

Cirrhosis of the liver: etiology, diagnosis and management research papers exampl...

[Health & Medicine](#), [Alcoholism](#)



Abstract

Cirrhosis is 12th on the list of leading causes of death in the US. Cirrhosis is characterized by scarring of the liver tissue due to inflammation that could lead to liver failure and death. Some patients develop cancer in due course of the illness. The scarring, which is usually permanent, covers the outer layer with collagen, makes the liver very rigid and limits the exchange of blood between the portal vein and the liver, thereby creating excess pressure in the hepatic portal vein. The scarring renders the removal of toxin such as alcohol difficult due to depletion of hepatocytes. Cirrhosis is caused by viral infection such as hepatitis B and C, excessive alcohol consumption, autoimmune disorders and genetic predisposition. Alcoholic cirrhosis is one of the leading causes of death in the US. Cirrhosis is asymptomatic until it becomes decompensated. A combination of abstinence and pharmaceutical therapy is known to reverse effects of cirrhosis in many patients. Patients with severe cirrhosis and alcoholic liver disease with imminent liver failure would have to undergo liver transplantation. There is a dire need for more drugs with better efficacy to treat cirrhosis.

Cirrhosis is an irreversible condition of the liver where the healthy tissue is replaced gradually by scar tissue. The scarring is permanent and occurs due to heavy drinking. The scarring reduces the number of hepatocytes in the liver that are responsible for toxin filtration from the body. Cirrhosis is one of the stages of chronic liver disease that, usually, commences with a benign fatty liver condition, progressing slowly to cirrhosis and leading to liver failure or liver cancer and death. Some patients may develop cirrhosis owing

to genetic predisposition, an autoimmune disorder or non-alcoholic liver disease (Shannon, 2010).

Prevalence and risk factors of liver cirrhosis

Cirrhosis was implicated in over thirty thousand fatalities in the US in 2007. It is twelfth on the list of leading causes of death in the US. As mentioned earlier, cirrhosis could be alcohol-related, hepatitis infection-related, non-alcoholic or genetic in nature. Currently, alcoholism and hepatitis C infection are the two most common causes of cirrhosis (Starr & Raine, 2011).

Demographically, women are twice as prone to alcoholic cirrhosis with half as much alcohol consumption when compared to men due to apparent differences in the proportion of body fat (O'Shea, Dasarathy & McCullough, 2010).

Hispanic males and females seem to be genetically predisposed to develop cirrhosis nearly 1.8 and 1.4 times more, respectively, than Caucasians and Black. Within the Hispanic group, Puerto Ricans seem to be the most affected, followed by Mexicans and Cubans. Even though, cirrhosis is the 12th leading cause of death, the rate of mortality has decreased considerably in the past four decades (Shannon, 2010).

The likelihood of developing alcoholic cirrhosis is not just dependent on the amount of alcohol taken, but also on the absolute alcohol content of the drink consumed and the genetic makeup of the population under study.

Studies have shown that only 6 to 41% of the population of heavy drinkers develop cirrhosis. Beer drinkers are more prone to cirrhosis when compared to wine drinkers. Drinking during non-meal time elevates the risk of cirrhosis

by 2.7 times. Malnourished individuals are more likely to develop a quick progressing form of cirrhosis. Alcoholism, when combined with viral hepatitis, becomes a lethal combination in patients with liver dysfunction (O'Shea, Dasarathy & McCullough, 2010)

Etiology

Viral

Hepatitis C is one of the two major causes of cirrhosis in the US and worldwide, which accounts for 47% of cirrhosis-related deaths. 15% of cirrhosis-related deaths can be attributed to Hepatitis B virus worldwide (Starr & Raines, 2011). Hepatitis A and E viruses are rarely a cause of cirrhosis. Hepatitis C virus is an RNA virus that results in chronic liver disease in 80% of those infected and may lead to cirrhosis in 15% of them. If such patients are alcoholics, then the damage to the liver and the probability of cancer increases dramatically. Since there are no vaccines available for hepatitis C virus, the number of deaths due to this virus is high. Hepatitis B is vaccine-preventable and therefore is responsible for cirrhosis only in non-vaccinated individuals (Lefton, Rosa & Cohen, 2009).

Alcohol

Alcohol is the other major cause of cirrhosis in the US. Typically, patients who do not exhibit signs of apparent cause of liver infection are checked for binge drinking. To avoid liver damage from binge drinking, men are advised not to drink more than two drinks a day and women are advised not to drink more than one drink a day (Shannon, 2010). Scientists suggest that alcoholic liver damage should be measured in terms of 'pint years', where one pint-

year would equal drinking one pint of whisky every day for one year. As mentioned earlier, comorbidity of alcoholism with Hepatitis C infection would accelerate the rate of disease progression (Lefton et al., 2009).

Autoimmune disease

Another etiology of cirrhosis is the development of autoimmune antibodies against the liver cells, resulting in primary biliary cirrhosis (PBC that affects young women) and primary sclerosing cholangitis (PSC that typically affects young men). Cirrhosis may also be caused by autoimmune hepatitis (Lefton et al., 2009).

Genetic factors

Cirrhosis may occur as a secondary complication in genetic diseases such as Wilson disease, hemochromatosis and α 1-antitrypsin deficiency (Starr & Raines, 2011).

Metabolic storage disease

Obesity is a metabolic storage disease that is becoming a national concern. Obesity-induced non-alcoholic fatty liver disease is a condition that leads to cirrhosis in obese children and adults (Lefton et al., 2009).

Signs and symptoms of liver cirrhosis

The earliest symptoms of cirrhosis are not apparent until substantial liver damage has occurred. The outward symptoms include vomiting, muscle wasting, fatigue, bleeding gut, abdominal bloating, abdominal swelling, jaundice, ascites, peripheral edema, spiderlike blood vessels (spider angiomas) and weight loss. A physical examination of the abdomen would

reveal a swollen spleen due to increased blood pressure in the organ and reduced blood flow through the scarred and shrunken liver. The physical attributes of the patients such as palmar fascia, palmar erythema, testicular atrophy, gynecomastia, sweet smelling breath (fetor hepaticus), sterility, painless enlargement of parotid gland may be helpful in indicating liver damage (Lefton et al., 2009). Testing of the bodily fluids is another route of diagnosis that might indicate elevated levels of aspartate transaminase and alanine transaminase that could indicate the presence of liver damage. A damaged liver will not be able to produce blood-clotting factors efficiently, which would be indicated by elevated serum prothrombin time. Increased bilirubin levels are also a certain indication of liver dysfunction (Shannon, 2010; Starr & Raine, 2011).

Pathophysiology

Cirrhosis is preceded by chronic liver inflammation and fibrosis. Fibrosis can be described as the wound healing process where the continuous inflammation from oxidative stress and production of reactive oxygen species due to alcohol consumption leads to continual healing by the body, resulting in encapsulation of the liver tissue by collagenous scar tissue (Schuppan and Afdhal, 2008). Prolonged fibrosis leads to portal vein hypertension, which creates pressure on the spleen due to lack of space for passage of blood through the scarred collagenous liver tissue (Starr & Raine, 2011). The hypertension gives cirrhotic patients a distinctly distorted liver that remodels the extracellular matrix of the hepatic sinusoids (Schuppan and Afdhal, 2008). The hypertension leads to endothelial dysfunction that

limits the release of vasodilators. The decrease in vasodilators such as nitric oxide can be attributed to the elevated scavenging that occurs due to oxidative stress created by alcohol consumption. Once inside the body, the alcohol is converted to acetaldehyde by alcohol dehydrogenase (ADH) and later into acetate by acetaldehyde dehydrogenase (ALDH). The metabolic products of alcohol metabolism are toxic and create an imbalance between the numbers of antioxidants and free radicals, thereby causing oxidative stress (Schuppan and Afdhal, 2008). The intrahepatic resistance to blood flow results in splanchnic vasodilation and aggravates the existing portal hypertension. End-stage cirrhotic patients display intense splanchnic vasodilation that causes hypoperfusion of the kidneys, increased salt and water retention in the body and elevated cardiac output to compensate. These conditions lead to ascites, mismatch in pulmonary ventilation/perfusion, hepato-renal syndrome and arterial hypoxemia. Sinusoid capillarization is a certain indication of imminent liver failure (Tsochatzis, Bosch & Burroughs, 2014).

Diagnosis

Imaging techniques

Imaging techniques such as ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI) are some of the non-invasive diagnostic methods for detection of cirrhosis. Ultrasonography can help determine portal vein hypertension, nodular liver, hepatic tissue inhomogeneity, caudate lobe enlargement and liver distortion.

Ultrasonography with contrast can help in identifying fibrosis. CT and MRI

when used with contrast can help identify and locate lesions within the liver and nodularity (Schuppan and Afdhal, 2008).

Liver biopsy

Even though, some scientists consider liver biopsy as the gold standard in establishing the diagnosis, it is contraindicated when the diagnosing has confirmed cirrhosis. However, a transcutaneous liver tissue biopsy is warranted when the liver damage is a result of an unknown cause where the extent of liver damage is not assessable through imaging or blood tests. Risks associated with any route of biopsy, namely, laparoscopic, transjugular and percutaneous, is profuse bleeding (Schuppan and Afdhal, 2008).

Physical checkup

Abdominal examinations are not conclusive tests for determining liver damage. Liver rigidity might be revealed when the liver does not surface when palpated (O'Shea et al., 2010).

Prognosis

There are five stages of cirrhosis. Stage 1 is the least life threatening that has a mortality rate of 1% and is characterized by compensated liver and absence of esophageal varices. Compensated liver and presence of esophageal varices characterize stage 2 cirrhosis, which has a mortality rate of 3. 4%. When the liver becomes decompensated and develops ascites, the cirrhosis is called as stage 3 cirrhosis that has a mortality rate of 20%. Stage 4 cirrhosis is marked by decompensated liver and bleeding in the gastrointestinal walls, which has a mortality rate of 57%. A stage 5 cirrhosis

is characterized by kidney failure and infection. Studies show that stage 5 cirrhosis has mortality rate of 67%. These stages indicate the survival rates and help in determining the need for organ transplantation in patients (Tsochatzis et al., 2014).

Management of liver cirrhosis

Treatment of cirrhosis involves management of each symptoms that make up the condition of cirrhosis. For example, ascites is treated through low sodium diet, diuretics and transjugular intrahepatic porto-systemic shunt (TIPSS). Kidney dysfunction is treated by rehydration, albumin infusion and avoiding diuretics. Encephalopathy is managed by treating bacterial and viral infections, introducing high protein diet, treating internal bleeding and treating electrolyte imbalance (Schuppan and Afdhal, 2008).

Abstinence

Abstinence from alcohol has shown to be effective in stopping the progression of liver damage. In patients with alcoholic cirrhosis, significant improvement in liver architecture and survival has been observed irrespective of their stage. Portal vein hypertension alleviates and a slight reversal in cirrhosis could be observed. Studies show that 66% of the patients showed improvements in three months. Alcoholism being an addiction requires counseling and support to prevent relapse. Medications such as naltrexone, acamprosate, nalmefene and baclofen are prescribed to help the patient sustain abstinence (O'Shea et al., 2010).

Nutrition and diet

Prognosis of cirrhotic patients is affected by insufficient protein in the body. Enteral nutritional supplements in combination with regular oral supplements has shown improvement in encephalopathy, liver function and Child-Pugh score in severely malnourished patients with decompensated liver. Apart from including proteins, the patients must be advised on low sodium intake (Runyon, 2013).

Pharmacological treatments

Many drugs have been studied for treatment and management of cirrhosis; however, very few have shown any promise. Vasopressin receptor antagonists are being pursued to discover possible therapeutic use. Diuretic drug such as spironolactone and a combination of furosemide and spironolactone are prescribed to reduce fluid retention in the body (Runyon, 2013).

Liver transplantation

Alcoholic cirrhosis is often viewed as a self-induced condition that warrants that the patient be sober for at least six months before they can even be considered for transplantation. Such harsh regulations have been implemented to provide transplantation organs to needy and deserving candidates due to the shortage of donor organs. Studies indicate that after receiving a new liver through organ transplantation, many receivers relapse to excessive drinking, rendering the transplantation a worthless effort. The priority for transplantation is based on Model for end-stage liver disease score (MELD) (Tsochatzis et al., 2014)

Conclusion

Cirrhosis is an irreversible condition of liver tissue scarring that could lead to liver failure and death. The scarring limits exchange of blood between the portal vein and the liver, thereby rendering the removal of toxin such as alcohol difficult. The alcohol creates oxidative stress that causes inflammation and leads to fibrosis. Cirrhosis is asymptomatic until it becomes decompensated. A combination of abstinence from drinking alcohol and pharmaceutical therapy has shown a positive result in a reversal of cirrhosis. There is a dire need of novel drugs with reduced contraindications and efficacy to treat and reverse cirrhosis.

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