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Study of Iron Status in Patients with Cirrhosis

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Annotation: Cirrhosis It is a medical condition resulting from scarring of healthy liver tissue Which affects the normal performance of its functions. Liver cirrhosis is considered a disease that, in advanced cases, can lead to the patient developing more serious diseases, such as cirrhosis, kidney failure, or portal hypertension. One of the most important causes of cirrhosis in industrialized countries is addiction. Alcohol consumption and viral hepatitis The liver plays a major role in iron homeostasis; thus, in patients with chronic liver disease, iron regulation may be disturbed. Higher iron levels are present not only in patients with hereditary hemochromatosis, but also in those with alcoholic liver disease, nonalcoholic fatty liver disease, and hepatitis C viral infection. Chronic liver disease decreases the synthetic functions of the liver, including the production of hepcidin, a key protein in iron metabolism. Lower levels of hepcidin result in iron overload, which leads to iron deposits in the liver and higher levels of non- transferrin-bound iron in the bloodstream. Iron combined with reactive oxygen species leads to an increase in hydroxyl radicals, which are responsible for

phospholipid peroxidation, oxidation of amino acid side chains, DNA strain breaks, and protein fragmentation. Iron- induced cellular damage may be prevented by regulating the production of hepcidin or by administering hepcidin agonists.

1. Introduction

Liver cirrhosis is a medical term used to describe a condition where the liver contains a large amount of scar (fibrosis) tissue. Scar tissue forms from ongoing injury to the liver, usually from a chronic viral infection such as chronic hepatitis B and chronic hepatitis C. It can also be caused from alcohol or too much fat in the liver [1]

It is usually associated with transmissible infectious diseases such as viral hepatitis. Consumption of alcohol, metabolic syndrome, autoimmune processes, storage diseases, toxic Substances and medications. [2]

It is known that up to 40% of patients remain asymptomatic for long periods; however, once The complications develop. A progressive deterioration occurs whose outcome is death if the patient undergoes a definitive treatment that is the liver transplant. [3]

In patients with compensated cirrhosis, there are no specific symptoms although people commonly complain of being lethargic and easily fatigued. They may notice poor sleeping at night, reduced appetite. As cirrhosis progresses the scar tissue reduces the blood flow through the liver, causing increase in pressure in the veins which may cause bleeding in the gullet and stomach. Specific symptoms which develop in the later stages of cirrhosis include jaundice, weight loss, swelling of legs and abdomen, confusion and bleeding into the bowel.[1]

The advances in diagnostic methods allow now early diagnosis, even before the development of complications, which are mostly related to development of portal hypertension.[4]

In view of the increasing clinical importance of the Diagnosis of cirrhosis in the asymptomatic patient, it Is disheartening to realize that diagnostic accuracy in Routine clinical practice is rather poor. While we require a sensitivity of more than 95% for etiologic tests like HBsAg and anti-HCV, we commonly use method- Ology (percutaneous liver biopsy) with a sensitivity of Below 80% in detecting cirrhosis. The diagnostic sensitivity can be increased by examining more than one Biopsy specimen (9,lO) or by combining liver biopsy With laparoscopy (1l), but neither approach has found General acceptance in routine clinical practice.[5]

Recently, with the development of new and very effective treatments, especially in the viral related cirrhosis scenario, there is increasing evidence that cirrhosis can regress and that histological Improvement is associated with better prognosis.[4]

Treatment liver damage from cirrhosis cannot be reversed, but treatment can stop or delay Further progression and reduce complications. Treatment for hepatitis- related cirrhosis involves medications used to treat the different types of hepatitis, such as interferon for viral hepatitis and corticosteroids for autoimmune hepatitis.Survival rates have improved over the past several years because of drugs such as cyclosporine and tacrolimus, which suppress the immune system and keep it from attacking and damaging the new liver.treatment for cirrhosis resulting from other diseases depends on the underlying cause.[6]

One of the major, and potentially treatable, causes of anemia in patients with liver cirrhosis is acute or chronic blood loss into the gastrointestinal tract, often resulting in iron deficiency anemia (IDA). The hemorrhage is usually secondary to complicationsof portal hypertension such as gastroesophageal variceal rupture, gastropathy, gastric antral vascular ectasia (GAVE) or peptic ulcers, more common in patients with cirrhosis [7].

The fact that patients with liver disease have also had impaired coagulation is a contributing factor to the Tendency of bleeding, as well as the thrombocytopenia due to spleen enlargement. Iron deficiency (ID), with or without anemia, is associated with many symptoms and complications that have a significant and negative impact on patients. It can increase cardiovascular homeostasis and liver disease Since the liver plays a major role in iron balance,it is obvious that liver diseases of different etiology, and especially advanced CLD with Portal hypertension, are directly related to abnormalities in iron homeostasis.[8]

The main complications include gastrointestinal variceal hemorrhage, ascites, spontaneous bacterial peritonitisInfection, hepatorenal syndrome, hepatic encephalopathy, and hepatocellular Carcinoma.]9[

Iron is one of the most important elements that plays an important role in the vital and basic functions that contribute to a person's survival and helps him perform the body's functions to the fullest extent. It is worth noting that ferritin is not iron, but rather a protein in the body that contains iron, and it is the main form in which iron is stored in the body. The human body stores iron in the form of ferritin and hemosiderin in the liver, spleen, marrow, duodenum, skeletal muscle, and other anatomical areas. [10]

Need to include ferritin among the routinely monitored markers used to evaluate disease progression in patients with cirrhosis. [11]

The intracellular iron storage primarily consists of ferritin and is mainly located in the liver and the bone marrow. Transferrin is the only protein transporting iron between enterocytes, iron storage and erythroblasts of the bone marrow.[18]

Hepcidin, a hormone mainly synthetized in the liver, is a very important regulator of the iron metabolism. It causes the internalization of ferroportin-1 (FPN1), a surface protein on macrophages, enterocytes and hepatocytes. FPN1´s function is the export of iron out of the cells. In sum, an increased production of hepcidin leads to a decreased resorption of iron in the intestine and reduced release of iron from the hepatocytes and macrophages. The synthesis of hepcidin is decreased in patients with iron deficiency, enhanced erythropoiesis and hypoxia while it is increased in case of full iron stores in the liver and inflammation. [18]

The liver performs a major role in iron homeostasis. It is the main organ for the production of the iron regulatory hormone hepcidin, expressed in iron excess conditions as well as in cases of inflammation, blocking the absorption of iron from cases of inflammation blocking the absorption of iron from the enterocytes.[13]

The liver is the second largest organ in the human body, it weights up to 5% of the total body weight. It is responsible for various, very important physiological processes such as storage of nutrients like carbohydrates and lipids as well as synthesis of coagulation factors, glucose, lipids and ketone bodies. Another key function is the transformation, activation and inactivation of endogenous substances such as steroids and bilirubin or exogenous substances like medicines and toxins Furthermore, the liver is an exocrine gland that produces gall for digestion of lipids and it is responsible for essential metabolic reactions such as urea synthesis.[18]

Cirrhosis is the end-stage of many types of liver disease, the most common being chronic viral hepatitis due to either hepatitis B virus (HBV) or hepatitis C virus (HCV) infections, alcohol abuse, and fatty liver (from obesity or diabetes). Cirrhosis may also be caused by conditions immune system damages the liver, such as autoimmune hepatitis, Primary Biliary Cholangitis and Primary Sclerosing Cholangitis. And in rare cases, cirrhosis may be caused by long-term exposure to some medicines or environmental toxins.[1]

The advances in diagnostic methods allow now early diagnosis, even before the development of complications, which are mostly related to development of portal hypertension.[4]

A study demonstrated that serum ferritin remains a useful tool for diagnosing iron restriction in patients with liver cirrhosis.[13]

The study also found that in cirrhotic chronic hepatitis B patients, the levels of serum transferrin were lower, while ferritin and serum iron were higher compared with the iron markers of non-cirrhotic patients. [14]

Another study highlighted that 10%-30% of patients with cirrhosis have excess iron, which can be particularly significant in individuals with nonalcoholic fatty liver disease, alcoholic liver diseases, CHC, and primary biliary cholangitis. Excess iron has been shown to increase the risk of hepatocellular carcinoma (HCC) and independently predict mortality.[15]

2. Cirrhosis of the Liver

2.1 Causes

A wide range of diseases and conditions can damage the liver and lead to cirrhosis. Some of the causes include:

- Long-term alcohol abuse.
- Ongoing viral hepatitis (hepatitis B, C and D).
- Nonalcoholic fatty liver disease, a condition in which fat accumulates in the liver.
- Hemochromatosis, a condition that causes iron buildup in the body.
- Autoimmune hepatitis, which is a liver disease caused by the body's immune system.
- Destruction of the bile ducts caused by primary biliary cholangitis.
- Hardening and scarring of the bile ducts caused by primary sclerosing cholangitis.
- Wilson's disease, a condition in which copper accumulates in the liver.
- Cystic fibrosis.
- Alpha-1 antitrypsin deficiency.
- Poorly formed bile ducts, a condition known as biliary atresia.
- Inherited disorders of sugar metabolism, such as galactosemia or glycogen storage disease.
- Alagille syndrome, a genetic digestive disorder.

2.2 Symptoms

Cirrhosis often has no symptoms until liver damage is severe. When symptoms do occur, they may include:

- Fatigue.
- Easily bleeding or bruising.
- Loss of appetite.
- Nausea.
- Swelling in the legs, feet or ankles, called edema.
- Weight loss.
- Itchy skin.
- Yellow discoloration in the skin and eyes, called jaundice.
- Fluid accumulation in the abdomen, called ascites (uh-SAHY-teez).
- Spiderlike blood vessels on the skin.
- Redness in the palms of the hands.
- Pale fingernails, especially the thumb and index finger.
- Clubbing of the fingers, in which the fingertips spread out and become rounder than usual.

2.3 Complications of Cirrhosis

Major Complications

- Complications of portal hypertension
- Variceal hemorrhage
- Portal hypertensive gastropathy
- Ascites
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome
- Hepatic hydrothorax
- Hepatopulmonary syndrome
- Portopulmonary hypertension
- Cirrhotic cardiomyopathy
- Hepatic encephalopathy
- Hepatic hydrothorax
- Hepatopulmonary syndrome
- Portopulmonary hypertension
- Cirrhotic cardiomyopathy
- Hepatic encephalopathy
- Hepatocellular carcinoma
- Portal vein thrombosis.[31]

2.4 Diagnosing Cirrhosis

Medical history and physical examination can identify patients with or at risk for cirrhosis. Most physical examination findings are not sensitive for cirrhosis but some offer specificity greater than 90%. Screening for cirrhosis in the general population is not currently recommended. However, patients with established chronic liver disease with abnormal liver enzymes, hepatic steatosis on imaging, or viral hepatitis should be evaluated for cirrhosis. Liver biopsy is considered the criterion standard to diag- nose cirrhosis, although it is being increasingly replaced by noninvasive methods for fibrosis assessment. Biopsy is reserved for patients with noninvasive testing that is inconclusive or technically inadequate or when the underlying chronic liver disease is unclear.

Serologic measures and imaging-based indices are used to diagnose cirrhosis. Compared with biopsy, these measures are less expensive, safer, and simpler to follow longitudinally safer, and simpler to follow longitudinally. The most common serologic tests capture indirect signs of liver fibrosis and dysfunction. [32]

2.5 Treatment cirrhosis

The best way to treat liver fibrosis is to address the root cause.

Successfully treating the cause of early to moderate liver fibrosis may reverse most, if not all, of the damage that the fibrosis has caused. [33]

Nearly every chronic liver condition eventually results in fibrosis, as each condition causes lasting inflammation in the liver. This inflammation can lead to the formation of scar tissue, which is fibrous.

When a person has advanced liver fibrosis or cirrhosis, they often require additional forms of treatment, and liver damage is generally irreversible.

Common treatment options for advanced fibrosis or cirrhosis include:

1. Taking medications to remove excess fluid from the body.
2. limiting salt intake.
3. Taking medications to remove toxins from the brain.
4. Taking medications that reducepressure in the veins of the stomach and esophagus.
5. Having transplantation surgery to replace the damaged liver with a healthy one from a donor.

Treatment can often reverse the effects of mild to moderate fibrosis. However, the condition tends not to cause noticeable symptoms until it has progressed.

This leads to irreversible damage and may cause conditions such as cirrhosis. For this reason, detecting fibrosis in an early stage is crucial.

FIGURE 1: Impact on treatment outcomes

This figure is self-created by the corresponding author.

2.6 Iron statue

The iron status in patients with cirrhosis is a complex issue that can involve both iron deficiency and excess iron.

1_ Excess Iron statue

thank Ryan Tlau *et al*) 2015 (Indicated explored the relationship of ferritin with TLC (as a marker of inflammation) and transferrin saturation (TS) (as a marker of iron overload). Serum hepcidin is influenced both by inflammation and iron overload and a positive correlation of hepcidin with ferritin and TS has been reported in patients with cirrhosis.[20]

And what you achieve G A Siregar Tlau *et al* (2018) Almost one-third of the total serum iron is in the portal system, sinusoidal mesenchymal cells and in the reticuloendothelial cells. Liver disorders can disturb iron homeostasis. Serum iron (SI), Totallron Binding Capacity (TIBC) and ferritin are important tests for evaluating iron abnormalities. Other parameters are transferrin saturation. Ferritin is an iron- containing protein in the human body and transferrin is a protein that acts as an iron transport protein. Ferritin is an acute phase protein and levels elevated in response to iron overload and systemic inflammation. The accumulation of iron in the liver will initiate a radical reaction that will ultimately damage the liver cells.

These lines of evidence suggest that iron is an important culprit in the pathogenesis of liver cirrhosis. In some previous studies, it has been shown that increased ferritin has significant prognostic value in chronic liver disease. Serum ferritin level has recently been reported to associate with early mortality in patients with liver cirrhosis. A recent study also showed that ferritin behaving as a cytokine might also directly induce the fibrogenic process by activating hepatic stellate cells. Their lines of evidence suggest that iron may be an important co-factor in the progression of liver cirrhosis. Finally, it might reflect an iron overload condition resulting in significant morbidity and arly mortality. [14]

Through the study he conducted Kosha J Mehta Tlau *et al.* (2019) this review narrates the role of iron in liver fibrosis. It Examines the underlying mechanisms by which excess iron can facilitate fibrotic Responses. It describes the role of iron in various clinical pathologies and lastly Highlights the significance and potential of iron-related proteins in the diagnosis And therapeutics of liver fibrosis.

Showed Iron-related proteins such as ferritin, hepcidin (hepcidin: ferritin ratio) and transferrin have successfully contributed to disease prognosis and acted as markers of fibrosis severity and progression in certain liver pathologies [19]

Previous studies made by Lalmuankima Tlau *et al*. (2023) indicated Excess iron deposition in the liver is known to be hepatotoxic and exacerbate liver injury. CLD also decreased synthetic functions of liver including decreased hepcidin level causing ultimately iron overload and deposits in liver and higher levels of non- transferrin- bound iron in the bloodstream. Excess iron can be harmful to the organism, in part through the generation of oxygen radicals, and Is potentially lethal. Excessive iron deposition in the liver leads to further injuries by triggering hepatocellular necrosis, inflammation, fibrosis and even carcinoma.

Showed The study concluded that Iron profile was deranged in chronic liver diseases where Serum ferritin and total iron binding capacity has increased in Relation to the severity of liver disease. This finding guided the management of Chronic condition of liver damage. [17]

Kanokwan Pinyopompanish Tlau *et al* (2023) achieved his studies into Iron overload is a condition involving excessive iron deposit in various organs, the liver being the main target organ for iron deposition and overload which are associated with significant liver morbidity and mortality Was Showed Iron overload is a well- recognized complication of chronic transfusion in patients with iron-loading anemias. It is associated with increased liver fibrosis and cirrhosis in these patients. [23]

Previous studies made by Sandra Milic *Tlau et al.* 2016.06.22The liver plays a critical role in the regulation of iron levels, particularly through pro- duction of hepcidin. In patients with chronic liver disease, iron metabolism changes result in iron overload. This is believed to occur mostly due to low levels of hepcidin. Iron deposits and NTBI are responsible for further damage to the liver by inflicting oxidative stress on hepatocyt.. These findings suggest that future studies should focus on the production of the agonists mini- and on manipulating various metabolic pathways to increase endogenous production of hipciden. [24]

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In studying this world Narendra Siddaiah Tlua et akb(2007)

Iron overload is associated with hepatocellular carcinoma in patients with end-stage liver disease, suggesting a possible carcinogenic or cocarcinogenic role for iron in chronic liver disease [29]

2_Anemia status

studies made by Eleana Gkamprela Tlau *et al* (2017) A study demonstrated into the serum ferritin remains a useful tool for diagnosing iron restriction in patients with liver cirrhosis. In the case of

iron deficiency, the most common cause of anaemia," increase of haemoglobin levels is usually intended to be achieved by iron supplementation, although the effects of iron supplementation in patients with cirrhosis has not been disease. These alterations might 'pretend' to satisfy iron levels despite the possible presence of iron deficiency. Hence, iron metabolism in patients with cirrhosis is difficult to interpret on the basis of blood work, and, finally, the reason for anaemia in these individuals often remains uncertain." Anaemia is very common in patients with cirrhosis and is known to be a predictor of negative outcomes, but little is known about the effect of iron substitution in these individuals. In our cohort, increase of haemoglobin levels improved transplant- free survival of patients with cirrhosis. The increase of haemoglobin levels was mainly induced by iron supplementation and was even stronger in the case of concomitant use of iron and rifaximin. Increased iron levels in plasma and increased iron storage stimulates hepcidin production which further blocks dietary iron absorption and storage. In iron deficiency states hepcidin production is suppressed, which ensures increased dietary iron abs Erythropoietic processes cause high. showed An increase of haemoglobin levels is as sociated with improvement of transplant- free survival in patients with cirrhosis. Because the prediction of haemoglobin increase significantly depends on rifaximin and iron supplementation, application of these two medications can have an important impact on the outcome of these patients.[13]

I achieved a study Sonal Singh Tlau *et al (2020)* After she indicated into The etiology of anemia in liver disease is diverse and often multifactorial. Anemia is more severe in advanced stages of liver cirrhosis and can be a predictor of the severity of liver disease. Showed that hemoglobin levels decrease with increasing severity of liver Disease; thus, this measure can be used in the initial assessment of patients to give a picture of the Severity of the disease. A larger prospective trial is needed to establish the use of hemoglobin levels For assessing severity and predicting mortality in patients with liver cirrhosis.[21]

Indicated studies submitted by Jakub Dawidowsk Tlau *et al* (2022) To Anemia is a common finding among patients with liver diseases. Patients who suffer from anemia are At a higher risk of liver function decompensation and hospitalization. It affects significantly their quality Of life and contributes tomortality. Anemia is present in70% of patients with liver cirrhosis and with varying Incidence accompanies other liver disorders. So the results were Anemia associated with liver disease is most frequently ascribed to blood loss from the gastrointestinal tract or micronutrient deficiency, with less common occurrence of hemolytic or aplastic anemia.[22]

In his study Manish Manrai Tlau *et al* (2022) found Anemia in a patient with cirrhosis is an important but often neglected disease association. The presence of anemia increases the risk of hepatic decompensation and Liver-related mortality. Increased severity of anemia is directly proportional to Worsening severity indices like model for end-stage liver disease score. Anemia May be seen in 66%-75% of patients with liver cirrhosis. Iron deficiency, which is The commonest type of anemia, has been observed in 22% of patients with Compensated cirrhosis and 78% in those with decompensated disease. The presence of anemia and various RBC indices, serum ferritin, TSAT, have allowed been independently associated with worsening disease severity and poor prognosis. Showed The evaluation and management of anemia in cirrhosis is an important aspect of disease management.

IDA is a potentially treatable cause of anemia wherein RBC indices and serum iron studies have prognostic significance. [15]

Jassin Rashidi-Alavijeh Tlau *et at* referred from his study conducted in (2023) Into Cirrhosis is the final common path of many different liver diseases, resulting in severe morbidity and high mortality Anaemia is frequently observed in patients with cirrhosis, and rates up to 66% were reporte. In the case of cirrhosis, in particular in advanced stages, iron Parameters undergo complex alterations. Transferrin synthesis is Reduced in patients with cirrhosis leading to elevated Transferrin saturation irrespective of lower iron levels, and Ferritin levels are often increased as ferritin is an acute-phase Protein reacting on inflammation. Showed Anaemia is frequently

observed in patients with cirrhosis and was identified as a predictor of adverse Outcomes, such as increased mortality and occurrence of acute-on-chronic liver failure. [16]

In the letter that Dr. med.univ submitted (2017) he referred to the Intracellular iron storage primarily consists of ferritin and is mainly located in The liver and the bone marrow. Transferrin is the only protein transporting iron between Enterocytes, iron storage and erythroblasts of the bone marrow. Hepcidin, a hormone Mainly synthetized in the liver, is a very important regulator of the iron metabolism. It causes The internalization of ferroportin-1 (FPN1), a surface protein on macrophages, enterocytes and Hepatocytes. FPN1´s function is the export of iron out of the cells. In sum, an increased Production of hepcidin leads to a decreased resorption of iron in the intestine and reduced Release of iron from the hepatocytes and macrophages. The synthesis of hepcidin is decreased In patients with iron deficiency, enhanced erythropoiesis and hypoxia while it is increased in Case of full iron stores in the liver and inflammation. In case of severe liver damage, the liver cannot longer fulfill its synthesis function, leading to a decreased production of hepcidin and thereby increased iron absorption. Iron deficiency anemia in patients with cirrhosis IDA in patients with liver cirrhosis is mainly due to acute and chronic hemorrhage of the gastrointestinal tract. iron metabolism is drastically influenced by changes due to cirrhosis and anemia. Especially iron deficiency anemia, can be a consequence of decompensation in patients with cirrhosis Showed Liver cirrhosis is a severe, life-limiting disease and its only curative therapy is liver Transplantation. This study concentrated on the prognostic value of iron parameters and anemia in patients with Cirrhosis. Iron metabolism is drastically influenced by changes due to cirrhosis and anemia. Especially iron deficiency anemia, can be a consequence of decompensation in patients with cirrhosis. Because of that, iron parameters and parameters defining anemia could be suspected to be predictive markers for patients with liver cirrhosis and diagnosis of IDA In patients with cirrhosis is challenging and ambiguous. In this study, transferrin saturation was chosen As the defining parameter in an attempt to avoid diagnostic error due to iron overload.[18]

Through the study he conducted Kosha J Mehta Tlau et al (2019) indicated Excess Iron can feed the Fenton reaction to generate unquenchable amounts of free Radicals that cause grave cellular and tissue damage and thereby contribute to Fibrosis. Moreover, excess iron can induce fibrosis-promoting signals in the Parenchymal and non-parenchymal cells, which accelerate disease progression And exacerbate liver pathology. Fibrosis regression is achievable following Treatment, but if untreated or unsuccessful, it can progress to the irreversible Cirrhotic stage leading to organ failure and hepatocellular carcinoma, where Resection or transplantation remain the only curative options. Therefore, Understanding the role of iron in liver fibrosis is extremely essential as it can help In formulating iron-related diagnostic, prognostic and treatment strategies. Thus, this review narrates the role of iron in liver fibrosis. It Examines the underlying mechanisms by which excess iron can facilitate fibrotic Responses. It describes the role of iron in various clinical pathologies and lastly Highlights the significance and potential of iron-related proteins in the diagnosis And therapeutics of liver fibrosis Showed Iron-related proteins such as ferritin, hepcidin (hepcidin: ferritin ratio) and transferrin have successfully contributed to disease prognosis and acted as markers of fibrosis severity and progression in certain liver pathologies[19].

Previous studies made by Sandra Milic *Tlau et al.* 2016.06.22The liver plays a critical role in the regulation of iron levels, particularly through pro- duction of hepcidin. In patients with chronic liver disease, iron metabolism changes result in iron overload. This is believed to occur mostly due to low levels of hepcidin. Iron deposits and NTBI are responsible for further damage to the liver by inflicting oxidative stress on hepatocyt. These findings suggest that future studies should focus on the production of the agonists mini- and on manipulating various metabolic pathways to increase endogenous production of hipciden. [24]

In studies made by European Association for the Study of the liver (2018) The natural history of cirrhosis is characterised by an asymp- tomatic compensated phase followed by a decompensated phase, marked by the development of overt clinical signs, the most frequent of which are ascites,

bleeding, encephalopathy, and jaundice. The following Clinical Practice Guidelines (CPGs) represent the first CPGs on the management of decompensated cirrhosis. In this context, the panel of experts, having empha- sised the importance of initiating aetiologic treatment for any degree of hepatic disease at the earliest possible stage, extended its work to all the complications of cirrhosis, which had not been covered by the European Association for the Study of the Liver guidelines, namely: ascites, refractory ascites, hypona- tremia, gastrointestinal bleeding, bacterial infections, acute kid- ney injury, hepatorenal syndrome, acute-on-chronic liver failure, relative adrenal failure, cirrhotic cardiomyopathy, hep- atopulmonary syndrome, and porto- pulmonary hypertensionpanel of experts, produced these GPGs using evidence from PubMed and Cochrane database searches providing up to date guidance on the management of decompensated cirrhosis with the only purpose of improving clinical practice. [25].

According to the study he conducte Rakesh Kumar Jagdish *Tlau et al (2023)* Early identification of the severity of PH and addressing downstream complications is central to the management of cirrhosis. Each complication merits detailed redressal, and overall management demands a holistic approach. ACLF needs to be identified early in the course with the institution of specific therapies. Newer modalities such as plasmapheresis and FMT have promising results. LT remains the definitive care in both advanced cirrhosis and ACLF. [26]

Based on the study he conducte Manish Manrai Tlua *et al* (2022). IDA is a potentially treatable cause of anemia wherein RBC indices and serum iron studies have prognostic significance. Patients should be screened for deficiency of micronutrients like Folic acid, Vit B12, Vit B6 at baseline and supplementation should be initiated. Future research into various aspects dealing with diagnosis, management of anemia, and newer therapeutic modalities is the need of the hour. In addition, the role of anemia in the prognostication of cirrhosis is an area that needs further research in prospective triald. [28]

3 Conclusions:

1. In case of severe liver damage, the liver cannot longer fulfill its synthesis function, leading to a decreased Production of hepcidin and thereby increased iron absorption.
2. Iron-related proteins such as ferritin, hepcidin (hepcidin:ferritin ratio) and transferrin have successfully contributed to disease prognosis and acted as markers of fibrosis severity and progression.
3. Serum ferritin could predict the prognosis of patients with cirrhosis Moreover, ferritin could express the severity of liver disease and might reflect an iron overload condition resulting in significant morbidity and early mortality. Iron overload associated in patient with cirrhosis associated with severity cirrhosis. The evaluation and management of anemia in cirrhosis is an important aspect of disease management.
4. Anaemia is frequently observed in patients with cirrhosis and was identified as a predictor of adverse Outcomes, such as increased mortality and occurrence of acute-on-chronic liver failure that hemoglobin levels decrease with increasing severity of liver Disease; thus, this measure can be used in the initial assessment of patients to give a picture of the Severity of the disease.
5. A larger prospective trial is needed to establish the use of hemoglobin levels For assessing severity and predicting mortality in patients with liver cirrhosis

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