INTRODUCTION

Esophageal varices are porto-systemic collaterals and they form as a consequence of portal hypertension (a progressive complication of cirrhosis), preferentially in the sub mucosa of the lower esophagus. Rupture and bleeding from esophageal varices are major complications of portal hypertension and are associated with a high mortality rate. Variceal bleeding accounts for 10–30% of all cases of upper gastrointestinal bleeding

The majority of cirrhotic patients will acquire esophageal varices at some point throughout their lives (5 to 15% per year), and the annual rate of esophageal haemorrhage is also 5 to 15%. In individuals with cirrhosis, the frequency of esophageal varices ranges from 30 to 70 percent, with 9–36 percent of patients having high-risk varices. Esophageal varices develop at a rate of 5–8% per year in people with cirrhosis, but only 1–2% of the time the varices are severe enough to cause bleeding. The transition from tiny to large varices occurs at an annual rate of 8%. Within the first year after being diagnosed with esophageal varices, about 30% of individuals will bleed. Despite advances in detection and treatment, the fatality rate for variceal haemorrhage remains significant (20 percent -35 percent). The severity of liver disease is linked to the occurrence of gastric varices. The size of the esophageal varices is the most important predictor of varices identication of large-sized esophageal before their first bleeding, is essential to prevent or

minimize this life threatening complication of liver cirrhosis.According to current standards, all cirrhotic patients should have an upper gastrointestinal endoscopy (UGIE) at the time of diagnosis to check for varices that are at high risk of bleeding. Surveillance endoscopies are also indicated every 1-2 years for patients with tiny varices, every 2-3 years for those with no varices in compensated cirrhosis, and once a year for decompensated cirrhosis patients. Even while UGIE is often regarded as the gold standard for diagnosing esophageal varices, it has its own set of limitations. First, diagnosis of esophageal varices by UGIE depends on the performance of individual endoscopists. Second, the vast majority of individuals who undergo UGIE screening do not have varices. Third, needless UGIE screening raises the expense of health-care services. Fourth, patients find the use of UGIE to be a painful treatment. Fifth, it may have negative consequences such as increased bleeding and infection risk.

Due to these problems in using UGIE, some noninvasive means have been proposed for prediction of esophageal varices in order to restrict UGIE to the population with high risk of variceal bleeding. Accurate identification of patients at the highest risk of bleeding allows stratification in an attempt to avoid unnecessary preventive measures in 60-75% of patients who will never have variceal bleeding in future. In a limited resources setting like ours, where

financial constraints are a major problem, predicting the presence and grade of varices by non-invasive methods serves to help a lot in various ways.

Because of the shared characteristics of these noninvasive methods, esophageal varices prediction is repeatable, cost-effective, easy, and quick, with no added strain on patients. Despite the fact that these criteria are obviously preferred by patients, none of them can match UGIE in terms of sensitivity and specificity in predicting variceal haemorrhage. Several predictive models based on various combinations of the above characteristics are proposed to increase the sensitivity and specificity of variceal prediction. The sensitivity and specificity of the recently suggested predictive models appear to vary with demographic, liver cirrhosis etiologies, and liver disease severity.

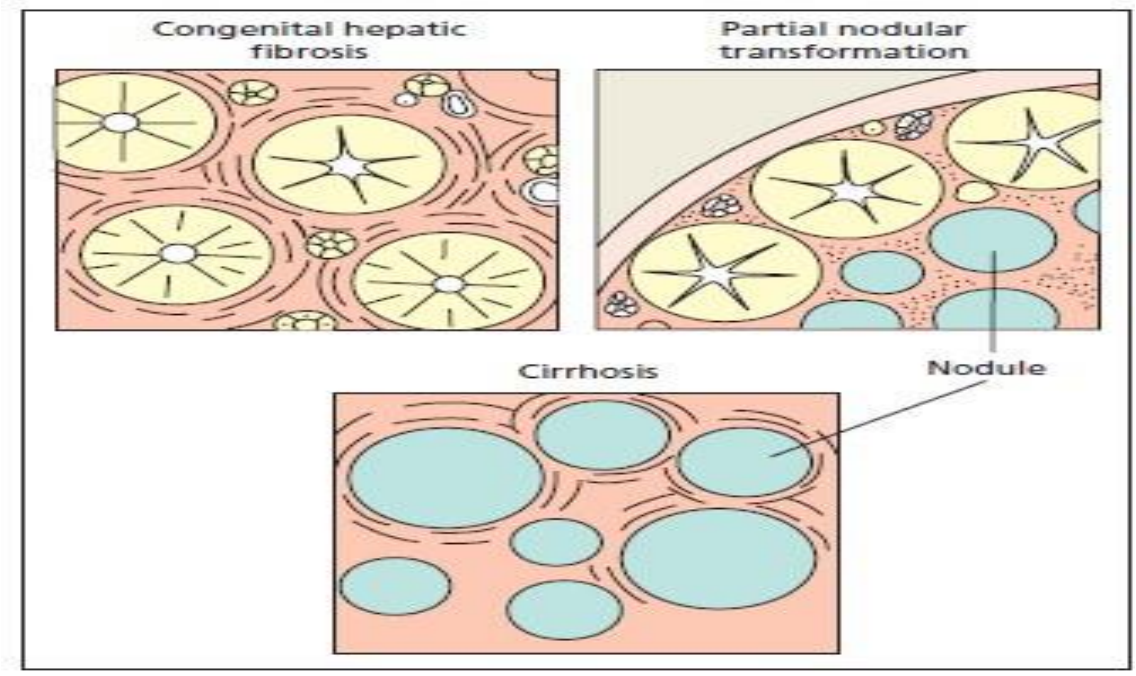
The common features of these noninvasive means that prediction of esophageal varices is reproducible, cost effective, simple and quick with no additional burden to patients. Even though these variables are clearly preferable to patients, none is comparable to UGIE in terms of sensitivity and specificity in prediction of variceal hemorrhage. To improve the sensitivity and specificity in variceal prediction, several predictive models are proposed using various combinations of the above variables. Apparently, the sensitivity and specificity of the currently proposed predictive models varies with population, the etiologies of liver cirrhosis and the severity of liver disease.

AIMS AND OBJECTIVES

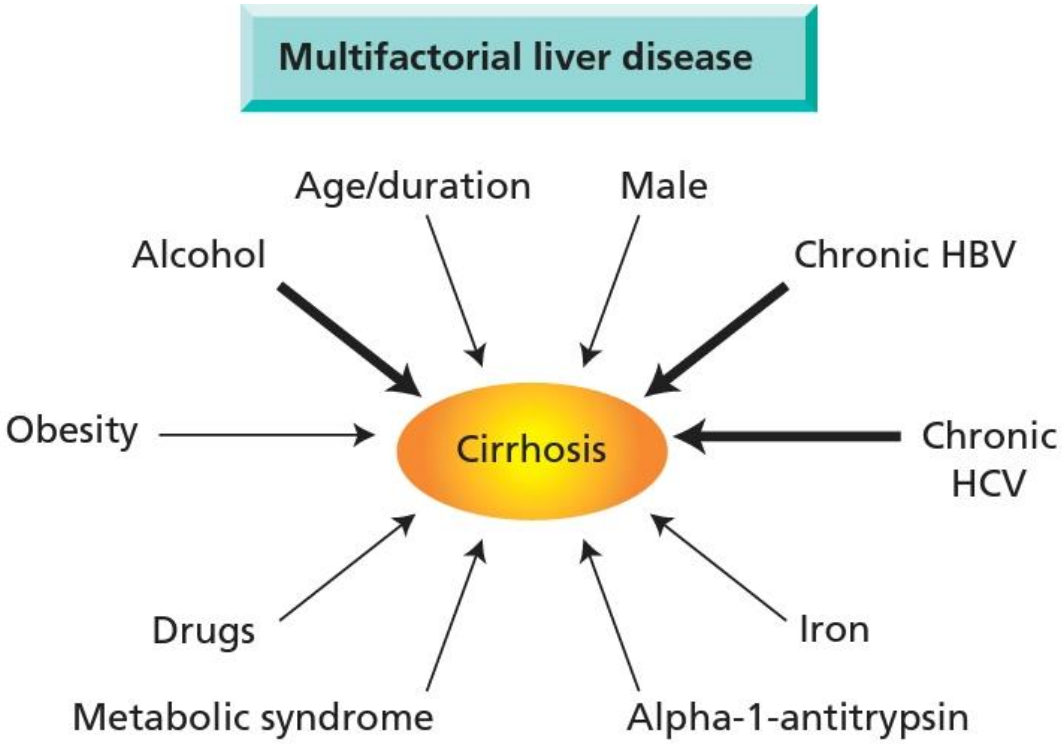
To identify and study noninvasive investigative parameters (clinical, biochemical, radiological) that could predict the presence and grades of oesophageal varices in cirrhosis patients.

REVIEW OF LITERATURE

Cirrhosis is a histopathologic diagnosis defined as diffuse hepatic fibrosis with the replacement of normal liver architecture by micro or macro nodules as a result of a wide range of chronic liver illnesses. The time it takes for chronic liver disease to progress to cirrhosis varies widely, depending on the underlying cause, such as weeks in patients with total biliary blockage to decades in individuals with chronic hepatitis C. Cirrhosis was once assumed to be incurable; however, fibrosis can be reversed if the underlying insult that created the cirrhosis is eliminated. This is seen in the successful treatment of chronic hepatitis C, hemochromatosis, and patients with alcoholic liver disease who have stopped drinking, as well as biliary obstruction.



CAUSES OF CIRRHOSIS



Alcoholic cirrhosis, NASH cirrhosis (non-alcoholic steatohepatitis), and viral cirrhosis, particularly hepatitis C, are all on the rise in developed countries. Hepatitis B and C are the most common causes in developing countries, although alcohol and autoimmune diseases are also on the rise. Cirrhosis can be caused by a number of factors, including:

1. alcoholism
2. chronic viral hepatitis (hepatitis B and C)
3. autoimmune hepatitis
4. biliary cirrhosis (primary cirrhosis, primary sclerosing cholangitis, and autoimmune cholangiopathy)
5. NASH (non-alcoholic steatohepatitis)

6. Cardiac cirrhosis
7. Hepatic metabolic disease that is hereditary (hemochromatosis, wilsons disease, alpha 1 antitrypsin deficiency,)
8. Cirrhosis due to cryptogenic cirrhosis

Cryptogenic cirrhosis is a term used to describe cirrhosis that has no identified origin (up to 20% of cases).

MORPHOLOGICAL CLASSIFICATION

It can classified based on the nodular size.

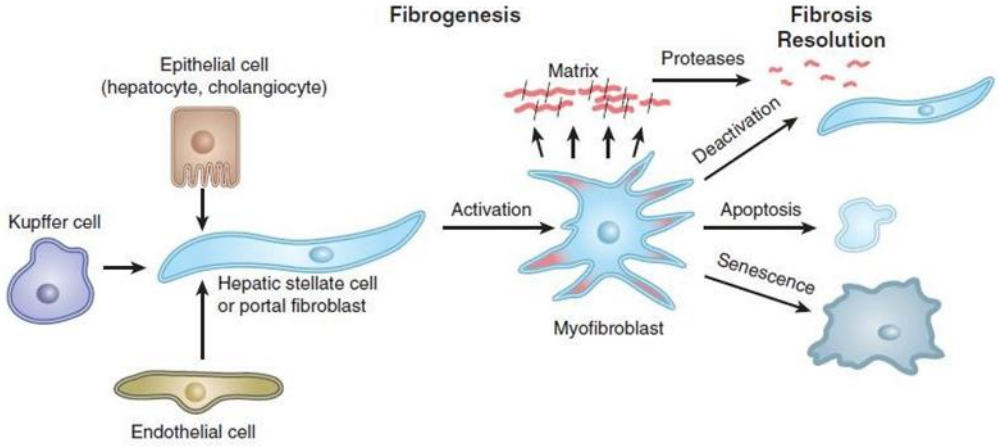
Nodules <3mm are said to be micronodular and >3mm as macronodular

1. Micronodular or Laennecǁs cirrhosis

2. Macronodular cirrhosis

3. Mixed type

PATHOGENESIS



Fibrosis is caused by the conversion of hepaticstellate cells to myofibroblasts, which results in the synthesis of more collagen and other extracellular matrix components, causing architectural distortion and a loss in function and bulk.

CLINICAL FEATURES

Patients may present for the first time with the complications of cirrhosis or may be asymptomatic and incidentally be identified during checkup for unrelated causes or because of abnormal liver tests

In clinical terms., cirrhosis is classified in to

- Compensated form and
- Decompensated form,

Cirrhosis worsened by one or more of the following symptoms, such as jaundice, ascites, hepatic encephalopathy, and bleeding varices, is referred to as decompensation. Decompensation is frequently preceded by ascites, but in compensated cirrhosis, these characteristics, as well as any complications related to Portal hypertension, are absent. Because of the implications for prognosis and therapy, this distinction is critical in clinical practise. Patients with compensated cirrhosis have a 50% ten-year survival rate, whereas those with decompensated cirrhosis have a 50% 18-month survival rate. When the inciting or precipitating reason is removed, a decompensated patient may become compensated, and the prognosis may improve.

COMPENSATED CIRRHOSIS

Patients may be asymptomatic or have non-localizing symptoms, or they may be picked up by chance due to changes in biochemical parameters or imaging examinations. Fatigue, anorexia, weight loss, flatulence, dyspepsia, and stomach pain are some of the symptoms that patients may experience.

Palmar erythema, pedal oedema, and spider naevi are all signs of cirrhosis. An epigastric mass, which is the enlarged left lobe of the liver, and splenomegaly may be discovered during an abdominal examination. Biochemical testing in this group are normally within normal norms. Mildly increased transaminases, or GGT, is the most common LFT anomaly in this population.

DECOMPENSATED CIRRHOSIS

Ascites, jaundice, altered sensorium, and other symptoms are common in these patients. Decreasing blood pressure — with progression of cirrhosis, mean arterial pressure often decreases. Hypertensive patients may become normotensive.

Patients can have mild fever (37.5 -38*C). This is probably because of bacteremia due to gram negative organisms. Ongoing hepatocyte necrosis and development of hepatocellular carcinoma may also contribute.

SYMPTOMS:

Patients may present with symptoms such as jaundice, pedal edoema, abdominal distension, and pruritis. Malena and hematemesis are the most typical side effects of an upper GI bleed. Hepatic encephalopathy causes changes in the sensorium, ranging from sleep problems to florid disorientation and coma. Anovulation is a common cause of menstrual irregularity in women. Impotence, decrease of sexual drive, testicular atrophy, and infertility are all symptoms of hypogonadism in men.

The development of ascites and bleeding from esophagogastric varices, which renders cirrhosis decompensated, is due to portal hypertension, which is a complicating aspect of decompensated cirrhosis.

GENERAL EXAMINATION:

Reduced blood pressure - as cirrhosis progresses, mean arterial pressure frequently drops. Patients who are hypertensive may become normotensive.

Patients may get a slight fever (37.5-38°C). This is most likely due to bacteremia caused by gram-negative bacteria. Ongoing hepatocyte necrosis and development of hepatocellular carcinoma may also contribute.

Jaundice (This happens once the functional impairment due to hepatocyte destruction has exceeded the process of regeneration. The deeper the jaundice, more severe is hepatic decompensation)

Dermatologic findings:

- Bronze piginentation of the skin, which occurs in hemochromatosis, may shed light on the pathogenesis.
- The presence of *"vascular spiders"* (arterial spiders/spider naevi / spider telengiectasia spider angioma) in the distribution of venous drainage areas of the superior vena cava is visible. New spiders may emerge as liver function deteriorates. They're more often linked to alcoholic cirrhosis. They're common throughout pregnancy and in some healthy people. Multiple spiders and clubbing are signs of hepatopulmonary syndrome.
- *Palmar erythema*: palms are warm and red, especially around the thenar eminence, hypothenar eminence, and finger pulp.
- Both arterial spiders and palmar erythema may be caused by an overabundance of oestrogen. In the liver, estrogens are inactivated. The level of estradiol in the blood is normal, but the level of free testosterone in the blood is low. As a result, the high estradiol/free testosterone ratio could be a factor in these findings.
- Hypoalbuminemia could be linked to leukonychia.
- Clubbing‖ can occur pan digitally especially with development of hepato pulmonary syndrome or in cystic fibrosis.‖Hypertrophic osteoarthropathy‖ has also been observed.

- Dupuytrens contracture‖ may be present.This is characterized by thickened
- palmar fascia resulting from unorganized proliferation of the fibroblasts.

Chest findings:

- In males, gynecomastia can appear alongside other signs of feminization, such as a change in pubic hair pattern, axillary hair loss, and chest hair loss. Because androstenedione, which is produced by the adrenals, is aromatized into estrone, which is then converted to estradiol in the adipose tissue.

Abdominal findings-

Abdominal examination may reveal the presence of ascites, hepatomegaly, splenomegaly, and dilated abdominal wall veins.

- Ascites refers to excessive collection of peritoneal fluid. In massive ascites fluid thrill may be present where as in moderate ascites shifting dullness is to be elicited. If flanks are full it is probably due to ascites and not fat
- Hepatomegaly is a condition in which the cirrhotic liver is enlarged, shrinking, or normal in size. Palpation reveals a solid, nodular consistency. As the assessment of liver size correlates less reliably with

imaging investigations, features such as form and consistency should be valued more on palpation. A palpable liver in cirrhosis usually indicates alcoholic liver disease, primary biliary cirrhosis, hemochromatosis, hepatocellular carcinoma, and Budd Chiari syndrome.

- Splenomegaly is a symptom of cirrhosis caused by congestion caused by portal hypertension. However, there is a poor association between splenic size and portal pressure, implying that other factors may be at play.
- Caput medusae - When portal hypertension develops, portal venous blood is transmitted through the periumbilical veins to the umbilical vein, which becomes patent in cirrhosis, and then to the upper and lower abdominal veins, where it enters the systemic circulation. These veins enlarge and become more visible. As a result, portal blood is diverted to systemic circulation. Because it resembles the head (Caput) of the mythological Gorgon Medusa, it is known as caput medusae.
- Dilated abdominal veins caused by SVC and IVC blockage should be distinguished from cirrhosis-related dilated veins. The direction of flow must be examined in order to determine the reason of blockage. The blood flow in an IVC obstruction is below upwards, however in cirrhosis, the blood flow is away from the cause of obstruction, and the

direction of flow must be determined. The flow is downwards when the IVC is obstructed. Due to the lack of valves in these veins in both scenarios, the flow may be bidirectional, and the test may be deceptive. Furthermore, due to blockage, dilated veins are more typically found in the back and loin.

- Peptic ulcer occur in 11% of cirrhosis patients. In comparison to stomach ulcers, duodenal ulcers are more common. In cirrhosis, helicobacter pylori colonisation is greater than in the general population. Patients with ascites are more likely to develop abdominal hernias. Only if they are bad enough to cause death in alcoholics should they be corrected. Because alcoholic cirrhosis patients with stomach discomfort may have associated chronic pancreatitis that might return, this should be considered a differential diagnosis.

Neurological findings

- Changes in sleep patterns
- Changes in thinking
- Forgetfulness
- Personality or mood changes
- Poor concentration and judgment
- Worsening of handwriting or loss of other small hand movements

- Abnormal movements or shaking of hands or arms
- Agitation, excitement, or seizures (occur rarely)
- Disorientation
- Drowsiness or confusion
- Slurred speech

Genitourinary findings - Testicular atrophy in males.

Endocrine changes - Hyperglycemia occurs in about 80% of cirrhotic patients in the form of glucose intolerance. Only around 10-20% are truly diabetic.

INVESTIGATIONS*:*

LIVER FUNCTION TEST ABNORMALITIES-

Aminotransferase (ALT) is raised higher than AST in chronic hepatitis. As hepatitis advances to cirrhosis, AST rises faster than ALT, reversing the ratio of AST to ALT from I to higher than 1. The enzymes in cirrhosis patients might be within normal ranges or considerably increased.

Alkaline phosphatase‖ - Alkaline phosphatase enzyme is elevated 2 to 3 times normal in cirrhosis. If elevated more than that, primary biliary cirrhosis or sclerosing cholangitis should be considered as the etiology.

GGT and alkaline phosphatase levels are frequently raised in proportion. In the case of alcoholic liver disease, GGT levels will be

abnormally high. Alcohol use increases the amount of GGT in the rnicrosomes. Bilirubin levels are frequently normal in the compensated stage of cirrhosis. Decompensation is defined as an increase in bilirubin levels, which is one of the prognostic indications in the Child Pugh score. Albumin is a protein that is only synthesised in the liver. Cirrhosis is deteriorating owing to a deterioration in the liver's synthetic function. Albumin levels are also depleted. In the kid pugh score system, it is also one of the prognostic indications for survival.

Prothrombin time‖ -Many of the coagulation factors are synthesized in liver. Prothrombin time which measures the extrinsic coagulation pathway, is a marker for the synthetic function of the liver. Thus coagulopathy worsens as cirrhosis progresses.

Serum electrolytes – "hyponatremia‖ can occur in patients with ascites. Severity can be correlated with worsening cirrhosis**.**

Hematologic abnormalities

- Thrornbocytopenia, anaemia, and leucopoenia are all possible side effects. Thrombocytopenia is the first anomaly to appear and is a predictor of the development of portal hypertension. In asymptomatic compensated cirrhosis, pancytopenia might even be the presenting characteristic. This is due to the cells being sequestered in the larger spleen. The platelet count should never go below 50,000. This does not

induce bleeding in and of itself, but it might increase bleeding in the context of coagulopathy.

- Anemia in cirrhosis is mainly because of upper G1 bleed. Anemia can also be present as a result of direct suppression of bone marrow by alcohol,splenic sequestration and hemolysis, folate deficiency

Other abnormalities - In cirrhosis, the globulin levels are high. This is because of shunting of bacterial antigens in the portal venous blood which are normally filtered by the liver in to systemic circulation leading which induces production of immunoglobulins. Marked elevations of IgG may point towards the presence of autoimmune hepatitis.

IMAGING MODALITIES:

- **Ultrasonography -** Ultrasonography is a non-invasive routinely used investigation to diagnose cirrhosis. The size of the liver, the nodularity, the portal vein diameter, presence of ascites and splenomegaly can be assessed. Doppler studies to check the direction of blood flow in the portal vein aids in the diagnosis of portal hypertension. Presence of HCC and portal vein thrombosis can also be made out**.**
- MRI may be useful in hermochromatosis to reveal iron overload. MRA can determine portal vein flow and dynamics.

- CT is not the first choice in the diagnosis of cirrhosis. It may be useful when investigating liver malignancy or secondaries or pancreatic pathology
- Elastography to assess the stiffness of the liver tissue is also available.
- Liver biopsy**:** A liver biopsy is the gold standard test for cirrhosis diagnosis. Cirrhosis is now diagnosed without the need for a liver biopsy In only rare cases, such as demonstrating the underlying metabolic aetiology of cirrhosis, such as NASH, Wilson disease, hemochromatosis, or alpha 1 antitrypsin deficiency, may a liver biopsy be required.

COMPLICATIONS OF CIRRHOSIS

- Ascites,
- Spontaneous bacterial peritonitis,
- Hepatic encephalopathy,
- Portal hypertension,
- Variceal bleeding
- Hepatorenal syndrome.
- Hepatocellular carcinoma.

PORTAL HYPERTENSION:

The rise of the hepatic venous pressure gradient (HVPG)>5 mmHg is described as portal hypertension.

Portal hypertension is caused by two mechanisms that occur at the same time:

1. Fibrosis and regenerating nodules affect the architecture of the liver, resulting in increased resistance to portal blood flow.
2. Splanchnic vasodilation causes increased blood flow.

The causes of portal hypertension are divided into pre-hepatic, post hepatic and intrahepatic causes.

Thrombosis of the portal vein and thrombosis of the splenic vein are pre-hepatic factors that result in sinistral hypertension or left sided portal hypertension. Cirrhosis, pancreatitis, abdominal trauma, infection, or haematological reasons such as essential thrombocytosis, polycythemia vera, and protein C and S deficiency can all induce portal vein thrombosis.

The hepatic veins and venous outflow into the heart are affected by post-hepatic causes. Budd Chiari syndrome, veno occlusive disease, constrictive pericarditis, persistent right sided congestion, and restrictive cardiomyopathy are among the conditions. Pre-sinusoidal causes include schistosomiasis and congenital portal fibrosis, as well as post-sinusoidal causes include veno-occlusive disease and cirrhosis, which cause the sinusoidal type of portal hypertension.

The primary complications of portal hypertension include ascites, bleeding varices splenomegaly, hypersplenism etc. Splenomegaly results from congestion due to increased portal pressure. Hypersplenism with development of thrombocytopenia may be the first presentation of portal hypertension even before ascites may develop.

PATHOPHYSIOLOGY:

Increased intrahepatic resistance and increased portal blood flow cause portal hypertension. Hepatic compliance diminishes as hepatic resistance increases. Small variations in blood flow occur when portal pressure rises. It is adaptable to a healthy liver. However, in the cirrhotic liver, it can have a significant stimulatory effect on portal pressure.

The portal venous inflow increases as a result of the hyperdynamic state. New vessels emerge from the dilated collateral vessels. The flow from high-pressure portal veins to low-pressure systemic veins is increasing. Esophageal varices can develop as a result of angiogenesis and collateral vessel development. Mechanical and vascular variables are the primary causes of variations in portal flow and resistance. The cirrhotic liver's fibrosis and nodularity, as well as the vascular architecture distortion and remodelling that occur in the systemic and splanchnic vascular systems in response to the chronic increases in flow and shear stress that characterise the "hyperdynamic circulatory state," are examples of "mechanical factors."

Intrahepatic vasoconstriction, which contributes to increased intrahepatic resistance, and splanchnic and systemic vasodilation, which accompany the hyperdynamic circulatory state, are two vascular factors. The decrease in the synthesis of the vasodilator NO and the increase in the production of the vasoconstrictor ET-1 are the key contributors to the increase in hepatic vascular resistance.

Other vasoactive mediators involved in the development of increased intrahepatic resistance in cirrhosis include cysteinyl leukotrienes, thromboxane, angiotensin, and hydrogen sulphide.

Peripheral and splanchnic vasodilation, lower mean arterial pressure, and enhanced cardiac output are all characteristics of the hyperdynamic circulation. Vasodilation allows more systemic blood to flow into the portal circulation, particularly in the splanchnic bed. Splanchnic vasodilation is largely generated by splanchnic arteriole relaxation and subsequent splanchnic hyperemia. Excess NO production by splanchnic vascular endothelial cells is principally responsible for splanchnic vasodilation and increased portal venous inflow, according to studies of experimental portal hypertension.

In the splanchnic and systemic circulation, excess NO production leads to vasodilation, hyperdynamic circulation, and hyperemia, in contrast to the hepatic circulation, where NO deficit leads to increased intrahepatic resistance. The vascular variables that produce portal hypertension are

especially relevant since they are both reversible and dynamic, making them attractive targets for experimental therapeutics

Because one-third of cirrhotic patients have gastric and esophageal varices, upper GI endoscopy is now required to screen all patients with established cirrhosis for the presence of varices. The extent of the varices, the severity of cirrhosis, tense ascites, and higher wedged hepatic vein pressure all influence the likelihood of variceal bleed. The presence of thrombocytopenia, an enlarged spleen, encephalopathy, the development of ascites, and esophageal varices with or without bleeding can all indicate the development of portal hypertension in individuals with liver cirrhosis. In dubious circumstances, a CT or MRI scan of the abdomen, as well as an interventional radiological procedure, can be used to determine the free and wedged hepatic vein pressures, as well as the gradient between the two. It is usually 5 mm Hg, but if it exceeds 12 mm Hg, it indicates a higher risk of bleeding. When bleeding occurs, the first step is to stop the bleeding, followed by prophylaxis to prevent more bleeding. Intravenous fluids and blood products, as well as octreotide at a rate of 50-100 micrograms per hour, are used for acute care. After that, the varices are destroyed using endoscopic variceal band ligation. Beta-blockers that are not selective can be used as a medicinal prophylactic. TIPS can be used if this manner of management fails.

GASTROESOPHAGEAL VARICES:

Varices are dilated, tortuous veins that typically occur within the oesophagus and stomach of cirrhotic patients. They are porto-systemic collaterals, which are vascular channels that connect the portal venous and systemic venous circulations and form as a result of portal hypertension (a dreaded cirrhosis complication), primarily in the lower esophageal submucosa but also in the stomach.

Portal collaterals can be found in the following locations:

1. Oesophageal and stomach varices
2. Hemorrhoids.
3. Caput medusae.
4. Retroperitoneal sites

Esophageal varices rupture and bleeding are connected with a significant mortality risk. Despite advances in diagnosis and treatment, the fatality rate for variceal haemorrhage remains significant (20%-35%). 10–30% of all cases of UGI bleeding are caused by variceal bleeding.

A patient with cirrhosis who does not have varices has not yet developed portal hypertension, or his or her portal pressure is not yet high enough for varices to form. Small varices begin to form as portal pressure rises. Blood flow via the varices will rise over time as circulation improves,

resulting in the creation of massive varices. The rupture of varices occurs when the expanding force surpasses the maximal wall tension, resulting in hemetemesis.

The annual rate of varices development in people with cirrhosis is roughly 5–8%, however only 1–2% of the time the varices are large enough to cause bleeding. Each year, between 4–30 percent of patients with tiny varices will become major varices, putting them at risk of bleeding. Variceal haemorrhage occurs at a yearly rate of 5-15 percent , and 6-week mortality after variceal haemorrhage is about 20 percent . In general, variceal bleeding resolves spontaneously in 40-50 percent of patients, although frequency of early rebleeding ranges between 30 percent and 40 percent within first 6 weeks, and about 40 percent of all rebleeding episodes occur within the first 5 days

Gastric varices (GV) bleed less frequently than esophageal varices, accounting for 10-30% of variceal haemorrhages. Gastric variceal haemorrhage, on the other hand, is more severe and has a greater death rate. Furthermore, a large percentage of patients, between 35 and 90 percent, rebleed after spontaneous hemostasis. The severity of liver disease is linked to the occurrence of gastric varices. The Child–Pugh classification system can be used to determine the severity of cirrhosis. Varices can affect 40 percent of Child–Pugh A patients and 85 percent of Child–Pugh C patients.

PATHOPHYSIOLOGY:

The development of esophageal varices is influenced by four unique zones of venous drainage at the gastroesophageal junction. The gastrointestinal zone, which extends 2 to 3 cm below the gastroesophageal junction, is made up of longitudinal veins in the submucosa and lamina propria. They join at the top of the stomach's cardia and drain into the short gastric and left gastric veins. The palisade zone reaches 2 to 3 cm into the lower oesophagus from the gastric zone. This zone has four groups of veins that run longitudinally and parallel to the oesophagus mucosal folds. These veins join up with veins in the lamina propria to form an anastomosis.

Because the perforating veins in the palisade zone do not connect with the distal oesophagus’s extrinsic (periesophageal) veins, there is a higher risk of bleeding. Between the portal and systemic circulations, the palisade zone is the most important watershed area.

The oesophagus’s 'perforating zone,' which has a network of veins, is closer to the palisade zone. These veins are called "perforating veins" because they connect the veins in the oesophagus submucosa with the exterior veins. They are less likely to be longitudinal. The longest zone, the truncal zone, is about 10 cm long and is positioned proximal to the perforating zone in the oesophagus

It is usually characterised by four longitudinal veins in the lamina propria, which are unlikely to bleed. Because the periesophageal veins drain into the azygos system, portal hypertension is characterised by an increase in azygos blood flow. The venous drainage of the lower end of the oesophagus is through the coronary vein, which also drains the cardia of the stomach, into the portal vein

The fundus of the stomach drains through short gastric veins into the splenic vein. In the presence of portal hypertension, varices may therefore form in the fundus of the stomach. Splenic vein thrombosis usually results in isolated —gastric fundal varices. Because of the proximity of the splenic vein to the renal vein, spontaneous splenorenal shunts may develop and are more common in patients with gastric varices than in those with esophageal varices‖.

A portal pressure gradient of at least 10 mm Hg is required for the formation of gastroesophageal varices. Further more, varices are assumed to require a portal pressure gradient of at least 12 mm Hg to bleed; other local factors that enhance variceal wall tension are also necessary because not all patients with a portal pressure gradient of greater than 12 mm Hg bleed. In the framework of Laplace's law, factors that influence variceal wall tension might be considered.

Laplace's law

$$T = Pr/w$$

T is variceal wall tension

P is the transmural pressure gradient between the variceal and esophageal lumen

r is the variceal radius

w is the variceal wall thickness

When the variceal wall thins and the varix increases in diameter and pressure, the tolerated wall tension is exceeded and the varix ruptures.

These physiologic observations are manifested clinically by the observation that patients with larger varices (r) in sites of limited soft tissue support (w), with elevated portal pressure (P), tend to be at greatest risk for variceal rupture from variceal wall tension (T) that becomes excessive. One notable site in which soft tissue support is limited is at the gastroesophageal junction.

The absence of tissue support and high vessel density at the gastroesophageal junction may contribute to a higher frequency of bleeding from varices. Measurement of portal pressure by HPVG, splenic pulp pressure, direct portal vein pressure, and other methods can be used to determine the severity of portal hypertension.

Prognostic Value of HVPG in Patients with Chronic Liver Disease	
Measurement	**Significance**
1-5 mm Hg	Normal
≥ 6 mm Hg	Risk of disease progression in persons with HCV recurrence after liver transplantation
≥ 10 mm Hg	Clinically significant portal hypertension
≥ 12 mm Hg	Increased risk for rupture of varices
≥ 16 mm Hg	Increased risk of mortality
≥ 20 mm Hg	Treatment failure and mortality in acute variceal bleeding

DIAGNOSIS OF VARICES:

Upper GI endoscopy is the most common and gold standard procedure for detecting varices. All patients with liver cirrhosis should have an endoscopy to check for esophageal varices, . Surveillance endoscopies are advised depending on the severity of cirrhosis and the existence and extent of varices.

Compensated cirrhosis and No varices - Every 2–3 years

Compensated cirrhosis with small varices - Every 1–2 years

Decompensated cirrhosis - Yearly intervals

In patients who are not candidates for upper endoscopy, alternative screening modalities include wireless video capsule endoscopy, CT imaging, Doppler ultrasonography, radiography/barium swallow of the oesophagus and stomach, and portal vein angiography and manometry.

ESOPHAGEAL VARICES

The grading of esophageal varices by endoscopy is subjective. To try to standardise the reporting of esophageal varices, many criteria have been utilised. The criteria developed by the Japanese Research Society for Portal Hypertension are the most widely used.

red color signs	location of the varix
color of the varix	form (size) of the varix

Red color signs include

- red wale marking, which are longitudinal whip-like marks on the varix
- diffuse redness
- cherry-red spots‖, which usually are 2 to 3 mm or less in diameter
- hematocystic spots, which are blood-filled blisters 4 mm or greater in diameter

The color of the varix can be white or blue

The form of the varix at endoscopy is described most commonly as

- small and straight(grade I)
- tortuous and occupying less than one third of theesophageal lumen (grade II)

- large and occupying more than one third of the esophageal lumen (grade III).

The oesophagus can have varices in the lower third, middle third, or upper third. The size of the varices in the bottom portion of the oesophagus is the most essential of the aforementioned characteristics. During the removal of the endoscope, the size of the varices in the lower portion of the oesophagus is measured. Small varices have a diameter of less than 5 mm, while large varices have a diameter of more than 5 mm.

Another grading which is used in this study is the Paquet classification, where varix size is graded on a 4-point Likert scale

Paquet classification

- grade 1 varices are small and flattened by insufflation of air;
- grade 2 varices are slightly larger and do not flatten;
- grade 3 varices are larger but do not touch in the middle of the lumen.
- grade 4 varices are large and touch each other in the middle of the lumen

Grade 1 and 2 are small varices and grade 3 and 4 are large varices. Others are two size, three size classifications. Patients with large esophageal varices, Child-Pugh class C cirrhosis, and red color signs on varices have the highest risk of variceal bleeding within 1 year.

The progression of tiny to large varices is linked to

- Child-Pugh B/C (decompensated cirrhosis)
- Red wale marks on baseline endoscopy (longitudinal dilated venules resembling whip marks on the variceal surface)
- Alcoholic cirrhosis

On endoscopy, variceal bleeding is detected by one of the following findings:

- Varices with no other potential cause of bleeding
- Active bleeding from a varix
- White nipple covering a varix
- Clots overlying a varix

The following are risk factors for an initial variceal bleeding episode includes:

- big varices with red colour signals (>5 mm)
- a high MELD or CTP score
- consuming alcohol indefinitely
- a high HVPG of more than 16 mm hg
- coagulopathy

GASTRIC VARICES:

For, Gastric varices there are three forms of classification that are typically utilised.

1. The classification of Sarin

2. Classification of rhizomes

3. The classification of Arakawa.

Most commonly used classification is Sarin’s classification of GV

SARIN’S CLASSIFICATION

Gastric varices are less common than esophageal varices and are seen in 5-33 percent of patients with portal hypertension, with a documented bleeding rate of roughly 25% in two years, with fundal varices having a higher bleeding rate.

Gastric varices are divided into four groups based on their relationship to esophageal varices and where they are located in the stomach.

The esophageal-paraesophageal varices (gastroesophageal venous system), the inferior phrenic vein (IPV) (gastrophrenic venous system), or both, empty GV into the systemic circulation. These drainage types roughly conform to Sarin et al classification.'s system. GOV1 drains through the esophageal and paraesophageal varices, IGV1 through the left IPV, and GOV2

through both the esophageal and paraesophageal varices and the IPV. GV originate at the hepatopetal collateral route, which develops as a result of localised portal hypertension, and drain into the gastric veins.

- Type 1 gastroesophageal varix (GOV): Esophageal varices extend along the lesser curve.
- Type 2 gastroesophageal varix: esophageal varices extend along the great curvature.
- Isolated gastric varix (IGV) type 1 - Stomach varices.
- Isolated gastric varix type 2: Varices in duodenum .

The size of fundal varices (large, medium, and small, defined as 10 mm, 5-10 mm, and 5 mm, respectively), Child class (C,B,A), and endoscopic presence of variceal red spots (defined as a localised reddish mucosal area or spots on the mucosal surface of a varix) are all risk factors for gastric variceal haemorrhage.

TREATMENT :

The goal of treatment for portal hypertension is to reduce portal blood flow with pharmacologic agents like beta blockers or vasopressin and its analogues, or to decrease intrahepatic resistance with pharmacologic agents like nitrates, or to create a portosystemic shunt with radiologic or surgical

means. Endoscopic or radiologic procedures can also be used to target the varices for treatment.

ENDOSCOPIC THERAPIES -

Sclerotherapy or endoscopic variceal ligation (EVL)‖, are local therapies that have no effect on either portal flow or resistance.

Except where low visibility prevents efficient band ligation of bleeding varices, endoscopic sclerotherapy has generally been replaced by endoscopic band ligation. A sclerosant is injected into (intravariceal) or close to (paravariceal) a varix in this procedure. Sodium tetradecyl sulphate, sodium morrhuate, ethanolamine oleate, and pure alcohol were utilised as sclerosants. Retrosternal pain, sclerosant-induced esophageal ulcer-related haemorrhage, strictures, and perforation are all possible complications.

VARICEAL LIGATION:

The preferred endoscopic approach for controlling acute esophageal variceal bleeding and preventing rebleeding is endoscopic variceal ligation; however, the efficacy of band ligation in the treatment of gastric varices is limited. Injection sclerotherapy is more difficult to execute than variceal ligation. The varix is suctioned into a cap attached to the endoscope's tip, and a band is placed around it. The band suffocates the varix, resulting in thrombosis.

Multi-band devices allow you to apply multiple bands without having to remove and re-insert the endoscope. The gastroesophageal junction is first banded, and then more proximal varices are banded in a spiral at intervals of roughly 2 cm before the endoscope is withdrawn. Banding is not required for varices in the mid- or proximal oesophagus. Endoscopic variceal ligation has fewer side effects than sclerotherapy, and it takes fewer sessions to achieve variceal obliteration. Furthermore, unlike sclerotherapy, esophageal variceal ligation after an acute haemorrhage does not result in a prolonged increase in HVPG.

Endoscopic variceal ligation is less likely than sclerotherapy to cause local problems such as esophageal ulcers, strictures, and dysmotility. If stomach fundal varices are banded, banding-induced ulcers can be severe and potentially fatal. After variceal ligation, a PPI is frequently indicated. Snare drums with detachable snares and clips are generally not recommended.

SHUNTING THERAPY

By bypassing the point of increased resistance, either radiologically (transjugular intrahepatic portosystemic shunt) or surgically, portal pressure is significantly reduced.

PHARMACOLOGIC THERAPY:

It consists of splanchnic vasoconstrictors (vasopressin and analogues, somatostatin and analogues, nonselective beta-blockers) and venodilators

(vasopressin and analogues, somatostatin and analogues, nonselective beta-blockers) (nitrates). Vasoconstrictors reduce portal venous inflow by causing splanchnic vasoconstriction. Venodilators work by lowering intrahepatic and/or portocollateral resistance in the liver.

Drugs that lower the flow of blood through the portal vein

- Agents that inhibit beta -adrenergic receptors in a non-selective manner
- Somatostatin and its derivatives
- vasopressin and terlipressin

Drugs that lower intrahepatic resistance,

- Nitrates
- 1-adrenergic blockers (e.g., prazosin)
- Angiotensin receptor blockers

Moreover, all venodilators (e.g., isosorbide mononitrate) have a systemic hypotensive action, and the decrease in portal pressure appears to be more due to hypotension (i.e., a decrease in flow) than resistance. The use of a vasoconstrictor and a vasodilator together reduces portal pressure in a synergistic manner.

Vasopressin is a endogenous peptide hormone produced by the body that causes splanchnic vasoconstriction, decreases portal venous inflow, and

lowers portal pressure. This medication has a lot of systemic side effects. Another semisynthetic counterpart with less negative effects is terlipressin.

Somatostatin is a peptide with 14 amino acids. Somatostatin has a half-life in the circulation of 1 to 3 minutes after IV injection, hence longer-acting analogues of somatostatin have been developed. Octreotide, lanreotide, and vapreotide are the most well-known analogues. By suppressing the release of glucagon, somatostatin lowers portal pressure and collateral blood flow. Somatostatin also lowers portal pressure by lowering splanchnic blood flow after a meal.

Following iv administration**, octreotide** has a half-life in the circulation of 80 to 120 minutes. However, it has a short-term effect on portal pressure. Furthermore, although lowering the postprandial increase in portal pressure, continuous octreotide infusion did not lower portal pressure. Long-acting octreotide does not reliably lower portal pressure, and higher doses have side effects that make it unsuitable for treating portal hypertension. Somatostatin or octreotide may be as effective as terlipressin or sclerotherapy in reducing acute variceal bleed, according to several randomised controlled trials. In clinical practise, somatostatin or octreotide is used in conjunction with endoscopic variceal haemorrhage treatment.

Carvedilol is a medication that acts as a nonselective -blocker as well as a weak - receptor blocker. -In the intrahepatic circulation, receptor

activation generally increases resistance. As a result, blocking the -receptor lowers intrahepatic vascular resistance, which lowers portal pressure even further. Carvedilol has antioxidant and antiproliferative properties, and it may be more effective than endoscopic variceal ligation in preventing a first variceal bleed. Carvedilol has been shown to reduce variceal rebleeding as effectively as a combination of nadolol and isosorbide mononitrate, with less adverse effects. Carvedilol is begun at a dose of 6.25 mg once a day and gradually increased to a maximum dose of 25 mg once a day. Arterial hypotension frequently limits dose increases.

Propranolol or **nadolol** are nonselective beta blockers that are recommended. The heart's cardiac output is reduced when 1adrenergic receptors are blocked. Blocking 2-adrenergic receptors, which promote vasodilation in the mesenteric circulation, permits 1-adrenergic receptors to act unopposed, resulting in a reduction in portal flow. A drop in portal pressure is caused by a combination of decreased cardiac output and decreased portal flow. Monitoring the HVPG is the most precise way to determine how effective beta blockers are. The initial hemodynamic response (a decrease in HVPG of 12 mm Hg, or 10%) 20 minutes after IV propranolol administration can be utilised to predict long-term bleeding risk reduction. When hepatic function deteriorates, the benefit of beta blockers is reduced. The most

common way to check for beta blocker efficacy is to look for a drop in heart rate, which is a measure of 1-adrenergic receptor blockade.

Nitrates- Vasodilation is caused by either short-acting (**nitroglycerin**) or long-acting (**isosorbide mononitrate**) nitrates. A reduction in intracellular calcium in vascular smooth muscle cells causes vasodilation. Nitrates cause venodilation rather than arterial dilation, and thus lower portal pressure by reducing portal venous blood flow. A combination of nitroglycerin and vasopressin has been used to control acute variceal haemorrhage. If the systolic blood pressure is greater than 90 mm Hg, the rate of **nitroglycerin** infusion is **50 to 400 mcg per minute**; nevertheless, the combination of vasopressin and nitroglycerin is rarely utilised currently. Nitrates are no longer indicated for primary prophylaxis to avoid initial variceal bleeding, either alone or in combination with a beta blocker. Isosorbide mononitrate may be given to a beta blocker for secondary prophylaxis (to avoid variceal rebleeding) if the beta blocker alone has not resulted in an adequate drop in HVPG.

BALLOON TAMPONADE AND STENTS

"Approximately 10% to 15% of individuals with acute variceal haemorrhage are resistant to pharmacologic and endoscopic therapy. Until TIPS can be carried out, balloon tamponade is utilised as a temporary treatment. Because varices are superficial and thin-walled, and blood flows

through submucosal veins, they are easily squeezed. The **Sengstaken-Blakemore tube** has three lumens: one for aspirating gastric contents, one for inflating a gastric balloon to a volume of 200 to 400 mL, and one for inflating an esophageal balloon. The Minnesota tube is a Sengstaken-Blakemore tube that has been modified. With any of these tubes, inflating a stomach balloon alone is desirable. In about 80 percent to 90 percent of patients, balloon tamponade can stop bleeding for up to 24 hours.

The use of an endotracheal tube reduces the risk of pulmonary aspiration. If bleeding persists after the tube is inserted, reinflate and adjust the stomach balloon before inflating the esophageal balloon. To tamponade esophageal varices, selfexpandable metallic coated stents have been employed due to the hazards involved with the deployment of tamponade balloons. These stents can be left in for up to two weeks before being withdrawn.

TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

A transjugular intrahepatic portosystemic shunt (TIPS) also known as a transjugular intrahepatic portosystemic stent shunt (TIPSS) – lowers portal pressure by connecting the hepatic vein to an intrahepatic branch of the portal vein. The shunt is inserted via a percutaneous transjugular technique. TIPS is a side-to-side portacaval shunt used to treat portal hypertension problems such as variceal haemorrhage and refractory ascites, as well as Budd-Chiari syndrome, hepatic hydrothorax, and hepatorenal syndrome.

TIPS has been used to control acute variceal bleeding and prevent variceal rebleeding when pharmacologic and endoscopic therapies have failed, particularly in patients with Child-Pugh class B or C cirrhosis, who are more likely than patients with Child-Pugh class A cirrhosis to have bleeding that is refractory to therapy. When compared to continued pharmacologic and endoscopic therapy, early TIPS (within 72 hours of control of variceal bleeding) in patients at high risk of rebleeding (Child-Pugh class C, class B with active bleeding, or a MELD score > 18 and a transfusion requirement of > 4 units of red blood cells [RBCs]) is associated with a lower rate of treatment failure and mortality, with no increased risk of hepatic encephalopathy. TIPS implantation is the conventional salvage treatment when bleeding from varices cannot be controlled following two sessions of endoscopic therapy within a 24-hour period.

The most common salvage treatment is TIPS placement. TIPS is also used to treat bleeding from isolated gastric fundal varices for both bleeding control and rebleeding prevention. TIPS cannot be advised as a first choice for preventing variceal rebleeding due to various problems; rather, it is reserved for patients who have failed endoscopic or pharmacologic therapy and have failed endoscopic or pharmacologic therapy.

SURGICAL THERAPY

There are three types of surgical treatments for portal hypertension:

• non-shunt procedures

• portosystemic shunt procedures

• a liver transplant

When noncirrhotic causes of portal hypertension and patients with Child-Pugh class A cirrhosis fail to respond to standard pharmacologic and endoscopic therapy, surgical techniques (other than liver transplantation) are utilised as salvage therapy. In all patients with cirrhosis and variceal haemorrhage, liver transplantation should be considered.

NON-SHUNT PROCEDURES :

Non-shunt procedures include esophageal transection‖ and gastroesophageal devascularisation‖. They are performed infrequently but may be required in selected cases.

SURGICAL SHUNTS:

The use of surgical shunts for refractory variceal haemorrhage has decreased dramatically as TIPS have become more widely available. Surgical shunts are almost exclusively used in children to treat refractory bleeding caused by noncirrhotic portal hypertension, such as congenital hepatic fibrosis and portal vein thrombosis. Selective shunts, such as distal

splenorenal shunts (WARRENS SHUNT), partial shunts, such as the side-to-side calibrated portacaval shunt, and whole portosystemic shunts, such as the side-to-side portacaval shunt or end-to-side portacaval shunt, are the three types of surgical portosystemic shunts.

GASTRIC VARICES TREATMENT:

- Endoscopic treatment modalities for gastric variceal bleeding.

1. Gastric variceal sclerotherapy (GVS).
2. Gastric variceal obturation (GVO) with glue.
3. Gastric variceal band ligation (GVL) with or without detachable snares.
4. Thrombin injection (bovine or human).
5. Combined endoscopic therapy.

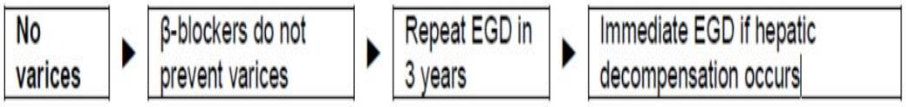
- Endoscopic ultrasound-guided therapy.
- Radiologic intervention –

— transjugular intrahepatic portosystemic shunt (TIPS)

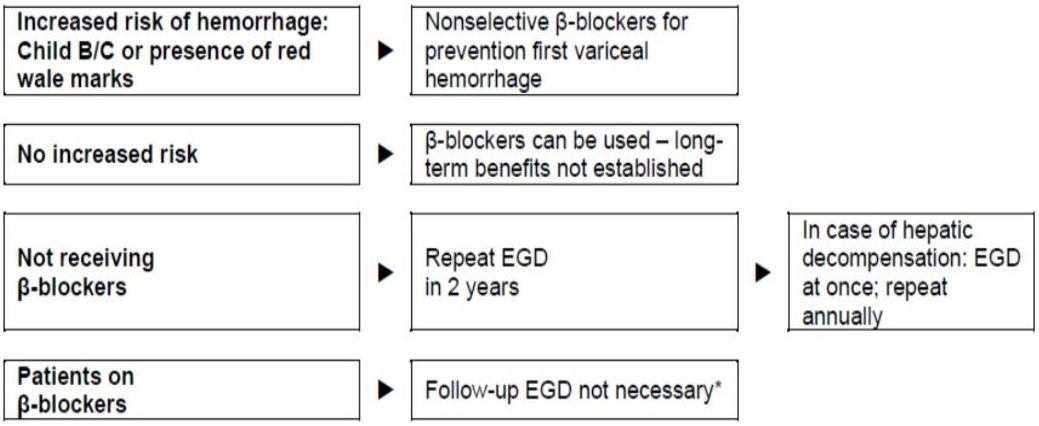
— Balloon-Occluded Retrograde Transvenous Obliteration (BRTO).

Management Recommendations:

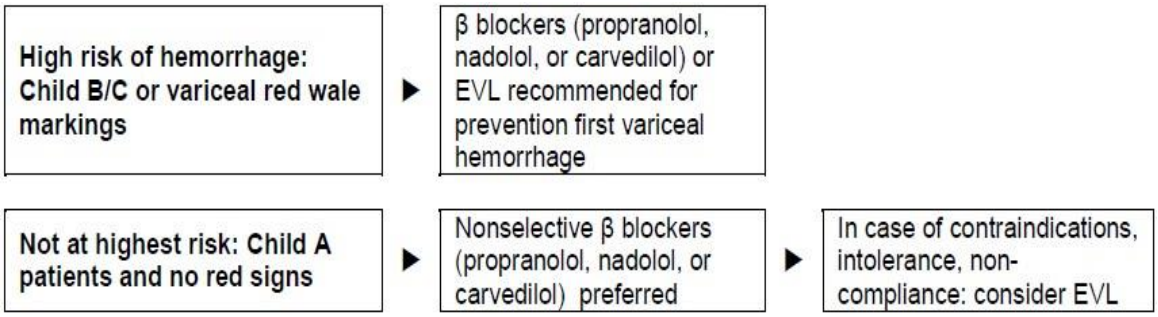
1) PATIENTS WITH CIRRHOSIS BUT NO VARICES:



2) PATIENTS WITH CIRRHOSIS AND SMALL VARICES, BUT NO HEMORRHAGE:



3) PATIENTS WITH CIRRHOSIS AND MEDIUM OR LARGE VARICES, BUT NO HEMORRHAGE:

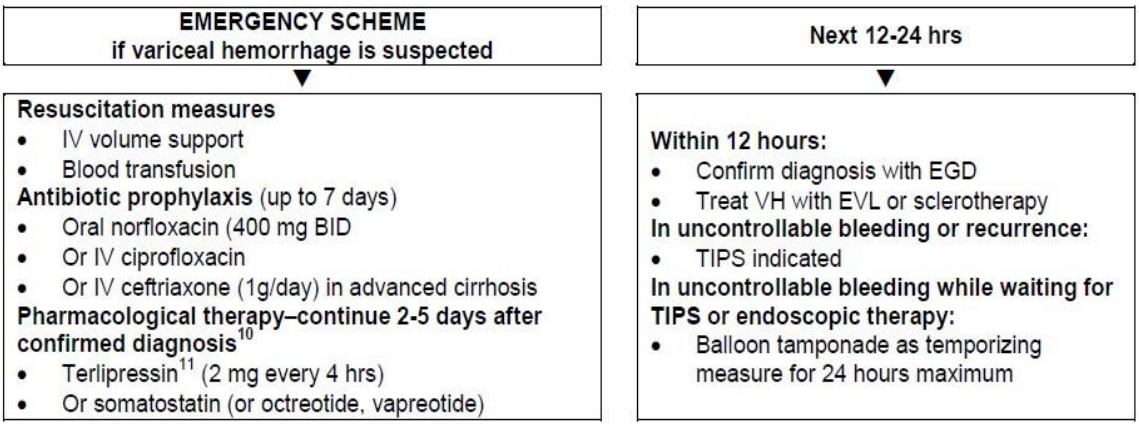


If a patient is given a nonselective beta-blocker, the dose should be adjusted to the maximum tolerated dose; an EGD follow-up is not required. It

is a cost-effective preventive treatment. It has substantial adverse effects and does not prevent the establishment or growth of modest to big varices. Patients who are currently on a selective -blocker (metoprolol, atenolol) for another cause should switch to a nonselective -blocker (propranolol, nadolol, or carvedilol).

If EVL is used to treat a patient, it should be done every 1-2 weeks until obliteration is achieved with the first surveillance. EGD is used to check for variceal recurrence 1-3 months after obliteration and then every 6-12 months after that. Nitrates (alone or in conjunction with beta-blockers), shunt therapy, or sclerotherapy should not be used to prevent variceal bleeding as a primary prophylactic.

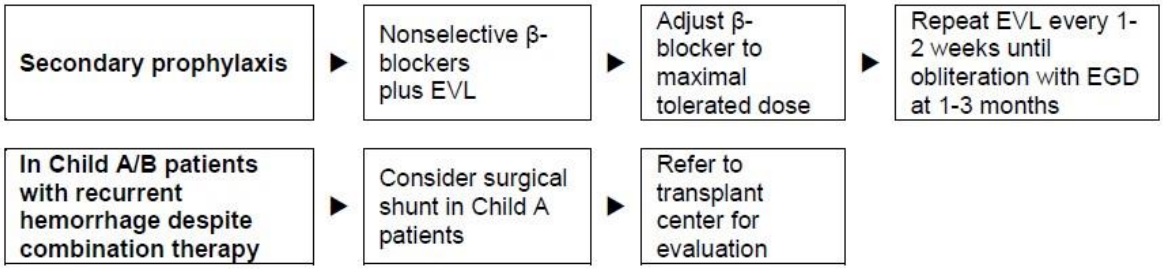
4) PATIENTS WITH CIRRHOSIS AND ACUTE VARICEAL HEMORRHAGE



In patients who bleed from gastric fundal varices, endoscopic variceal obturation using tissue adhesives such as cyanoacrylate is preferred, where available. Otherwise, EVL is an option. TIPS should be considered in patients

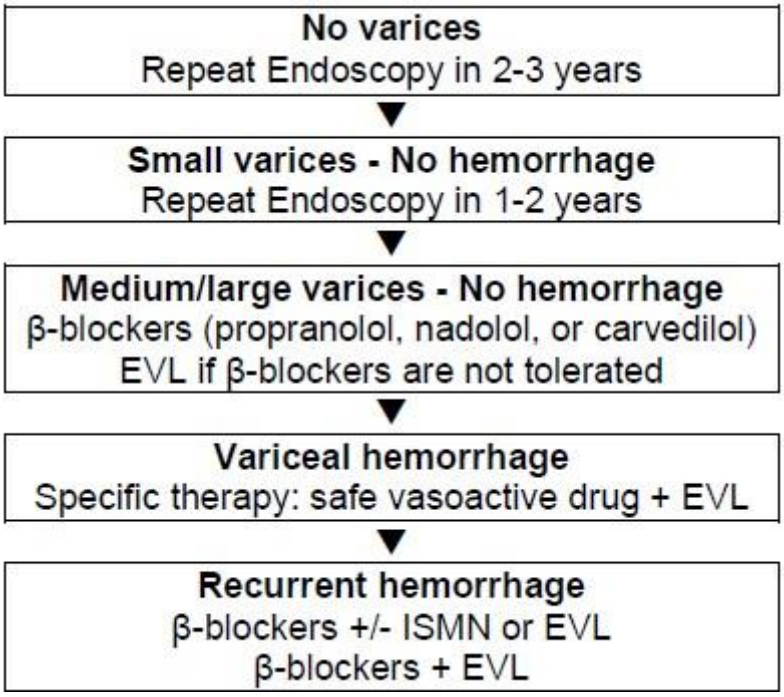
in whom hemorrhage from fundal varices cannot be controlled or in whom bleeding recurs despite combined pharmacological and endoscopic therapy

5) PATIENTS WITH CIRRHOSIS WHO HAVE RECOVERED FROM ACUTE VARICEAL HEMORRHAGE



RECOMMENDATIONS FOR FIRST-LINE MANAGEMENT OF CIRRHOTIC

PATIENTS AT EACH STAGE IN THE NATURAL HISTORY OF VARICES:



WHY DO NONINVASIVE PREDICTORS OF SUCCESS ARE REQUIRED? VARIATIONS IN THE ESOPHAGEAL SYSTEM?

Endoscopy units will be overworked as a result of this method, and patient compliance may suffer as a result of the repetitive testing. Patients at the highest risk for oesophageal varices could be identified noninvasively, limiting research to those who are most likely to benefit. Although upper GI endoscopy is considered the gold standard against which all other tests are measured, it is not without flaws. The evidence for interobserver agreement for endoscopic diagnosis of variceal presence, grade, or presence of red signals is inconsistent. Several studies have been conducted to evaluate clinical symptoms and factors related to liver function, liver fibrosis, portal hypertension, and hypersplenism, as well as portal hypertension and hypersplenism. While some techniques are clearly preferred by patients, none appear to be as accurate in diagnosing oesophageal varices as upper GI endoscopy. Noninvasive tests are still being sought.

Nonselective beta-blockers have been proven to reduce bleeding in more than half of patients with medium or large varices, but they do not prevent the development or expansion of small to large varices and have serious side effects. As a result, patients with cirrhosis should have endoscopic screening for varices at the time of diagnosis. The majority of people having screening EGD either do not have varices or have varices that do not require

preventive medication, due to the point prevalence of medium/large varices being between 15% and 25%. Furthermore, EGD is costly and frequently necessitates sedation, and it can be avoided in cirrhotic patients who are already on nonselective beta-blockers for other reasons (e.g., arterial hypertension).

1) Physical Signs and Variables Related to Liver Function:

Physical Signs and Variables Associated with Liver Function: "A variety of clinical signs and various laboratory markers have been identified as predictors indicating the existence of oesophageal varices, either alone or in combination." Spider naevi, splenomegaly or ascites, Child-Pugh classification, serum albumin, and prothrombin time are among them."

In a research by Garcia-Tsao et al., spider naevi, low albumin, and low platelet count were found to be independent risk factors for the existence of varices. Berzigotti et al. discovered that spider naevi, ALT, and albumin might predict oesophageal varices, with the optimal cutoff having a sensitivity of 93%, specificity of 37%, and accurately categorising 72 percent of patients. When platelet count, prothrombin index, and spider naevi were combined, they found that spider naevi were predictive of major oesophageal varices with a diagnostic accuracy of 72 percent. Splenomegaly revealed on clinical examination was determined to be an independent risk factor for the development of big varices, according to Chalasani et al. Zaman et al. found

that cirrhotic patients in Child-Pugh classes B or C were nearly three times more likely than those in Child-Pugh class A to have oesophageal varices or big oesophageal varices.

The Baveno IV International Consensus Workshop on Diagnostic and Treatment Methodology decided that no study had attained a high enough level of significance to justify the widespread adoption of noninvasive oesophageal varices markers.

2) Variables Related to Liver Fibrosis:

Through the deposition of extracellular matrix (ECM) complexes, chronic liver damage and inflammation leads to fibrosis and eventually cirrhosis. Secondary processing causes the collagen fibrils in the complex to cross-link, conferring resistance to degradative enzymes and irreversibility. Normally, ECM deposition is a dynamic, reversible process, with ECM removal mediated by a number of particular matrix metalloproteinases (MMPs), which are regulated by soluble inhibitors known as TIMPs (tissue inhibitor of metalloproteinase). A number of serum indicators for ECM deposition and removal have been studied as potential candidates for liver fibrosis, and a small number of studies have looked into their utility in predicting oesophageal varices. Glycoproteins, hyaluronic acid, and laminin, as well as members of the collagen family such as procollagen III and type IV collagen, have all been investigated as potential markers so far.

There have been several discrepancies in the results. Galal et al. evaluated serum hyaluronic acid's ability to predict medium-to-large oesophageal varices and found that the sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy at a cutoff of 207 g/L were 94 percent, 77.8%, 88.7%, 87.5 percent, and 88.3%, respectively. Körner et al. found no link between hyaluronic acid or laminin concentrations and the severity of oesophageal varices, and Bahr et al. found no link between serum laminin and the size of oesophageal varices.

When looking at the evidence on the role of collagens, there is a similar debate. The aminoterminal propeptide of type III procollagen was demonstrated to have a slight link to the degree of oesophageal varices in the first of only two research in this field. Mamori et al second .'s study included 44 patients with alcoholic liver disease and found a significant difference in serum type IV collagen levels between patients with and without varices (712.3 versus 404.3 ng/mL, p value 0.001), resulting in an AUROC of 0.78 for predicting the presence of oesophageal varices.

Because none of the aforementioned markers can now predict oesophageal varices in portal hypertension, multiple distinct biomarkers have been combined in order to improve their diagnostic potential. FibroTest is a composite score derived from the results of five serum blood tests (alpha-2 macroglobulin, apolipoprotein A1, haptoglobin, and corrected for the patient's

age and gender (glutamyltranspeptidase, bilirubin, and alanine). Patients with chronic hepatitis C, chronic hepatitis B, fatty liver disease, and chronic alcoholic liver disease had strong predictive values for severe fibrosis, according to the findings.

A single study has assessed the predictive value of fibroTest in the diagnosis of large oesophageal varices in 99 cirrhotic patients. Significant differences in FibroTest value (0.89 versus 0.82), platelet count (110 versus 150), and prothrombin time (50 versus 66%) were seen between patients with and without large oesophageal varices. FibroTest had the highest discriminative power of all the variables with an AUROC curve of 0.77. Using a cutoff of 0.80, this gave a sensitivity of 92%, specificity 21%, PPV 33%, and NPV 86%. A fibroTest score < 0.75 was found to be associated with the absence of large oesophageal varices with a NPV of 100%. The limitations to the study are that it was a retrospective study with significant population bias and has not been reproduced in a prospective study of compensated cirrhotics. FibroTest is not readily available to most clinicians, which limit its utility as a screening test

3) Variables Related to Portal Hypertension and Hypersplenism:

Due to platelet sequestration, thrombocytopenia can occur in portal hypertension-induced splenomegaly, and a great number of studies have been conducted to examine the association between platelet count and oesophageal

varices. Low platelet counts are frequently used to predict oesophageal varices and big oesophageal varices, although the cut-off levels employed vary widely, ranging from 68,000 to 160,000 platelets, with sensitivities ranging from 71–90 percent and specificities ranging from 36–73 percent. With the bulk of studies being retrospective in nature and having varied cohorts of patients, selection and spectrum bias are likely to contribute for much of this heterogeneity.

In a study of 214 individuals with compensated cirrhosis and portal hypertension but no varices, Qamar et al. found that the median platelet count at the time of varices onset was 91,000. There was no platelet count that accurately indicated the presence of oesophageal varices (AUROC curve 0.62), hence they concluded that platelet count is an insufficient noninvasive marker for predicting the presence of oesophageal varices. The platelet count has been coupled with other variables in an attempt to improve its predictive value, and the outcomes of these studies are given below.

As a result of portal hypertension, oesophageal collaterals occur as a result of vascular remodelling and angiogenesis. Nitric oxide and vascular endothelial growth factor are two substances hypothesised to be involved (VEGF). The potential of serum nitrate levels to detect oesophageal varices was investigated in a single study of 85 cirrhotic individuals. When patients with large oesophageal varices were compared to those without oesophageal

varices, significant changes in serum nitrate levels were discovered. The optimum cut-off level for predicting oesophageal varices was 38 mol/L, with a sensitivity of 86.5 percent, specificity of 83.3 percent, positive predictive value of 95 percent, and negative predictive value of 62.5 percent. According to animal studies, oesophageal varices arise not just as a result of the opening up of preexisting collateral arteries, but also as a result of angiogenesis, which may be mediated in part by VEGF. Only one study has looked into the use of VEGF as a noninvasive biomarker, and no link has been found between VEGF and cancer. Use of VEGF as a noninvasive biomarker has only been investigated in a single study, and no correlation between VEGF levels and grade of oesophageal varices was detected ."

The development of portosystemic collaterals and the resultant shunting is responsible for the complication hepatic encephalopathy, in which ammonia plays a role. One study has examined the role of blood ammonia concentrations in the noninvasive detection of oesophageal varices. In this study of 153 cirrhotic patients, a significant correlation was demonstrated between oesophageal variceal grade and venous ammonia levels. The AUROC curve for predicting the presence of oesophageal varices was 0.78, and using a cut-off of 42 μM/L this gave a sensitivity of 92% and a specificity of 60%."

Therefore, variables associated with portal hypertension and hypersplenism are not accurate enough to be used as noninvasive markers of oesophageal varices

PREDICTIVE SCORES:

1. Platelet count /spleen diameter Ratio:

This ratio is derived by multiplying the platelet count per millimetre by the maximal spleen bipolar diameter in millimetres as determined by abdominal ultrasonography. A lot of studies have now been conducted to evaluate this. On multivariate analysis, Giannini et al. found the platelet count/spleen diameter ratio to be the only independent variable linked with the presence of OV, with a cut-off value of 909, giving a PPV of 96 percent and NPV of 100 percent. In compensated cirrhotic individuals, the second portion of the study verified the reproducibility of this cut-off level, with a PPV of 74% and NPV of 100%.The same researchers then performed a repeat endoscopy and calculated the platelet/spleen diameter ratio in 68 patients who did not have OV. Patients with a platelet count/spleen diameter ratio of 909 had a 100% NPV and an 84 percent PPV at follow-up, and the researchers concluded that when cirrhotic patients were followed longitudinally, the platelet count spleen diameter ratio was successful in ruling out the existence of OV.

In 215 patients, a multicenter, international validation study employing the 909 ratio was conducted. With a PPV of 76.6 percent and an NPV of 87.0 percent, the test fared worse than in the original research. This has been a persistent feature in all following investigations, which range in nature from retrospective to prospective and use varied cut off points. As a result, despite early promising results, the platelet count/spleen diameter ratio is not a viable technique for detecting oesophageal varices.

2. GALL BLADDER WALL THICKNESS

Gallbladder wall thickening and impaired contractility are currently reported in cirrhotic patients and often related to portal hypertension and hepatic failure. Gallbladder emptying in response to a meal is a physiological phenomenon, mainly coordinated by the rate of gastric emptying of foods in duodenum and by the subsequent release of cholecystokinin (CCK), which triggers, gallbladder contraction. In normal subjects gallbladder emptying is affected by several factors: age, body surface area, wall thickness, fasting volume, hormonal factors, and meal composition. Impaired gallbladder contractility has been suggested to increase the incidence of gallstones in cirrhotic patients, although incongruous results are report. Because it allows for repeated measurements at short intervals and offers information for the study of gallbladder wall thickness, content, and contraction, real-time ultrasonography (US) is the approach employed for direct gallbladder viewing

under normal and pathological settings. The measurement of the spleen's size and the diameter of the portal vein with ultrasound is a noninvasive way for diagnosing portal hypertension. Furthermore, echo doppler flowmetry can quantify portal flow and mean blood velocity quantitatively. In the research, there is a substantial link between the decline in portal flow velocity and the severity of the disease as measured by the Child-Pugh score.

3. PORTAL VEIN VELOCITY

Normal main portal vein (MPV) peak systolic velocities range between 20 cm/sec and 40 cm/sec. A low flow velocity of <16 cm/sec in addition to a caliber increase in the MPV are diagnostic features of portal hypertension. Cirrhosis results in intrahepatic portal hypertension secondary to the increased resistance in hepatic venules caused by the intrahepatic fibrosis. A type of secondary flow is helical blood flow (defined as a minor flow superimposed on the primary flow pattern). A disruption in the laminar flow causes a helical flow [11,12]. Enhanced helical patterns can be caused by variations in viscosity, vessel shape, local asymmetries along the vessel wall, and changes in flow direction and speed.

To and fro portal venous flow pattern

The portal venous flow velocities gradually decrease with rising portal venous pressure, approaching the state of stagnation. As a result, the practically stationary blood column in the portal veins may be observed

shifting into and out of the liver with the respiratory cycle, resulting in a to-and-fro movement. The Valsalva manoeuvre, which also results in a temporary hepatofugal flow, can be used to replicate the effect of transient flow reversal or halt of forward flow during inspiration (Fig. 5). Stagnation of the blood column can develop to thrombosis or a frank flow reversal when portal hypertension worsens.

4. AST/ALT Ratio

The AST/ALT ratio has been used to predict cirrhosis, and research have being conducted to see if it may also be used to predict oesophageal varices. In a retrospective analysis, patients with varices had significantly higher AST/ALT ratios than those without (ratio: 1.8 versus 1.0). An AST/ALT ratio > 1.12 was found to be substantially linked with the occurrence of varices at initial endoscopy in another prospective trial (OR 3.9, 95 percent CI 1.3–11.8). With this threshold, the sensitivity was 47.8%, the specificity was 87 percent, the PPV was 42.3 percent, the NPV was 89.2 percent, and the AUROC was 0.69. A second study using a different cut-off of 1.0 found that predicting the existence of oesophageal varices had a sensitivity of 68 percent, specificity of 89 percent, PPV of 77 percent, and NPV of 83 percent, with an AUROC of 0.83 (0.72–0.94). This had a sensitivity of 68 percent, specificity of 77 percent, PPV 41 percent, and NPV 92 percent for the prediction of big oesophageal varices, and an AUROC of

0.79 (0.64–0.94). Overall, the AST/ALT ratio properly identified varices in 81 percent of patients and 76 percent of those with significant varices. As a result, these studies, which included individuals with various etiologies of liver disease and utilised varied AST/ALT ratio cutoffs, cannot reliably predict the existence of oesophageal varices in real practise, allowing clinicians to forgo screening all cirrhotic patients with endoscopy

5. Platelet Count and Child-Pugh Class

Burton et al. published the validation of a model based on platelet count and Child-Pugh class for predicting the size and presence of varices in 2009. The first model showed a sensitivity of 58 percent, specificity of 79 percent, PPV of 30 percent, and NPV of 92 percent for detecting major varices in Child-Pugh A patients with a platelet count of 80. The second model, which had a sensitivity of 60%, specificity of 59 percent, PPV of 80%, and NPV of 34%, was designed to detect any varices in Child B/C patients with a platelet count of 90. Once again, the accuracy of these models in predicting the occurrence of oesophageal varices is questionable.

6. Right Lobe Liver Albumin Ratio

The right hepatic lobe diameter (as determined by abdominal ultrasonography in mm) is divided by the serum albumin concentration (g/L) to get this ratio. A total of 94 cirrhotic patients were studied in a single study. The number and extent of oesophageal varices were linked to the right hepatic

lobe/albumin ratio. This resulted in a sensitivity of 83.1 percent and a specificity of 73.9 percent for a cut-off value of 4.425, indicating that it cannot be utilised as a viable screening test once more

7. Liver Stiffness

The noninvasive technology transient elastography (TE, FibroScan, Echosens, France) was developed to assess hepatic fibrosis in patients with chronic liver disorders. Fibrosis generates an increase in liver stiffness, which is measured by TE, which is painless, quick, and simple to perform. Gender, BMI, disease aetiology, and the existence of necro inflammatory alteration have all been linked to a wide range of liver stiffness values ranging from 2.5 to 75 kPa. Normal TE values are 3.8–8 kPa in men and 3.3–7.8 kPa in women, severe fibrosis (Metavir fibrosis stage 2) 7-8 kPa, and cirrhosis 13–17 kPa, as a general reference. APRI was another measure that revealed no meaningful association. Studies show a link between liver stiffness measurements and the existence of oesophageal varices, but opinions differ on the relationship between liver stiffness and variceal size. Therefore, the predictive performance of liver stiffness measurement is poor for the diagnosis of OV with low specificity and PPV, particularly with regard to large OV. However, it may be useful as a screening test to identify patients in whom variceal screening is not required.

The existence of abdominal portosystemic collaterals, portal vein diameter, portal blood velocity and congestion index, spleen size, flow pattern in the hepatic veins, and portal vein diameter were all previously assumed to have prognostic importance but had low sensitivity and specificity. Regardless of the incidence of big varices, using CT as the initial screening modality for the detection of varices was much less expensive than using endoscopy.

Capsule endoscopy is viable in the majority of patients, and in terms of patient preference, it appears to be preferred to traditional endoscopy and may enhance screening programme compliance, however this has yet to be determined, and cost effectiveness is a big factor.

In conclusion, based on all the available evidence to date, upper GI endoscopy remains the gold standard for the diagnosis of oesophageal varices in cirrhotic patients despite its own limitations. Clinical, biochemical, and radiological parameters currently are not accurate enough to avoid screening endoscopy, due to the risks associated with missing patients with large oesophageal varices. In a limited resources setting like ours, where financial constraints are a major problem, predicting the presence and grade of varices by non-invasive methods serves to help a lot in various ways‖

The common features of these noninvasive means that prediction of esophageal varices is reproducible, cost effective, simple and quick with no additional burden to patients. Even though these variables are clearly

preferable to patients, none is comparable to UGIE in terms of sensitivity and specificity in prediction of variceal hemorrhage. To improve the sensitivity and specificity in variceal prediction, several predictive models are proposed using various combinations of the above variables. Apparently, the sensitivity and specificity of the currently proposed predictive models varies with population, the etiologies of liver cirrhosis and the severity of liver disease.

MATERIALS AND METHODS

STUDY POPULATION:

The present study was conducted on 50 patients admitted with a diagnosis of cirrhosis of liver at general medicine and medical gastroenterology wards of Government Rajaji Hospital, Madurai during the period of August 2021 to November 2021.

INCLUSION CRITERIA:

50 patients admitted with a diagnosis of cirrhosis of liver to the general medicine and medical gastroenterology wards of Government Rajaji Hospital, Madurai. Diagnosis of cirrhosis was based on clinical, biochemical and ultrasonographic findings.

EXCLUSION CRITERIA:

Individuals presenting with

- Cholecystectomy history
- Cholecystitis/ cholelithiasis
- Viral hepatitis
- Gall bladder polyp
- Gall bladder carcinoma

- Congestive cardiac failure
- Renal failure
- Pancreatitis
- Coagulopathy
- Nephrotic syndrome
- Diabetic mellitus
- portal vein thrombosis, Hepatoma

Ethics Statement :

The study protocol was approved by the institutional ethical committee of Madurai Medical College. Informed written consent was obtained from all the participants and all the clinical investigations were performed according to the principles which were expressed in the declaration of Helsinki. All patients gave consent to publication of their clinical data.

DATA COLLECTION

A previously designed proforma was used to collect the demographic and clinical details of the patients. All the patients underwent detailed clinical evaluation, appropriate investigations, imaging studies (ultrasound with Doppler) and upper g.i endoscopy

STUDY PROTOCOL:

DESIGN OF STUDY:

Observational Cross sectional study

PERIOD OF STUDY:

August 2021 To November 2021 (4 months)

METHODOLOGY:

History was taken on details and duration of alcoholism, jaundice, ascites, oliguria, pedal edema and gastrointestinal bleed. Presence or absence of jaundice, ascites, splenomegaly and hepatic encephalopathy was noted. Platelet count, prothrombin time and INR, liver function tests including serum bilirubin, serum transaminases, serum albumin was estimated. ultrasonogram abdomen and Doppler study of portal venous system, the portal vein Diameter ,flow pattern and velocity and spleen diameter along with echo texture of the liver, spleen size and direction of blood flow, ascites was noted. At UGI endoscopy, the esophageal varices was graded as large (Grade III-IV) or small (Grade I-II), based on Paquet's grading system.

COLLABORATING DEPARTMENTS:

- Department Of Medical Gastroenterology
- Department of Radiology

Statistical analysis

Statistical analysis were performed with IBM SPSS version 26 (SPSS Inc., Chicago, IL). Descriptive statistics was computed. Data were tested for normality using Shapiro wilks normality test. Due to the skewed data levels, mann whitney U test was used for between group analysis. Kruskal wallis test was used to analyse between cholesterol levels and PPI. Chi square test was used to analyse categorical variables. Spearman rank correlation test was used to analyse between cholesterol and PPI. Receiver Operating Characteristic Curve was used to find out cut-off point of marker (PPI) in predicting LVDD. A significance was set as $p < 0.05$.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

RESULTS AND OBSERVATIONS

Table 1. Comparison of baseline parameters between the patients with and without esophageal gastric varices (EGV) in the study

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Age in years	45.5	7.3	42.6	8.1	1.31	48	0.195(NS)

COMMENTS:

Median age group in esopaheal varies are 45 years

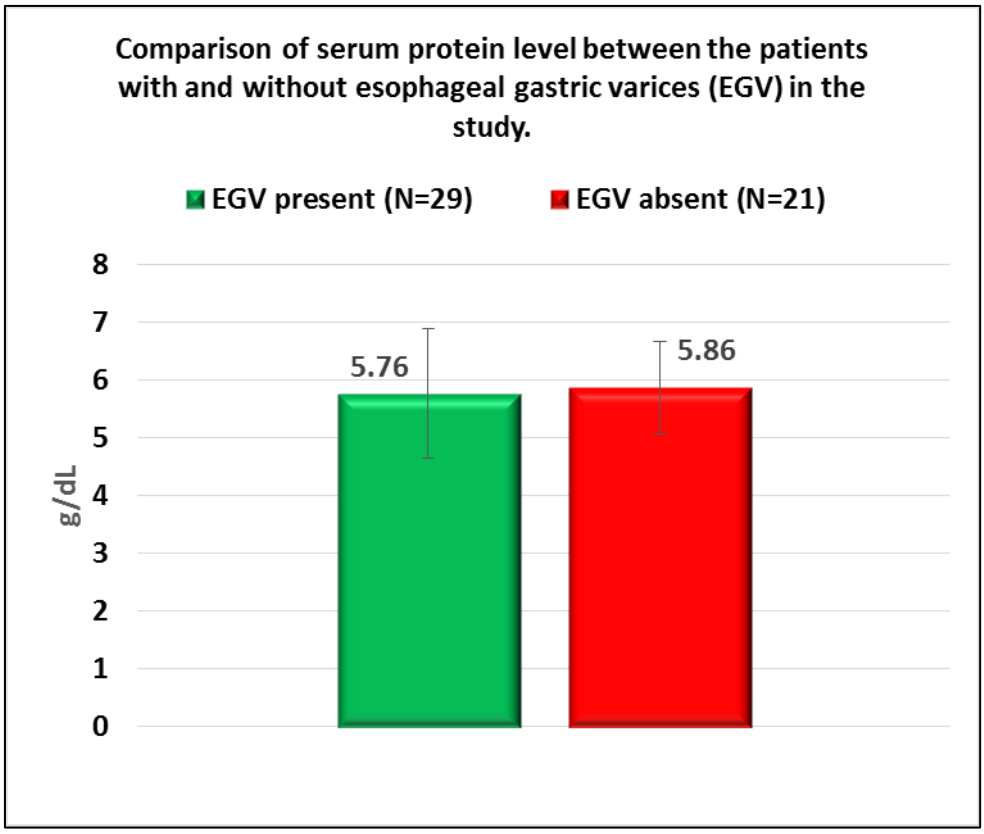


Table 2. Comparison of gender distribution between patients with and without esophageal gastric varices (EGV) in the study.

S.No	Gender	EGV present (N=29)		EGV absent (N=21)		Chi square value	df	P value
		n	%	n	%			
1	Female	5	17.2	3	14.3	0.079	1	0.999 (NS)
2	Male	24	82.8	18	85.7			

COMMENT: Among portal hypertensive patients predominantly male genders are affected

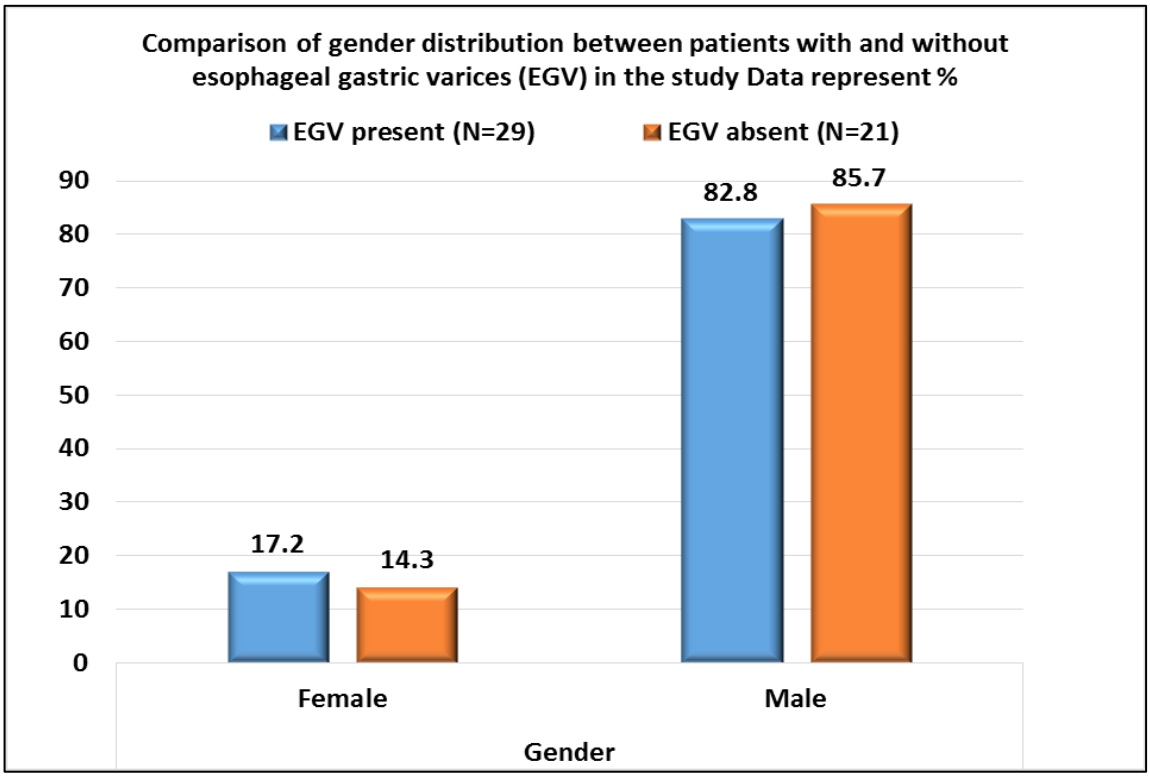


Table 3. Comparison of alcoholism between patients with and without esophageal gastric varices (EGV) in the study.

S.No	Alcoholic	EGV present (N=29)		EGV absent (N=21)		Chi square value	df	P value
		n	%	n	%			
1	Yes	24	82.8	17	81	0.027	1	0.999 (NS)
2	No	5	17.2	4	19			

COMMENT: Alcohol was the most common etiology and out of 24 patients 17had ESOPHAGEAL varices

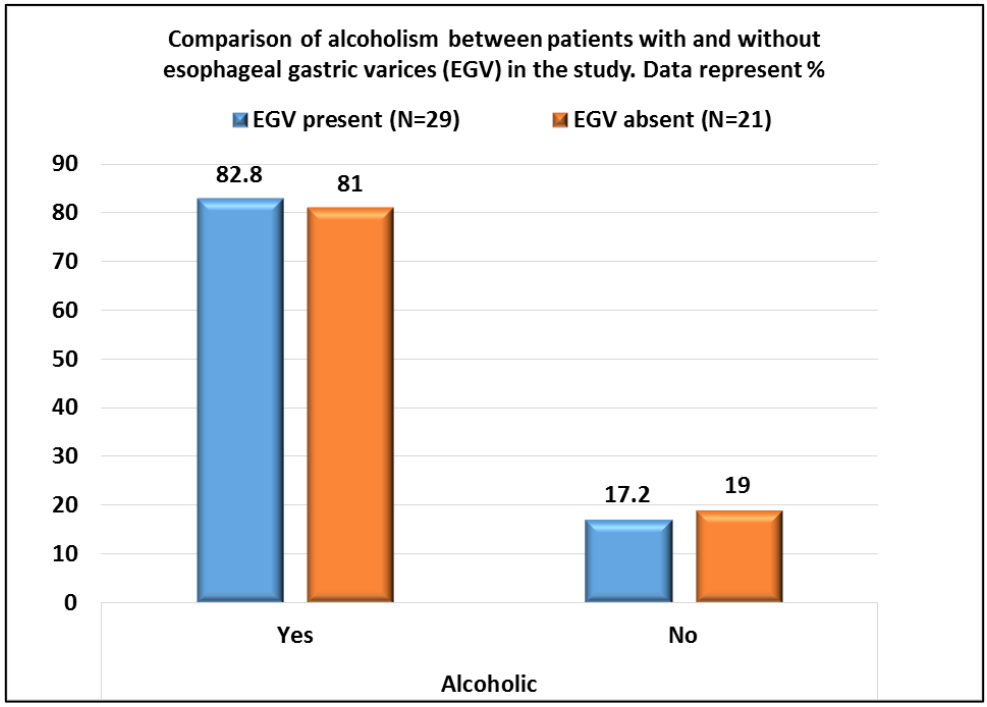


Table 4. Comparison of haemoglobin level between the patients with and without esophageal gastric varices (EGV) in the study

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Hemoglobin (g/dL)	8.9	1.04	9.86	1.4	2.75	48	0.008*

COMMENT: Mean haemoglobin level with portal hypertension is 8.9 gm/dL

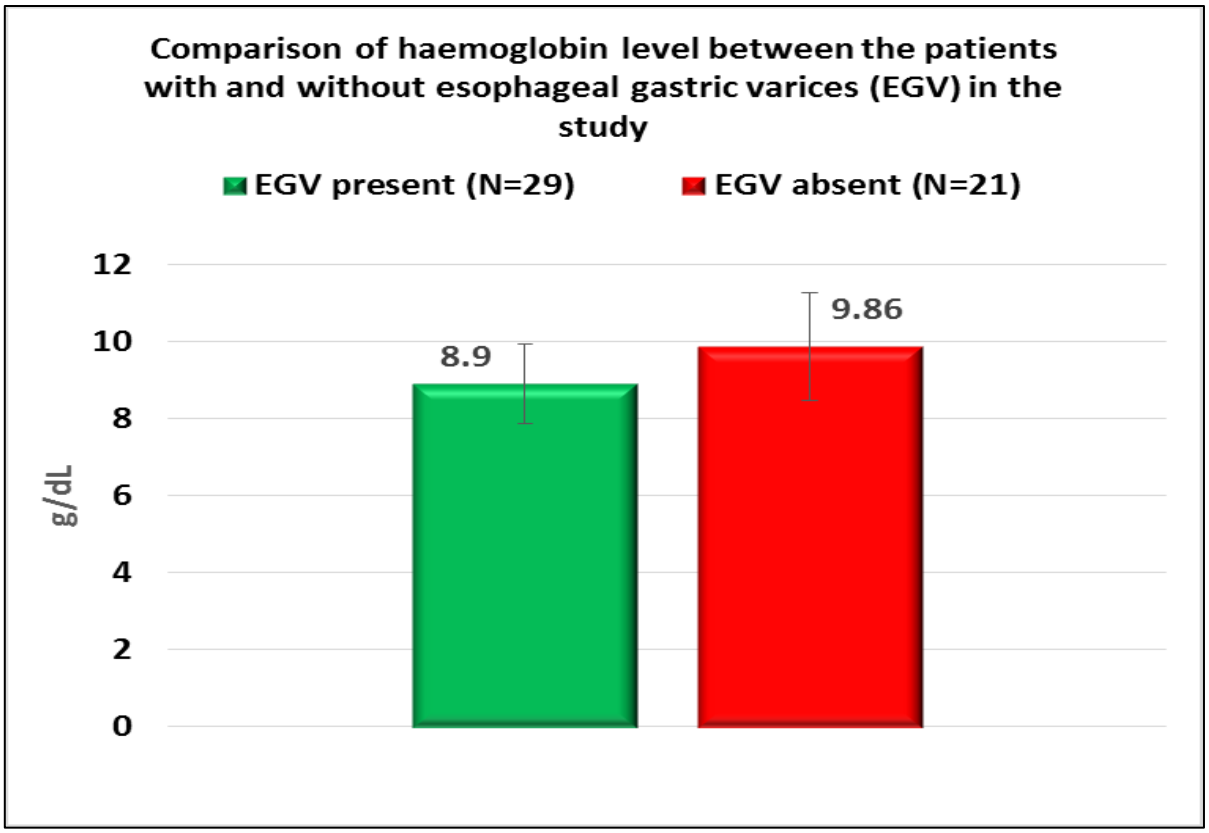


Table 5. Comparison of serum albumin level between the patients with and without esophageal gastric varices (EGV) in the study.

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Serum albumin (g/dL)	2.31	0.6	2.33	0.65	0.128	48	0.899 (NS)

COMMENT:

Median albumin level in esopageal varices group was 2.31 g/dL

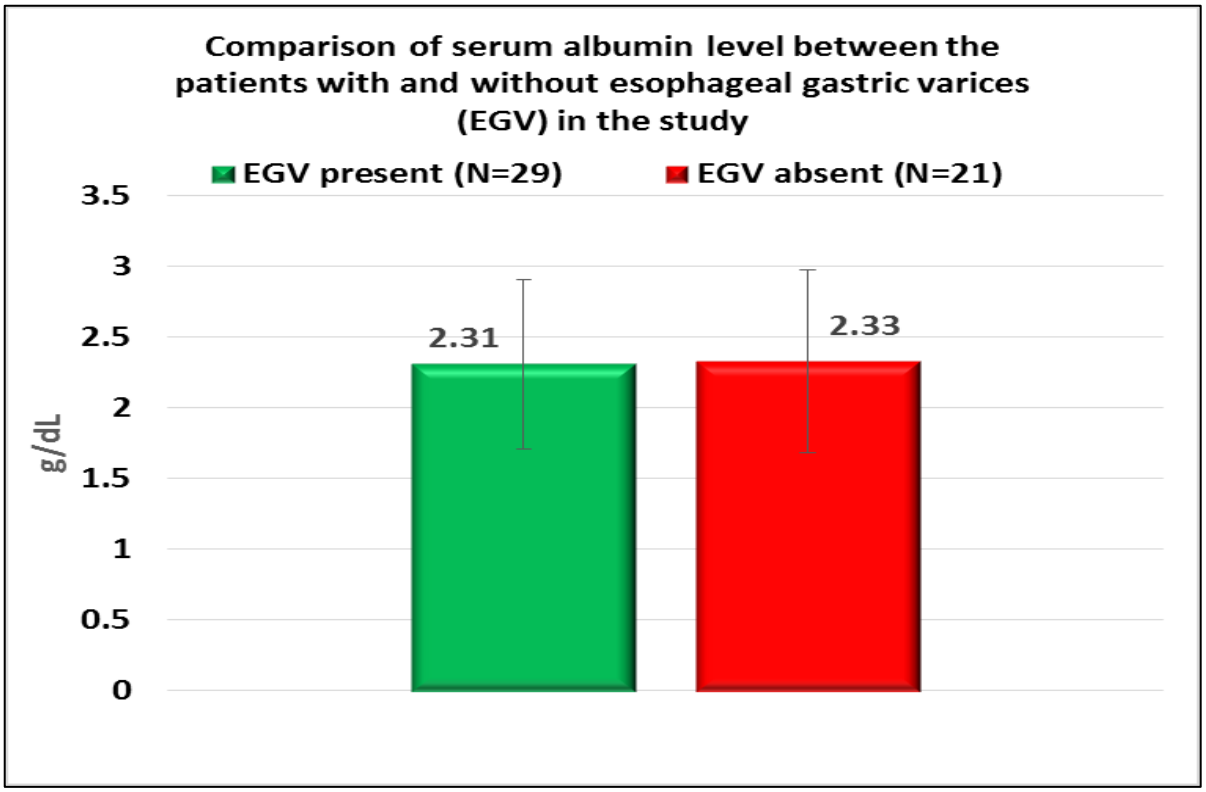


Table 6. Comparison of platelet level between the patients with and without esophageal gastric varices (EGV) in the study.

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Platelet count (1000 cells/cc)	82.1	12.8	127	43.5	5.26	48	<0.0001*

COMMENT: Median platelet count in portal hypertension with esophageal varices was 82000 with p value(<0.0001) low platelet count was significantly correlated with esophageal varices.

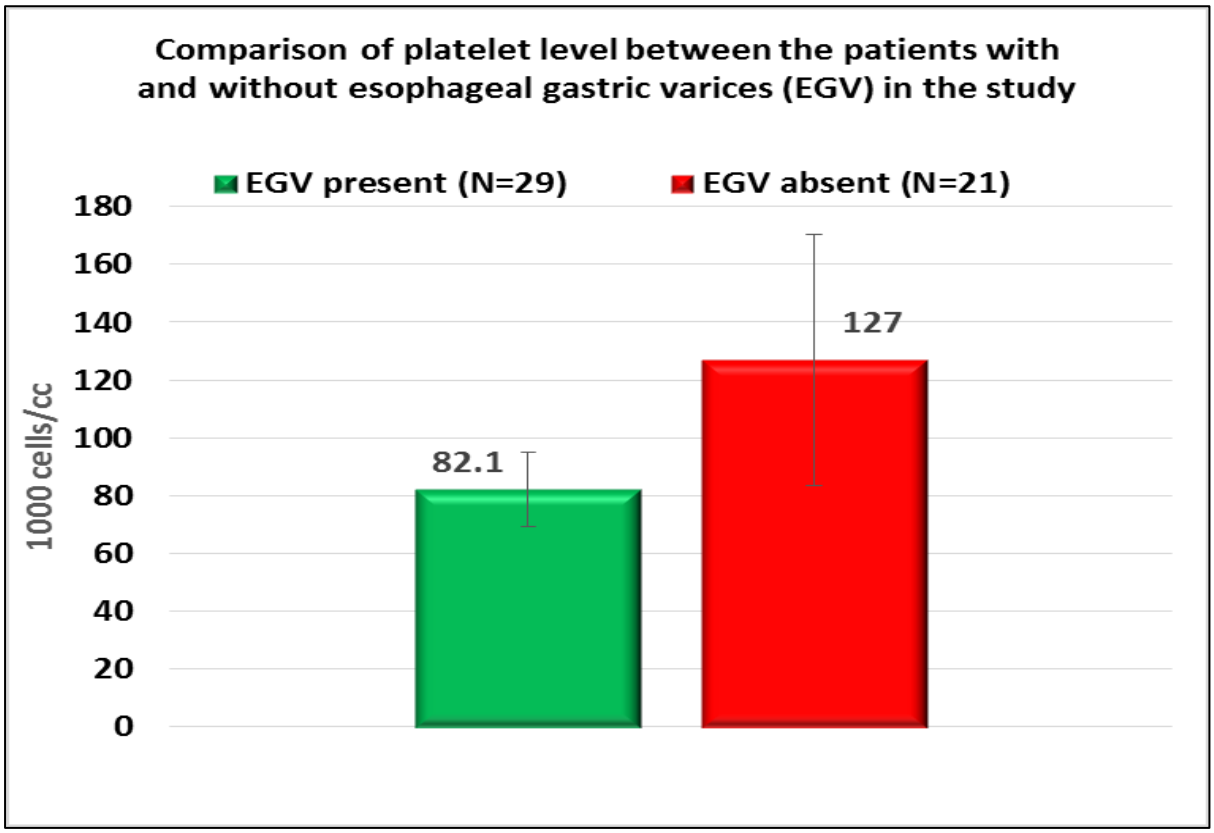
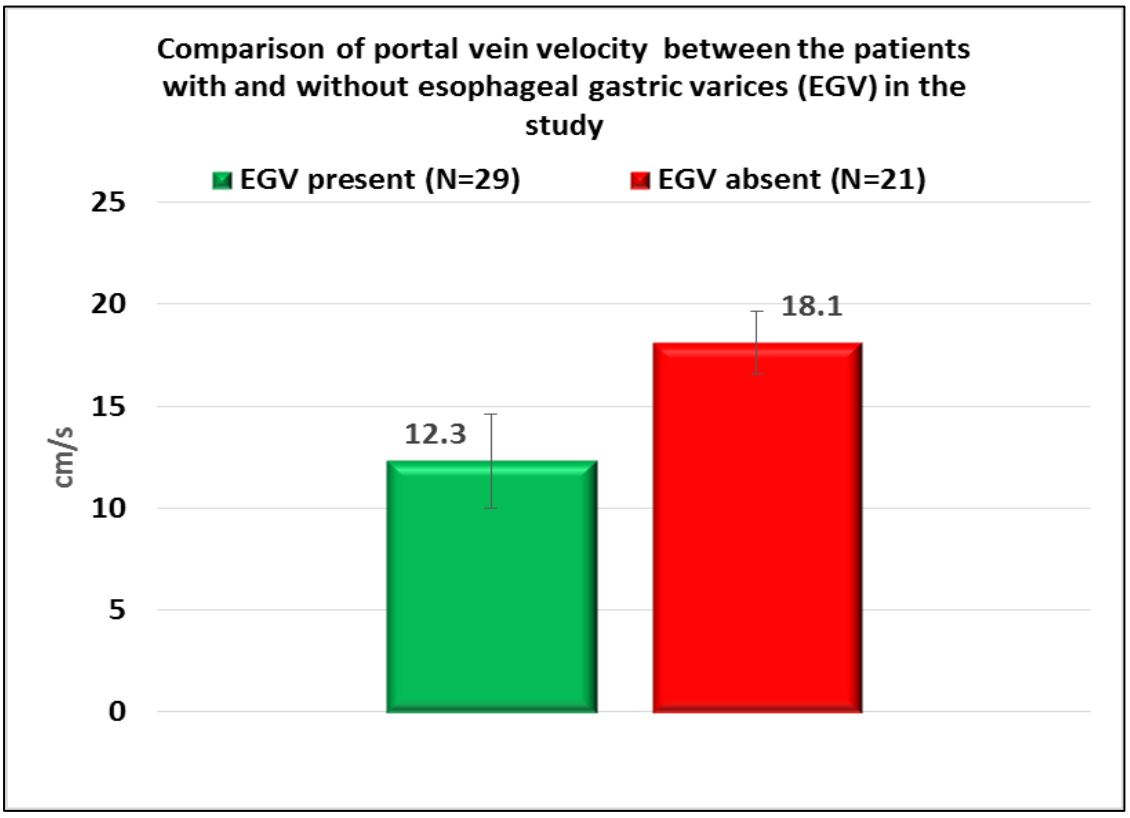


Table 7. Comparison of portal vein velocity between the patients with and without esophageal gastric varices (EGV) in the study.

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Portal vein velocity (cm/s)	12.3	2.3	18.1	1.54	9.74	48	<0.0001*



COMMENT:

Median Portal vein velocity in esophageal varices group was 12.3 cm/s With p value (<.0001) low portal vein velocity was significantly associated with esophageal varices

Table 8. Comparison of Gallbladder wall thickness between the patients with and without esophageal gastric varices (EGV) in the study

S.No	Parameters	EGV present (N=29)		EGV absent (N=21)		T value	df	P value
		Mean	SD	Mean	SD			
1	Gallbladder wall thickness(mm)	5.55	1.1	3.14	1.1	7.29	48	<0.0001*

.

COMMENT : Median Gall bladder wall thickness in esophageal varices group was 5.55 cm with p value (<0.0001).

Increased gall bladder wall thickness was significantly correlated with portal hypertension with esophageal varices patients

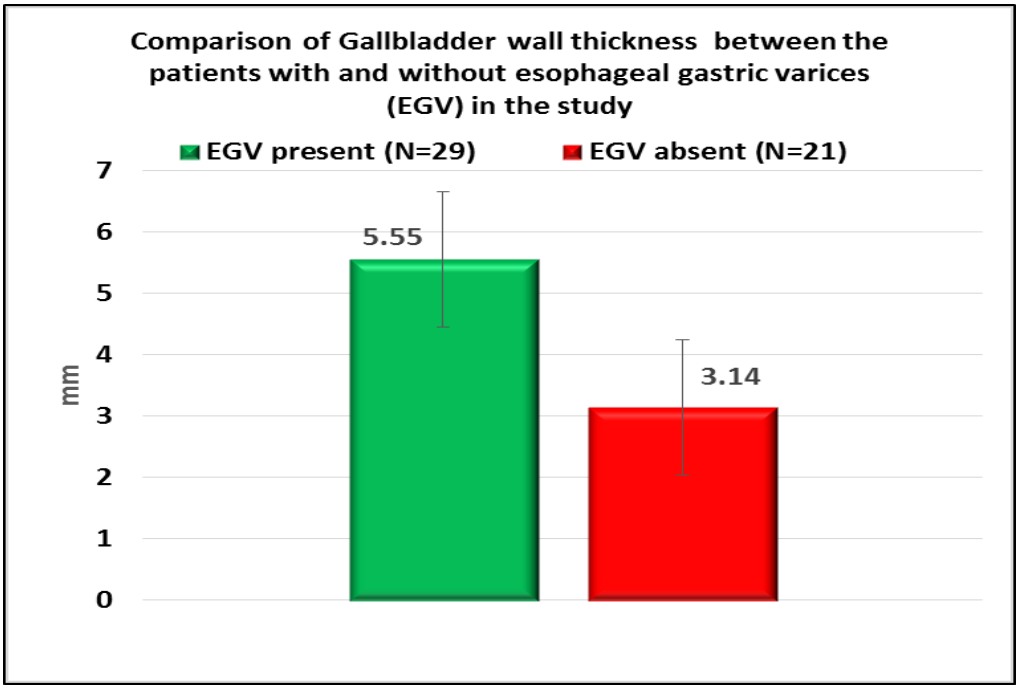


Table 9. Correlation of gallbladder wall thickness with portal vein velocity in patients with liver

S.No	Correlation of	Pearson's r	P value	Inference
1	Gallbladder thickness(mm) with portal vein velocity (cm/s)	-0.742	<0.0001*	Significant negative correlation of strong strength

COMMENT : Relationship of Gall bladder wall thickness and portal vein velocity among portal hypertension patients shows positive correlation (r=0.626) which was statistically significant (p<0.001failure signs.

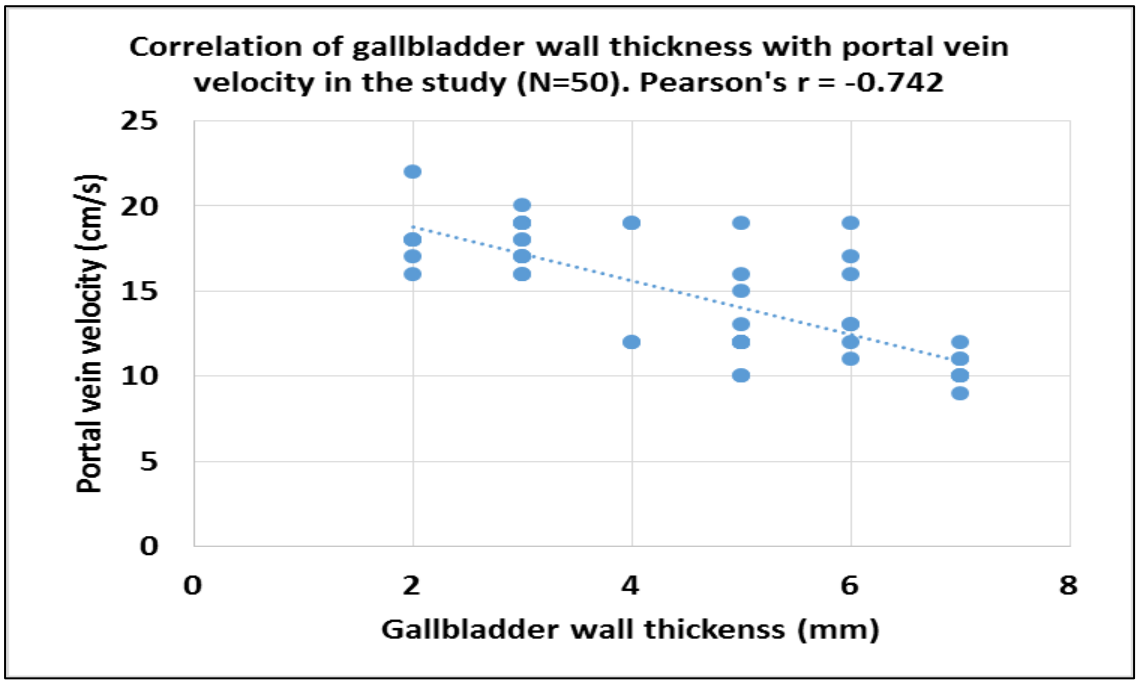
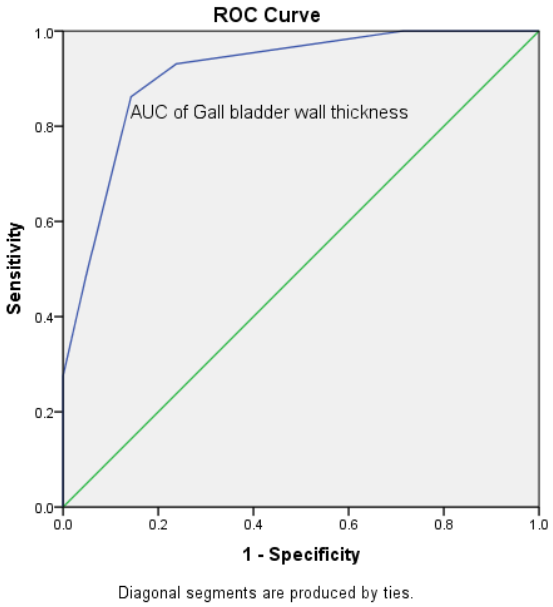
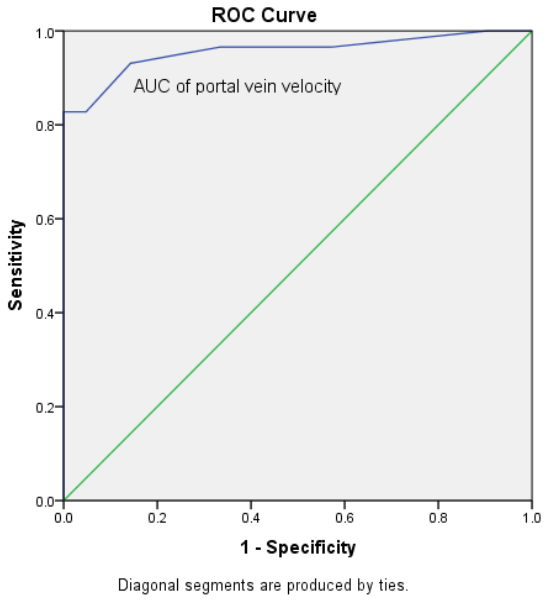


Table 10. Comparison of ROC curve for different parameters in predicting the esophageal gastric varices in the study.

S.No	Parameter	Area under curve (AUC)	P value	Cutoff value	Sensitivity (%)	Specificity (%)
1	Gallbladder wall thickness (mm)	0.913	<0.0001*	≥4.5mm	86.2%	86%
2	Portal vein velocity (cm/s)	0.956	<0.0001*	≤16.5 cm/s	93.1%	86%

COMMENT : Increased Gall Bladder Wall Thickness And Decreased Portal Vein Velocity occurs significantly more often in patients with Esophageal varices due to portal hypertension with p Value (<0.0001) with high sensitivity and specificity values





DISCUSSION

- Our study was done to assess various noninvasive predictors that could predict the presence of large esophageal varices
- Out of 50 total cirrhotic with portal hypertension patients,28 had esophageal varices and 22 had without varices.
- Alcohol was the most common etiology and out of 24 patients 17had ESOPHAGEAL varices
- Esophageal varices were associated with increasing grade of ascites ,p value<0.001 median platelet count in varices group was 82000,p value <0.001,low platelet count was significantly associated with large varices
- varices were correlated with low albumin levels, median value -2.3 mg/dl
- varices were significantly correlated with increasing portal vein velocity median value- 12.6 cm/s (p value- 0.001).
- varices were significantly correlated with increasing gall bladder wall thickness ,median value- 5.5mm (p value- < 0.001).

SUMMARY

A cross sectional observational study was done at Government Rajaji Hospital, Madurai among 50 cirrhosis of liver patients for assessing various noninvasive predictors that could predict the presence of large esophageal varices. From the present study, gall bladder wall thickness, portal vein velocity, low platelet count, AST/alt raio emerged as significant predictors for the presence of large varices.

We believe that these predictors may be of help to the physicians practicing in areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients. Accurate identification of patients at the highest risk of bleeding allows stratification in an attempt to avoid unnecessary preventive measures in 60-75% of patients who will never have variceal bleeding in future. In a limited resources setting like ours, where financial constraints are a major problem, predicting the presence and grade of varices by non-invasive methods help to avoid unnecessary upper G.I endoscopies.

CONCLUSION

- **Increased gall bladder wall thickness and decreased portal vein velocity** emerged as significant predictors for the presence of large esophageal varices.
- Cirrhosis of the liver can cause large esophageal varices, which can be dangerous. Given the significant endoscopic stress and cost of variceal screening, finding a less expensive, noninvasive method for accurately predicting big esophageal varices is critical.

LIMITATIONS OF THE STUDY

- This study involves inly small number of samples
- Patients with gall bladder pathology are not included in the study, as most common in alcoholics had associated with gall bladder pathology
- Hypercoagulable state and pre existent portal vein thrombosis has excluded in the study are most common in alcoholics

BIBLIOGRAPHY

- Evolving consensus in portal hypertension report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2005;43:167–176 Merli M, Nicolini G, Angeloni S, Rinaldi V, De Santis A, Merkel C, et al.
- Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol Sarin, Negi. Management of gastric variceal hemorrhage. Indian journal of gastroenterology 2006 Vol 25 (Supplement 1) November S25-28,
- Spiegel BM, Esrailian E, Eisen G. The budget impact of endoscopic screening for esophageal varices in cirrhosis. Gastrointest Endosc. 2007 Oct;66(4):679-92.
- Reiberger T, Ulbrich G, Ferlitsch A, Payer BA, Schwabl P, Pinter M, Heinisch BB, Trauner M, Kramer L, Peck-Radosavljevic M; Vienna Hepatic Hemodynamic Lab. Gut. 2013 Nov;62(11):1634-41. doi: 10.1136/gutjnl-2012-304038. Epub 2012 Dec 18.
- Carvedilol for primary prophylaxis of variceal bleeding in cirrhotic patients with haemodynamic non-response to propranolol D'Amico G, Pagliaro L, Pietrosi G, Tarantino I. Emergency sclerotherapy versus vasoactive drugs for bleeding oesophageal varices in cirrhotic patients. Cochrane Database Syst Rev. 2010 Mar 17;(3) .

- Avgerinos A, Armonis A, Stefanidis G, Mathou N, Vlachogiannakos J, Kougioumtzian Sustained rise of portal pressure after sclerotherapy, but not band ligation, in acute variceal bleeding in cirrhosis. Hepatology 2004;39:1623–1630
- Villanueva C, Piqueras M, Aracil C, Gomez C, Lopez-Balaguer JM, Gonzalez B, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. J Hepatol
- Banares R, Albillos A, Rincon D, Alonso S, Gonzalez M, Ruizdel-Arbol L, et al. Endoscopic treatment versus endoscopic plus pharmacologic treatment for acute variceal bleeding: a metaanalysis. Hepatology 2002;35:609–615 Shiv Kumar Sarin, Ashish Kumar, Peter W. Angus, Sanjay Saran Baijal, Soon Koo
- Baik et.al. Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations Hepatol Int (2011) :607–624 11. de
- Franchis R. Review Somatostatin, somatostatin analogues and other vasoactive drugs in the treatment of bleeding oesophageal varices. Dig Liver Dis. 2004 Feb; 36 Suppl 1:S93-100.

- Khan S, Tudur Smith C, Williamson P, Sutton R. Portosystemic shunts versus endoscopic therapy for variceal rebleeding in patients with cirrhosis. Cochrane
- Database Syst Rev 2006;(4):CD000553 (17054131). Banding ligation versus beta-blockers for primary prevention in oesophageal WGO Practice Guideline Esophageal Varices 13 © World varices in adults.Gluud LL, Krag A.Cochrane Database Syst Rev. 2012 Aug 15;8:CD004544. doi:
- Hou MC, Lin HC, Liu TT, Kuo BI, Lee FY, Chang FY, et al. Antibiotic prophylaxis after endoscopic therapy prevents rebleeding in acute variceal hemorrhage: a randomized trial. Hepatology 2004;39:746–753
- Bernard B, Grange JD, Khac EN, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: A meta-analysis. Hepatology 1999;29:1655–1661
- Ioannou GN, Doust J, Rockey DC. Systematic review: terlipressin in acute esophageal variceal hemorrhage. Aliment Pharmacol Ther 2003;17:53–64
- Gall bladder wall thickening as non-invasive screening parameter for esophageal varices – a comparative endoscopic – sonographic study Birgit Tsaknakis, Rawan Masri, Ahmad Amanzada, Golo

Petzold, Volker Ellenrieder, Albrecht Neesse & Steffen Kunsch Gall-bladder wall thickening in patients with liver cirrhosisT F Wang [1], S J Hwang, E Y Lee, Y T Tsai, H C Lin, C P Li, H M Cheng, H J Liu, S S Wang, S D Lee

- Gall Bladder Wall Thickness as a Marker of Portal Hypertension in Patients of Alcoholic Cirrhosis of Liver Jaya Pathak1 , Shivangi Gharia2 , Zeal Kishor Thakkar3 , Kesar Prajapati4 , Darshankumar M Rava
- Evaluation of the Gallbladder Wall Thickening as a Non-invasive Predictor of Esophageal Varices in Cirrhotic Patients Nora M. Shehata Alsiagy A. AbdelAziz Medhat Abd El-Megid Yasser M. Hafe
- Altered Doppler flow patterns in cirrhosis patients: an overview
- Pooya Iranpour,[1] Chandana Lall,[1] Roozbeh Houshyar,[1] Mohammad Helmy,[1] Albert Yang,[1] Joon-Il Choi,[2] Garrett Ward,[1] and Scott C Goodwin[1]

- Portal hypertension: Imaging of portosystemic collateral pathways and associated image-guided therapy Murad Feroz Bandali, Anirudh Mirakhur, Edward Wolfgang Lee, Mollie Clarke Ferris, David James Sadler, Robin Ritchie Gray, and Jason Kam Wong “Congestion Index” of the Portal Vein Furninori Moriyasu1 Osamu Nishida1 Nobuyuki Ban1 Takefumi Nakarnura1 Masahiko Sakai1 Takeo Miyake2 Haruto Uchin& The