widespread contract it at a young age, namely in those under 40. Ninety percent of them will show signs of chronic infection if they are babies or young children under five. On the other hand, only 5% of people will have the infection for the rest of their lives. Within five years, 6% of patients with chronic hepatitis B will develop hepatocellular

carcinoma, and 15 to 30% will advance to liver cirrhosis (50). HBV can spread through direct contact with blood or bodily fluids from infected people, such as vaginal secretions, saliva, or semen. It can happen sexually, during pregnancy, vertically, or by the use of non-sterile objects (needles, syringes, surgical equipment) (51). Chronic hepatitis B can be avoided with a safe and efficient hepatitis B vaccine. Treatment for an acute HBV infection is not required. Only supportive care is given during the acute phase of the illness. Antiviral medication has been shown to improve survival in the chronic phase by halting the disease's course, lowering the risk of decompensation, and halting the development of hepatocellular carcinoma (52).

FATTY LIVER DISEASE WITHOUT ALCOHOLISM

A chronic pathology known as non-alcoholic fatty liver disease (NAFLD) comprises mild disorders ranging from simple steatosis, which has no effect on morbidity or mortality in the short term, to more serious conditions like non-alcoholic steatohepatitis, which is characterized by fat with varying degrees of fibrosis and inflammatory infiltration that, in 3-8% of cases over a 5-year period, may progress to hepatic cirrhosis (53). It is distinguished by a hepatic fat accumulation greater than 5% of the weight of the liver and the presence of cytoplasmic triglyceride droplets in the hepatocytes (54). Obesity and diabetes are linked to NAFLD. Globally, there are an estimated 1.46 billion obese adults, according to current data. Nonalcoholic steatohepatitis (NASH) affects six million people in the US, and 600,000 cases of cirrhosis are caused by this etiology (55). There isn't a recognized pharmacological treatment for NAFLD at this time. However, it is advised to alter one's lifestyle to stop its advancement (56,57).

Autoimmune disorders

Primary biliary cholangitis, primary sclerosing cholangitis, and autoimmune hepatitis together account for less than 5% of the etiologies of cirrhosis.

Autoimmune hepatitis

The histological investigation indicates that the presence of autoantibodies, hepatitis interface, and high levels of gamma globulins is suggestive of chronic liver inflammation (58). In the US and Europe, the prevalence is estimated to be between 0.1 and 1.2 instances per 100,000 persons. It accounts for about 6% of liver transplant procedures, with 80% of patients being female. It can be fatal without treatment; more than half of patients die within five years, and almost all die within ten years of the disease starting (59). The foundation of the treatment is immunosuppressive therapy with corticosteroids and azathioprine, which has been demonstrated to dramatically increase survival rates in patients with and without cirrhosis, reaching 89% and 90% survival, respectively, after 10 years of treatment (60).

PRIMARY CHOLANGITIS CAUSED BY SCLEROSING

The pathogenesis of this chronic sickness is uncertain; nevertheless, it is characterized by an inflammatory response and progressive fibrosis of the extrahepatic and intrahepatic bile ducts (61). The prevalence is 6.3 cases per 100,000 people in the US and Europe. Men older than 40 account for 70% of those impacted. After diagnosis, the typical survival period is 12 years (62). It is near related with inflammatory bowel illness, considering that between 70 and 90 percent of PSC patients had the ailment While there is no cure for liver cirrhosis, symptoms can be managed and associated consequences can be attended to. The only available therapy is liver transplantation. It has been demonstrated to increase longevity (63).

PRIMARY BILIARY CHOLANGITIS

Over time, this autoimmune liver disease worsens and often leads to cirrhosis and cholestasis. Small and medium-sized intrahepatic bile ducts exhibit pathological deterioration. It results in fibrosis and biliary excretion issues [64]. Antimitochondrial antibodies have also been demonstrated to be characteristically present. It is more common in women between the ages of four and six. The disease is developing a little more slowly (65). Within 5 to 7 years of the disease's beginning, 40 to 68% of patients will exhibit signs of tiredness and cholestasis. Patients with symptoms have a 7-year survival rate, whereas those without symptoms may have up to 16 years left after diagnosis because of cirrhosis and associated sequelae. The only treatment with the potential to be curative is liver transplantation. The primary medication used to stop the disease's progression and postpone the need for a transplant is acid ursodeoxycholic (66).

CRYPTOGENIC CIRRHOSIS

A diagnosis of exclusion of chronic liver disease, whose cause remained unknown despite completion of all clinical, laboratory, and/or histological investigations, is cryptogenic cirrhosis (67). Viral causes, alcohol, autoimmunity, medications, genetic factors or illness of the biliary tract must be excluded. The majority of cases are now understood to be caused by NAFLD. Up to 14% of liver transplants in cirrhotic patients have a cryptogenic etiology, which accounts for 3% to 31% of cases (68).

ADDITIONAL REASONS

Less than 5% of patients have other reasons, which include medications, hereditary illnesses such hemochromatosis and Wilson's disease, heart problems, and deficiencies in alpha 1 antitrypsin (69, 70).

IDENTIFICATION

Most people with liver cirrhosis do not exhibit any symptoms until the onset of the decompensated phase. Liver cirrhosis is an indiscernible illness. Clinical suspicion is most often the consequence of an incident—a physical examination stigma associated with chronic liver disease being discovered, a hepatogram being altered in a laboratory analytical control, or cirrhosis decompensation occurring during a surgical procedure (laparotomy or laparoscopy) that is recommended for another reason (71).

MEDICAL HISTORY AND EXAMINATION

Most people with liver cirrhosis don't exhibit any symptoms at all or only have nonspecific ones like asthenia, weight loss, and decreased libido, which can cause a delay in diagnosis. When a patient enters the decompensated phase, they may experience a variety of symptoms, such as jaundice, hematemesis and melena from gastrointestinal hemorrhage, ascites and hepatomegaly-related abdominal distention, mental changes in hepatic encephalopathy, hypoxemia in cases of hydrothorax or hepatopulmonary syndrome, and/or altered mental state. (18) . During the physical examination, there are several indications that should raise suspicions about the illness: asterixis, ascites, "jellyfish head" collateral abdominal circulation, telangiectasias and spider veins, palmar erythema, and nail abnormalities (nail streaks and reddening) dupuytren's contracture, gynecomastia, hepatomegaly, splenomegaly, bruising, testicular atrophy, and jaundice (69).

LAB EXAMINATIONS

Laboratory tests cannot identify liver cirrhosis because they are unable to adequately reflect how the liver operates on its own. Laboratory studies are paired with clinical and imaging examinations to arrive at a diagnosis. When suspected liver pathology is found, a complete hepatic profile encompassing blood biochemistry, including platelet count, prothrombin time, transaminases, bilirubin, alkaline phosphatase, gamma-glutamyl transferase (GGT), and albumin, should be performed (72). Serum glutamic-pyruvic transaminase (SGPT) and glutamic oxaloacetic transaminase (SGOT) levels are typically elevated in cirrhosis and suggest hepatocellular damage, while they can also be seen within normal ranges. More than one in the SGOT/SGPT ratio is a reliable indicator. of cirrhosis, with the exception of alcoholic liver disease, and the association may be inverse in more advanced stages (73). The diagnostic use of alkaline phosphatase and gamma-glutamyl transferase (GGT), two enzymes related to cholestasis, is limited. Its rise indicates primary sclerosing cholangitis or primary biliary cholangitis when other obstructive bile tract illnesses have been ruled out. When the GGT rises on its own, it can be a sign that some drugs are actively activating specific enzymes (74). Albumin is a diagnostic for hepatic synthesis failure since it is solely produced by the liver (75). The liver synthesizes a large number of coagulation factors that block the extrinsic pathway of coagulation. A change in hepatic synthesis is indicated by a prolonged prothrombin time (76). Hyponatremia is a common observation in cirrhotic patients with ascites due to the kidney's retention of water and sodium, and it is linked to a poor prognosis (77,78). It's important to remember that conditions other than liver illness may also have an impact on the results on the hepatogram Examples include alkaline phosphatase (79), bilirubin in hemolysis situa bone illnesses, and transaminases in thyroid, muscle, and heart ailments.

IMAGING RESEARCH.

No sufficiently sensitive imaging study is available to be the sole means of diagnosing cirrhosis. The techniques employed are:

DOPPLER ULTRASOUND ABDOMINAL.

This diagnostic method is recommended since it is less expensive, non-invasive, and easier to use. It has a 91.1% sensitivity and 93.5% specificity for the diagnosis of liver cirrhosis. It enables evaluation of the blood flow via the hepatic and portal veins as well as the macroscopic appearance of the liver. It can even identify ascites, and when paired with the Doppler, it can assist in recognizing portal hypertension symptoms. Nodularity, elevated echogenicity, caudate lobe enlargement, and parenchymal atrophy are among the sonographic signs of cirrhosis (80,81).

ELASTOGRAPHY OF THE LIVER.

This imaging technique allows the hardness and rigidity of tissue to be measured in relation to the sound wave's speed of propagation [82]. Using this method, it may determine the extent of fibrosis in its various stages, exhibiting an 83% association with biopsies. The sensitivity and specificity of fibrosis in stages 2 (F2) and 3 (F3) are 84.7% and 78.3%, respectively, and 92% and 81%, respectively. Additionally, it achieves a sensitivity of 91.2% and a specificity of 80% in stage F4 (advanced fibrosis) (83,84).

MAGNETIC RESONANCE AND COMPUTED TOMOGRAPHY.

When it comes to detecting early-stage fibrosis, these imaging tests are not particularly useful. They make it possible to identify morphological changes that occur later in the disease, like nodularity. ascites, varicose veins, atrophy, and caudate lobe hypertrophy. These are not the preferred approaches due to their high cost and, in the case of computed tomography, significant radiation exposure. These days, its application is restricted to the diagnosis of hepatocellular carcinoma (85, 86).

LIVER BIOPSY

It is the most reliable method for cirrhosis diagnosis. The range of its sensitivity and specificity is 80–100%. But it's an expensive, intrusive procedure with a significant chance of problems. This can result in pain, moderate to severe bleeding, sepsis, peritonitis, and/or organ perforation, with a mortality rate of about 1 in 10,000 surgeries (87). It ought to be saved for situations where the patient's therapy would be altered by the results, such as when the etiology cannot be determined and the clinical, laboratory, and radiographic findings do not result in a diagnosis. Percutaneous, laparoscopic, surgical, or transjugular methods are available for implementation (88,89).

CONCLUSION

Conducting a comprehensive prospective assessment of the clinical history and etiology of liver cirrhosis is crucial since therapy and/or removal of the stimuli can halt the progression of the illness and keep it at a compensated condition for an extended period of time, increasing its survival. We advocate for the establishment of interdisciplinary work groups for close monitoring of the pathology and early diagnostic evaluation in primary care. Since non-alcoholic steatohepatitis has become more common in recent years, it is critical to emphasize that each person must regulate their metabolic risk variables and make prompt corrections to them. prior to the onset of liver or cardiovascular problems. We think that preventative initiatives should be started at a young age and that health policies should be enhanced.

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