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Evaluating The Complications Of Liver Cirrhosis

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Abstract
The types of liver cirrhosis were discussed, including the definition, causative factors, and the solutions. Liver cirrhosis is defined as a diffuse process characterized by fibrosis and transformation of the normal architecture of the liver into structurally abnormal nodules Liver cirrhosis was described as the final stage of liver disease, which was a resultant effect of previous stages of damage. The causes of Liver cirrhosis comes from the condition that leads to permanent or recurrent hepatocyte death can lead to cirrhosis, such as: chronic alcohol abuse, chronic viral hepatitis (hepatitis B and C), autoimmune hepatitis, nonalcoholic steatohepatitis, primary biliary cholangitis, hereditary metabolic liver diseases, or the cause may be unknown (cryptogenic cirrhosis). Characteristics of cirrhosis depicts that fibrous septa appears in the form of thin strips or wide scars/partitions around several adjacent lobules. Signs and symptoms of cirrhosis are that it can be asymptomatic for years. Often the first symptoms are non-specific; these include general fatigue (due to cytokine release), anorexia, weakness, and weight loss. The main complications of liver cirrhosis are associated with portal hypertension, liver failure and increased risk of developing hepatocellular carcinoma. Some complications caused by portal hypertension include: ascites, esophageal varices, bacterial infections, splenomegaly, and hepatopulmonary syndrome. While some complications due to reduced liver function include: jaundice, hepatic encephalopathy, hepatorenal syndrome, malnutrition, osteoporosis, hematological abnormalities. There are several lifestyle changes one can make to reduce the chances of further problems and complication of cirrhosis. These include: avoiding alcohol, quitting smoking, losing weight if one is overweight or obese, and practicing good hygiene.
Keywords*: Cirrhosis, Disease, Liver, Complication, Portal Hypertension*

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I. INTRODUCTION

Background of the study

Liver cirrhosis is the final stage of liver disease, which occurs as a result of previous stages of damage. It is an increasing cause of morbidity and mortality in developed countries; it is the fourteenth most common cause of death in the world, and the fourth in Central Europe (Tsochatzis E.A, 2014). The main causes of cirrhosis are: chronic viral infections, alcoholic and non-alcoholic steatohepatitis, autoimmune diseases, metabolic causes, hereditary diseases, etc. (Kumar *et al*., 2015). In the past, it was thought that cirrhosis was never reversible; however, it has become apparent that when the etiological nox that caused the cirrhosis is removed, fibrosis can be reversed (Fauci *et al*., 2009). In cirrhosis, healthy liver cells are replaced by inflammatory cells and fibrous tissue, leading to fibrosis and the formation of regenerative nodules, leading to liver failure, and complications that can be life-threatening.

The pathogenesis of cirrhosis is represented by progressive fibrosis and reorganization of the architecture of the liver. In the normal liver, the extracellular matrix consisting of interstitial collagen (collagen types I, III, V, and XI) is concentrated in the portal spaces and around the central veins. Hepatocytes do not have a true basement membrane, but they contain type IV collagen and other proteins in the space of Disse (Kumar *et al*., 2015). In cirrhosis, types I and III are deposited in the space of Disse, and the main source of excess collagen in cirrhosis is the perisinusoidal cells (formerly known as Ito cells). Normally, in healthy tissues, stellaxte cells store vitamin A. When hepatocytes are affected, they secrete paracrine factors, free radicals, growth factors, tumor necrosis factor (TNF) which activates stellate cells and turns them into myofibroblasts, which then lose vitamin A, they produce growth factors, cytokines and chemokines that cause their further proliferation and collagen synthesis. The excess of produced collagen is deposited in the perisinusoidal space, which leads to blockage of endothelial fenestrations and sinusoidal capillarization occurs, which prevents the free exchange of dissolved substances between hepatocytes and plasma. Vascular shunts lead to abnormal vascular pressures in the liver and contribute to liver dysfunction and portal hypertension (Kumar *et al*., 2015).

Definition of liver cirrhosis

Cirrhosis is defined as a diffuse process characterized by fibrosis and transformation of the normal architecture of the liver into structurally abnormal nodules (Kumar *et al*., 2015).

Characteristics of cirrhosis

Cirrhosis is a diffuse liver damage. Fibrous septa appear in the form of thin strips or wide scars/partitions around several adjacent lobules. Parenchymal nodules containing regenerating hepatocytes surrounded by fibrosis, have a diameter that varies from very small (<3 mm-micronodules) to large (over >1 cm-macronodules) (Kumar *et al*., 2015).

Causes of liver cirrhosis

Any condition that leads to permanent or recurrent hepatocyte death can lead to cirrhosis, such as: chronic alcohol abuse, chronic viral hepatitis (hepatitis B and C), autoimmune hepatitis, nonalcoholic steatohepatitis, primary biliary cholangitis, hereditary metabolic liver diseases, or the cause may be unknown (cryptogenic cirrhosis) (Fauci *et al*., 2009).

Signs and symptoms of cirrhosis

Cirrhosis can be asymptomatic for years. A third of patients never develop symptoms. Often the first symptoms are non-specific; these include general fatigue (due to cytokine release), anorexia, weakness, and weight loss. The liver is typically palpable and firm, with blunt edges, but is sometimes small and difficult to palpate. Nodes are usually not palpable unless they are large.

Clinical signs suggestive of chronic liver disease or chronic alcohol use, but not specific to cirrhosis, include sarcopenia, palmar erythema, parotid swelling, koilonychia, Dupuytren's contracture, spider nevus, gynecomastia, loss of libido, testicular atrophy, and peripheral neuropathy (Jesse, 2018). Most cases of ultimately fatal cirrhosis involve one of the following mechanisms: progressive liver failure, development of hepatocellular carcinoma, complications related to portal hypertension (Kumar *et al*., 2015).

II. COMPLICATIONS OF LIVER CIRRHOSIS

The main complications of liver cirrhosis are associated with portal hypertension, liver failure and increased risk of developing hepatocellular carcinoma (Kumar *et al*., 2015). Some complications caused by portal hypertension include: ascites, esophageal varices, bacterial infections, splenomegaly, and hepatopulmonary syndrome. While some complications due to reduced liver function include: jaundice, hepatic encephalopathy, hepatorenal syndrome, malnutrition, osteoporosis, hematological abnormalities.

Portal Hypertension

Portal hypertension is defined as an increase in the hepatic venous pressure gradient (HVPG) to more than 12 mmHg. The increase in pressure occurs due to the blockage of blood flow through the liver, which will cause the development of varicosities of the esophagus and stomach. Varicose veins become brittle and bleed easily (Danielle, 2004). The portal vein receives blood from the entire intestine and from the spleen, pancreas, and gallbladder and carries that blood to the liver. After entering the liver, the portal vein divides into right and left branches, and then into small venules that pass through the liver. When the blood leaves the liver, it returns to the general circulation through the hepatic vein. It is caused by a combination of two simultaneous hemodynamic processes: increased intrahepatic resistance to blood flow through the liver due to cirrhosis and regenerative nodes, and increased splanchnic blood flow due to vasodilatation within the splanchnic vascular bed (Fauci *et al*., 2009).

Causes of portal hypertension

The causes of portal hypertension are usually subcategorized as prehepatic, intrahepatic, and posthepatic. Prehepatic causes of portal hypertension are those that affect the portal venous system before it enters the liver; include portal vein thrombosis and vein thrombosis. Posthepatic causes include those affecting the hepatic veins and venous drainage to the heart; they include Budd-Chiari syndrome, veno-occlusive disease, and chronic right-sided heart congestion. Intrahepatic causes account for over 95% of cases of portal hypertension. They can be presinusoidal and postsinusoidal. Postsinusoidal causes include veno-occlusive disease, while presinusoidal causes include congenital hepatic fibrosis and schistosomiasis (Fauci *et al*., 2009).

Signs and symptoms of portal hypertension

Portal hypertension is asymptomatic; symptoms and signs arise from its complications. The most dangerous is acute variceal bleeding. Patients usually present with sudden (often massive) painless bleeding

from the upper gastrointestinal tract. Bleeding from portal hypertensive gastropathy is often subacute or chronic. Ascites, splenomegaly or portosystemic encephalopathy may be present (Albillos *et al*., 2017).

Diagnosis of portal hypertension

Ultrasound or CT often reveals dilated intra-abdominal collaterals, and Doppler ultrasound can determine patency and flow through the portal system. Esophageal varices, gastric varices, and portal hypertensive gastropathy are best diagnosed by endoscopy, which can also identify predictors of variceal bleeding.

Complications of portal hypertension

The three primary complications of portal hypertension are: bleeding varices, ascites, and hypersplenism.

Treatment of portal hypertension

When possible, the underlying disorder is treated. In patients with bleeding esophagogastric varices, combined endoscopic treatment and drug treatment reduce mortality and reduce the risk of rebleeding. In order to eradicate esophageal varices, endoscopic band ligation is used, and periodic endoscopic monitoring is performed to identify and treat recurrent varices. Long-term drug therapy usually includes non-selective beta-blockers. These drugs reduce portal pressure primarily by reducing portal flow. Medicines used include propranolol (40 to 80 mg orally twice daily), nadolol (40 to 160 mg orally once daily), timolol (10 to 20 mg orally twice daily) and carvedilol (6.25 to 12.5 mg orally twice a day), with dose titration. The addition of 10 to 20 mg of isosorbide mononitrate orally twice daily can further reduce portal pressure (Albillos *et al*., 2017).

Ascites

Ascites is defined as the accumulation of fluid in the peritoneal cavity. The most common cause of ascites is portal hypertension associated with cirrhosis, but it can also be caused by malignant or infectious causes (Fauci *et al.,* 2009).

Pathology of ascites

Splanchnic vasodilatation, mediated mainly by nitric oxide, causes systemic arterial pressure to fall as cirrhosis progresses. This leads to activation of the renin-angiotensin system, secondary aldosteronism, increased sympathetic activity, increased secretion of atrial natriuretic hormone. These systems tend to normalize arterial pressure, but produce salt and water retention (Ralston *et al*., 2018). The combination of splanchnic vasodilatation and portal hypertension changes intestinal capillary permeability, promoting fluid accumulation in the peritoneum (Ralston *et al.,* 2018).

Signs of ascites

Small amounts of ascitic fluid do not cause symptoms. Moderate amounts cause increased abdominal girth and weight gain. Large amounts may cause nonspecific diffuse abdominal pressure, but actual pain is uncommon and indicates another cause. If ascites results in elevation of the diaphragm, dyspnea may occur. Clinical signs are revealed by physical examination. Volumes <500 mL may not be detectable by physical examination. Massive ascites causes abdominal wall tightness and umbilical herniation. In liver disease or peritoneal disorders, ascites is usually isolated or out of proportion to peripheral edema; in systemic diseases (e.g heart failure) it is usually the other way around (Danielle *et al*., 2004). Ascites greater than 1 L causes abdominal distension, fullness in the hips, change in dullness to percussion. Other signs include umbilical hernia, scrotal edema, and enlarged abdominal veins (Ralston *et al.,* 2018).

Diagnosis of ascites

Diagnosis can be based on physical examination if there is a large amount of fluid, but imaging methods are more sensitive. Ultrasound and CT detect much smaller amounts of fluid (100 to 200 ml) than physical examination. Spontaneous bacterial peritonitis (SBP) is suspected if a patient with ascites has abdominal pain, fever, or unexplained worsening of the general condition. A diagnostic paracentesis should be performed if any of the following occur: ascites is recently diagnosed, its cause is unknown, and spontaneous bacterial peritonitis is suspected (Danielle *et al*., 2004).

Treatment of ascites

Successful treatment of ascites reduces symptoms but does not prolong life. If it is massive, it can cause severe fluid and electrolyte imbalance and cause hepatic encephalopathy. A hygienic-dietary regimen includes: restriction of sodium intake, diet without added salt ,, avoidance of drugs rich in sodium (eg, many antibiotics, antacids) and those that retain sodium (eg, steroids, NSAIDs). Most patients require diuretics in

addition to sodium restriction. Spironolactone is the drug of choice, but it can cause gynecomastia. Some patients will also need loop of Henle diuretics, e.g. furosemide. Large-volume paracentesis with intravenous albumin replacement can be used as first-line treatment for refractory ascites or when other treatments have failed. Transjugular intrahepatic portosystemic stent shunt may relieve resistant ascites, but does not prolong life and may worsen encephalopathy (Ralston *et al.,* 2018).

Esophageal Varices

Varicose veins are dilated veins in the distal esophagus or proximal stomach caused by increased pressure in the portal venous system, typically due to cirrhosis (Parswa, 2021). Venous blood from the gastrointestinal tract is normally distributed to the liver via the portal vein before reaching the vena cava. Diseases that interfere with this flow cause portal hypertension and can lead to the development of esophageal varices, an important cause of esophageal bleeding (Kumar *et al*., 2015).

Pathogenesis of esophageal varices

One of the places where the splanchnic and systemic venous circulation can communicate is the esophagus. Therefore, portal hypertension results in the development of collaterals that allow portal blood to enter the caval system. However, these collaterals augment the subepithelial and submucosal venous plexus within the distal esophagus. Varicose veins develop in 90% of patients with cirrhosis (Kumar *et al*., 2015).

Signs and symptoms of esophageal varices

Most patients have no symptoms until the varicose veins bleed. When the bleeding is sudden and severe, the patient vomits large amounts of blood. When the bleeding is less severe, the patient may swallow blood, which can cause black, tarry stools. If bleeding is not controlled, shock can occur.

Diagnosis of esophageal varices

Esophageal varices are best diagnosed by endoscopy, which can also identify varices with a high risk of bleeding. Endoscopy is also critical to rule out other causes of acute bleeding (eg, peptic ulcer), even in patients known to have varices. Namely, as many as one third of patients with known varices who have bleeding from the upper gastrointestinal tract have a non-variceal cause of bleeding. Because varices are usually associated with significant liver disease, it is important to evaluate for possible coagulopathy. Laboratory tests include complete blood count with platelets, prothrombin time (PT), partial thromboplastin time (PTT), and liver function tests (Parswa, 2021). CT or MRI are also used to diagnose esophageal varices.

Treatment of esophageal varices

Treatment of esophageal varices can be pharmacological (usually with non-selective beta-blockers) or endoscopically. The decision between pharmacological or endoscopic prevention is quite complex and depends on factors such as the size of the varices and the severity of cirrhosis. In patients with previous variceal bleeding, secondary prevention is carried out, which again can be pharmacological (typically with non-selective beta-blockers), endoscopic or rarely, radiological (TIPS) or surgical (Garcia *et al*., 2007, Gonzalez *et al*., 2015, Takashi *et al*., 1985).

In the case of acute variceal bleeding, treatment includes resuscitation with intravenous fluids and blood products, administration of vasoactive drugs (such as terlipressin or octreotide), intravenous antibiotics, and endoscopic ligation (Garcia, 2007). In severe cases, refractory to standard treatment, rescue therapy can be attempted using the Sengstaken-Blakemore probe or the Minnesota probe (Takashi *et al*., 1985).

Bacterial Infections

The risk of bacterial infection in cirrhosis is due to multiple factors including: liver dysfunction, dysbiosis, immune dysfunction associated with cirrhosis, and genetic factors. Bacterial peritonitis can be spontaneous bacterial peritonitis or secondary bacterial peritonitis. Spontaneous bacterial peritonitis is defined as bacterial infection of ascitic fluid without any intra-abdominal surgically treatable source of infection. It is a very common occurrence in patients with liver cirrhosis and ascites (Fernandez *et al.*, 2002; Fasolato *et al.*, 2007). The most common causative agents are Escherichia coli and other intestinal bacteria. The diagnosis of SBP is based on diagnostic paracentesis (Rimola *et al.,* 2000). 5% of patients with cirrhosis may develop peritonitis due to perforation or inflammation of intra-abdominal organs, which is called secondary bacterial peritonitis. Secondary bacterial peritonitis should be suspected in patients who have localized abdominal symptoms or signs, the presence of multiple organisms in the ascites culture, a very high ascites neutrophil count, and/or a high ascites protein concentration, or in those patients with an inadequate response to therapy. Patients with suspected secondary bacterial peritonitis should undergo CT and early consideration of surgical treatment (Soriano *et al*., 2010).

Hepatopulmonary Syndrome

Hepatopulmonary syndrome (HPS) is a pulmonary complication of liver cirrhosis and/or portal hypertension, in which patients develop hypoxemia as a result of changes in pulmonary microvascular tone and architecture. Dyspnea and hypoxemia worsen when the patient is in an upright position. This occurs in up to 30% of patients with cirrhosis. Although the degree of hypoxemia is not reliably correlated with the severity of liver disease, patients with HPS have a higher mortality than patients with liver cirrhosis without this disorder (Koch *et al.,* 2014).

Pathophysiology of Hepatopulmonary Syndrome

Hepatopulmonary syndrome results from the formation of microscopic intrapulmonary arteriovenous shunts in patients with chronic liver disease complicated by portal hypertension. The mechanism is unknown, but it is thought to be due to increased production or decreased hepatic clearance of vasodilators. Vascular dilatations cause excessive perfusion relative to ventilation, leading to hypoxemia, especially as patients have increased cardiac output as a result of systemic vasodilation (Mark and Andrea, 2020). Hepatopulmonary syndrome is associated with reduced levels of bone morphogenetic protein 9 (BMP9) and BMP10 compared to patients with advanced liver disease without hepatopulmonary syndrome. Lower levels of BMP9 were associated with more severe hepatopulmonary syndrome (Rochon *et al*., 2020). Since the lesions are often more pronounced at the bases of the lungs, hepatopulmonary syndrome can cause platypnea (dyspnea) and orthodeoxia (hypoxemia), which occur when the patient is sitting or standing, and pass in the supine position. Most patients also have characteristic findings of chronic liver disease, such as spider naevus. About 20% of patients have only pulmonary symptoms (Mark and Andrea, 2020).

Diagnosis of Hepatopulmonary Syndrome

Hepatopulmonary syndrome should be suspected in patients with known liver disease who report dyspnea (especially platypnea). Patients with such symptoms should undergo pulse oximetry. If the symptoms are pronounced (for example, dyspnea at rest), the partial pressure of gases in the arterial blood should be measured. Useful diagnostic tests are: contrast echocardiography, scintigraphy and pulmonary angiography. Pulmonary angiography may reveal a diffusely fine or patchy vascular configuration. Angiography is generally not required unless thromboembolism is suspected (Rochon *et al*., 2020).

Treatment of Hepatopulmonary Syndrome

The main treatment is oxygen therapy. Other therapies, such as somatostatin to inhibit vasodilation, have a modest benefit in only some patients. Chemoembolization is practically impossible due to the number and size of the lesions. Inhalation of nitric oxide synthesis inhibitors may be the therapy of the future. Hepatopulmonary syndrome may regress after liver transplantation or if the underlying liver disease regresses. The prognosis is poor without treatment (survival <2 years) (Rochon *et al*., 2020).

Hepatic Encephalopathy

Hepatic encephalopathy is also known as portosystemic encephalopathy (PSE). Deterioration of brain function occurs in people with severe liver disease because toxic substances that are normally removed by the liver accumulate in the blood and reach the brain (Danielle, 2004). Hepatic encephalopathy is characterized by personality changes, intellectual impairment and reduced level of consciousness (Shawcross *et al*., 2016).

Pathogenesis of Hepatic Encephalopathy

Cirrhosis leads to the accumulation of scar tissue in the liver, this scar tissue blocks blood flow and affects the liver's ability to filter toxins, hormones and nutrients. These toxins can accumulate and reach the brain, affecting brain function and causing cognitive impairment (American Liver Foundation, 2020). Two factors seem to be important in the development of this disorder: shunting of portal blood directly into the systemic circulation bypassing the liver, and severe hepatocellular damage and dysfunction (Kumar *et al*., 2015). Absorbed products that would otherwise be detoxified in the liver enter the systemic circulation and reach the brain, causing toxicity, especially in the cerebral cortex.

Signs and symptoms of Hepatic Encephalopathy

Symptoms usually do not become apparent until brain function is moderately impaired. Construction apraxia, in which patients cannot reproduce simple designs, develops early. Agitation and mania may develop, but are uncommon. Asterixis is a characteristic fluttering tremor that occurs when patients hold their arms outstretched with flexed joints. Neurological deficits are usually symmetrical. Neurological signs in coma usually reflect bilateral diffuse hemispheric dysfunction. Signs of brainstem dysfunction develop only in

advanced coma, often in the hours or days before death. A characteristic smell (fetor hepaticus) can appear regardless of the stage of encephalopathy (Danielle, 2004)

Diagnosis of Hepatic Encephalopathy

Diagnosis is ultimately based on clinical findings, but testing can help. Psychometric testing can reveal subtle neuropsychiatric deficits, which can help confirm early encephalopathy. Blood ammonia levels are usually measured. EEG usually shows diffuse slow-wave activity, even in mild cases, and may be sensitive but not specific for early encephalopathy. Examination of the cerebrospinal fluid is not routinely necessary, the only common abnormality being a mild elevation of protein (Danielle, 2004)

Treatment of Hepatic Encephalopathy

Treatment is multifactorial and includes elimination and correction of precipitating factors, sometimes hydration and correction of electrolyte imbalance is necessary. The use of lactulose, a non-absorbable disaccharide, results in acidification of the colonic contents. The goal of applying lactulose is to provoke 2-3 soft stools per day. Poorly absorbed antibiotics (rifaximin) are often used as adjunctive therapy for patients who cannot tolerate lactulose. Zinc supplementation is helpful and relatively harmless (Fauci *et al*., 2009).

Hepatorenal Syndrome

Hepatorenal syndrome (HRS) is a complication of advanced cirrhosis characterized by functional renal insufficiency and changes in systemic blood pressure due to increased activity of endogenous vasoactive systems. Functional renal insufficiency is a consequence of severe ischemia of the renal cortex and a decrease in the rate of glomerular filtration that develops in the late stages of cirrhosis (Dragana *et al*., 2005). Patients with hepatorenal syndrome have no identifiable cause of kidney dysfunction, and the kidneys themselves are not structurally damaged. Therefore, hepatorenal syndrome can be called a functional form of kidney damage. In fact, if a kidney from an individual with hepatorenal syndrome were transplanted into an otherwise healthy person, it would function normally.

Pathophysiology of Hepatorenal Syndrome

A hallmark of hepatorenal syndrome is renal vasoconstriction, although the pathogenesis is not entirely clear. Multiple mechanisms are probably involved, involving the interplay between disturbances in systemic hemodynamics, activation of vasoconstrictor systems, and reduction in the activity of vasodilator systems. The hemodynamic pattern of patients with hepatorenal syndrome is characterized by increased cardiac output, low arterial pressure, and decreased systemic vascular resistance. Renal vasoconstriction occurs in the absence of reduced cardiac output and blood volume, which is in contrast to most clinical conditions associated with renal hypoperfusion (Arroyo *et al.,* 2007; Turban *et al.,* 2007; Al-Khafaji *et al.,* 2015).

Types of Hepatorenal Syndrome

There are two subtypes of hepatorenal syndrome. Hepatorenal syndrome type 1 is characterized by progressive oliguria, a rapid rise in serum creatinine, and a very poor prognosis. There is usually no proteinuria, sodium excretion in the urine is <10 mmol/day, and the urine/plasma osmolarity ratio> 1.5. Treatment consists of albumin infusion in combination with terlipressin and is effective in about two-thirds of patients. Hemodialysis should not be used routinely because it does not improve outcome. Hepatorenal syndrome type 2 usually occurs in patients with refractory ascites, is characterized by a moderate and stable increase in serum creatinine, and has a better prognosis (Ralston *et al.,* 2018). Hepatorenal syndrome type 1 progresses rapidly, while kidney function in hepatorenal syndrome type 2 deteriorates slowly over weeks or months. Type 1 hepatorenal syndrome can be caused by sepsis or acute alcoholic hepatitis and occasionally develops in patients who already have type 2 hepatorenal syndrome (Al-Khafaji *et al.,* 2015)

Clinical characteristics of Hepatorenal Syndrome

Hepatorenal syndrome can occur spontaneously, while in most patients with decompensated cirrhosis it occurs after SBP, acute alcoholic hepatitis, gastrointestinal bleeding, prolonged diarrhea, forced diuresis (diuretics) or paracentesis with evacuation of large volumes of fluid (Cardenas *et al*., 2003). In recent years, spontaneous bacterial peritonitis (SBP) has become the most common factor leading to hepatorenal syndrome (HRS) type I (occurring in one third of patients with SBP despite the use of aggressive antibiotic therapy) (Rimola *et al*., 2000). The development of hepatorenal syndrome is not correlated with the severity of liver failure, but patients with severe retention of sodium (excretion less than 10 mEq/d) and water, dilutional hypernatremia (serum sodium level less than 130 mEq/l), low arterial pressure are under increased risk.

Treatment of Hepatorenal Syndrome

Liver transplantation is the definitive treatment for hepatorenal syndrome). However, transplantation for type 1 HRS is limited by the fact that many patients die before surgery because of the short survival compared to the long waiting time for transplantation, in most centers. If liver transplantation can be performed, the probability of 3-year survival after transplantation in patients with hepatorenal syndrome treated with terlipressin and albumin is similar to that of patients with cirrhosis without hepatorenal syndrome (Restuccia *et al*., 2004).

Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) can occur as a complication of liver cirrhosis. It is an aggressive malignant tumor with high mortality. In cirrhotic patients, hepatocellular carcinoma usually arises after malignant transformation of a dysplastic regenerative nodule.

Signs and symptoms of Hepatocellular Carcinoma

Hepatocellular carcinoma is most often manifests as previously stable patients with cirrhosis develop abdominal pain, lose weight, develop a palpable mass under the right rib cage, and have an inexplicable deterioration in their general condition. They may have a fever. In some patients, the first manifestation of hepatocellular carcinoma may be the appearance of hemorrhagic ascites, shock or peritonitis.

Diagnosis of Hepatocellular Carcinoma

The diagnosis is based on the determination of alpha-fetoprotein (AFP) and the application of imaging techniques (CT, ultrasonography or MRI). If imaging shows characteristic findings and alpha-fetoprotein is elevated, the diagnosis is clear. However, sometimes a definitive diagnosis requires a liver biopsy, guided by ultrasound or CT (Danielle, 2004).

Screening for Hepatocellular Carcinoma

An increasing number of hepatocellular carcinomas are being detected through the screening program. One common screening method is ultrasound and AFP determination every 6 or 12 months.

Treatment of Hepatocellular Carcinomas

Treatment of hepatocellular carcinoma depends on the stage of the disease. Liver transplantation is possible if the Milan criteria are met (one tumor diameter <5 cm or three tumors diameter <3 cm without vascular invasion and alpha-fetoprotein <500 mcg/L). In patients with solitary tumors <5 cm in diameter and without portal hypertension, surgical resection is potentially curative, with a 5-year survival rate of 60 to 80%. Ablative treatments (hemoembolization of the hepatic artery, radiofrequency ablation) provide regression of the disease and are used in specially indicated conditions. Chemotherapy is administered with drugs such as sorafenib, levatinib, regorafenib and immunotherapy such as nivolumab (Llovet *et al*., 2008). Atezolizumab and bevacizumab are now available as combination therapy for patients with advanced hepatocellular carcinoma who have not received prior systemic therapy (Finn *et al*., 2020).

III. CONCLUSION

The treatment for cirrhosis depends on what has caused it. Cirrhosis cannot usually be cured, but there are ways to manage the symptoms and any complications, and stop the condition getting worse. If one has cirrhosis, there are several lifestyle changes you can make to reduce your chances of further problems and complications. These include: avoid alcohol, quit smoking, lose weight if one is overweight or obese do regular exercise to reduce muscle loss, practice good hygiene to reduce your chance of getting infections by getting the vaccinations you may need, such as the annual flu vaccine or travel vaccines speak to a pharmacist if you're taking over-the-counter or prescription medicines, because cirrhosis can affect the way some medicines work (NHS, 2020).

For dietary changes, malnutrition is common in people with cirrhosis, so it's important you eat a healthy, balanced diet to help you get all the nutrients you need. Cutting down on salt can help reduce the chance of swelling in your legs, feet and tummy caused by a build-up of fluid. The damage to your liver can mean it's unable to store glycogen, which is a type of fuel the body needs for energy. Certain blood pressure medicines may control increased pressure in the veins that supply the liver, called portal hypertension, and prevent severe bleeding. Your provider will regularly perform an upper endoscopy to look for enlarged veins in the esophagus or stomach that may bleed. These veins are known as varices.

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