"STUDY TO CORRELATE SERUM –ASCITES ALBUMIN GRADIENT (SAAG) WITH THE ESOPHAGEAL VARICES AND IT'S GRADES IN PATIENTS WITH PORTAL HYPERTENSION".

By:

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Under The Guidance Of

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ABSTRACT

INTRODUCTION: Esophageal varices are one among the major after effect of portal hypertension. Serum ascites albumin gradient (SAAG) is one of the non-invasive parameters for predicting the presence and the degree of esophageal varices. The aim of the study was to correlate the SAAG ratio with the presence and grades of esophageal varices in patients with portal hypertension.

METHODOLOGY: This Case series was carried out in the Department of General Medicine at R.L.Jalappa Hospital, Kolar. All the eligible subjects were recruited into the study consecutively till the sample size is reached. A detailed clinical case history of study participants including demographic data, history, clinical examination and details of investigation were recorded in study proforma. The investigations included CBC, RFT, LFT, RBS, serum albumin.Serum Ascitic Albumin Gradient (SAAG) was calculated by subtracting the ascitic albumin concentration from serum albumin concentration (SAAG=serum albumin – ascitic albumin) g/dl.

RESULTS: A total of 50 people were included in the final analysis. The mean age was 50.26 ± 14.42 years. 48(96%) participants were males and remaining 2(4%) were females. The mean of SAAG was 1.86 ± 0.52. Minimum level was 1.10 and maximum level was 3.70 in study population. (95% CI 1.72 to 2.01). Among the study population 9(18%) had grade 1 Esophageal Varices, 14(28%) had grade2, 15(30%) had grade 3 and 12(24%) had no Esophageal Varices. The mean SAAG in people with Esophageal varices was 2.04 ± 0.46 and was 1.3 ± 0.2 in people without Esophageal varices. There was a statistically significant difference in the proportion of SAAG between Esophageal varices. (P value <0.001). The

SAAG had excellent predictive validity in predicting Esophageal varices**,**as indicated by area under the curve of 0.932 (95% CI 0.863 to 1.00, P value <0.001). SAAG had sensitivity of 84.21% (95% CI 68.75% to 93.98%) in predicting Esophageal varices, specificity was 100.00% (95 CI 73.54% to 100.00%), Positive predictive value was 100.00% (95 CI 89.11% to 100.00%), Negative predictive valuewas 66.67% (95 CI 40.99% to 86.66%), and the total diagnostic accuracy was 88.00% (95 CI 75.69% to 95.47%).

Conclusion: The current study found that there is a statistically significant association between both presence and severity of EV and SAAG value. There is need for more longitudinal studies with large sample size for it to replace the oesophagogastro-duodenoscopy.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

Glossary	Abbreviations
AASLD	American association for study of liver diseases
ABC	Airway, breathing and circulation scheme
AFP	Ascites fluid proteins
AFTP	Ascitic fluid total protein
APASL	Asian-pacific association for study of the liver
AVH	Acute variceal hemorrhage
AVH	Acute variceal hemorrhage
CLD	Chronic liver disease
CSPH	Clinically significant portal hypertension''
EASL	European association for study of the liver
EBL	Endoscopic band ligation
EGD	Esophagogastroduodenoscopy
EV	Esophageal varices
HVPG	Hepatic venous pressure gradient
HVPG	Hepatic venous pressure gradient
INR	International normalized ratio
IVC	Inferior vena cava
LDH	Lactate dehydrogenase
LMIC	Low and low-middle income
NAFLD	Non-alcohol related fatty liver disease
NCPH	Non-cirrhotic pht
NSBB	Non-selective beta blockers
PH	Portal hypertension
PHG	Portal hypertensive gastropathy
PHT	Portal hypertension
PHTN	Portal hypertension
SAAG	Serum ascites albumin gradient
TIPS	Transjugular intrahepatic portosystemic shunt
VB	Variceal bleeding

INTRODUCTION

INTRODUCTION:

Portal hypertension (PH) is a common clinical syndrome, most frequently arising due to chronic liver disease, characterized by an increased pressure gradient between the portal vein and the inferior vena cava (IVC).[1] Portal hypertension can be defined as a hepatic venous pressure gradient (HVPG) ≥5 mmHg and is clinically significant at 10 mmHg.[2]

Esophageal varices is one among the major after effect of portal hypertension. It is detected in about 50% of cirrhosis patients, and approximately 5–15% of cirrhosis patients show newly formed varices or worsening of varices each year. It is a hemodynamic abnormality characterized by sudden bleeding episode; about a third of all patients with esophageal varices show bleeding episode.[3] Variceal bleeding (VB) a major complication of PH, still carries a mortality of up to 20% within 6 weeks of the bleeding episode.

The grade of esophageal varices often varies with the severity of liver disease. Even though EV are present only in 45% of the individuals with Child-Pugh A cirrhosis, they are present in 85% of individuals with Child-Pugh C cirrhosis. Large size varices, the presence of red color signs, severe liver disease and portal pressure greater than 12 mm Hg predict greater risk of bleeding.[4] Variceal bleeding (VB) contribute to the estimated 32,000 deaths annually attributed to cirrhosis[5] and the rebleeding risk after acute variceal hemorrhage (AVH) is highest within the first 6 week with a peak in the first 5 days.[6] Varices may not develop and bleed when the HVPG is lower than 12 mmHg. That is, varices are related with the condition of HVPG higher than 12 mmHg.[3] The Baveno IV Consensus Conference on PHT recommended that all cirrhotic patients must be periodically screened for occurrence of esophageal varices. In cirrhotic patients with small varices, endoscopy should be performed at 1-2 yearly intervals and at 2-3 yearly intervals in patients without varices.[7] Incidence of first variceal hemorrhage ranges from 20 to 40% within two years. Recurrent bleeding occurs in 30 to 40% of patients within the next two to three days and in up to 60% within one week.

Thus, prevention of esophageal variceal bleeding remains at the forefront of long-term management of cirrhotic patients.[8] Nevertheless, routine screening of every cirrhotic patients has its economic implications because only 50% of patients have esophageal varices on their very first esophagogastroduodenoscopy (EGD) and fewer than 30% have large varices, with a higher risk of bleeding. [9] Furthermore, there is a low prevalence of varices which requires primary prophylaxis. Also, the upper endoscopy is an invasive and uncomfortable procedure which may not be acceptable for the patients. Therefore, to recognize the patients who gets benefit from routine endoscopy screening, it is important to predict the presence of EV through non-endoscopic and non-invasive markers. This considerably reduces the number of avoidable endoscopies.[10]

There are some non-invasive parameters for predicting the presence and the degree of esophageal varices, which are the biochemical, clinical and ultrasonography parameters. Those parameters could be performed separately or in combination. Among them, the parameters that mostly applied for predicting the occurrence of EV are splenomegaly, thrombocytopenia, Child-Pugh score, ascites, portal flow pattern, thickness of gall bladder wall, platelet count-splenic size ratio, serum ascites albumin gradient (SAAG), and right lobe liver diameter-albumin ratio.[11]

SAAG is a minimally invasive method. It is based on the difference between the albumin level of serum and ascitic fluid and is thought to reflect the colloid osmotic pressure gradient and the degree of portal hypertension. Literature documents that the SAAG is an indicator of PHTN, and that a direct relationship probably exists between SAAG and different PHTN measurements such as the, net portal pressure, portal pressure gradient or corrected portal pressure, these parameters being obtained by invasive methods. It is also of particular utility to differentiate between congestive heart failure and malignant ascites without liver metastases (both of them with elevated ascites fluid proteins -AFP-). [12] The SAAG appears to

retain its predictive value despite diuresis, infusion of albumin, therapeutic paracentesis or infection in the ascitic fluid. [13] So many studies has been conducted recently to determine the predictive effect of SAAG in portal hypertension. A study by Rahman et al reported that the SAAG value correlates both with incidence of oesophageal varices and severity of EV among patients with cirrhosis of liver disease. [14] Gurubacharya DL et al 2005 reported that, the occurrence of EV among individuals with ascites and high SAAG is directly related to the degree of SAAG and the size of the esophageal varices in patients with ascites and high SAAG is not associated with the degree of SAAG.[15] Budiyasa DGA et al[11] reported that, there was a negative correlation between serum albumin level and the degree of esophageal varices(EV) in patients with liver cirrhosis and therefore, the serum albumin level could be used as a predictor for determining the degree of EV. Whereas a study by Demirel U et al could not find any correlation between SAAG and esophageal varices among patients with non-alcoholic cirrhosis.[16] Even though literature had reported SAAG as a predictive diagnostic tool for portal hypertension among childrens[17], its use in detecting esophageal varices are scarce and not accurate among adults.[16]

There are limited number of studies showing this relation between SAAG and esophageal varices in adult's patients with portal hypertension especially in Indian context. Hence the aim of the current study was to correlates the SAAG ratio with the presence and grades of esophageal varices in patients with portal hypertension.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES:

- To determine the SAAG ratio in patients with portal hypertension.
- To determine the presence and grades of esophageal varices in patients with portal hypertension.
- To correlates the SAAG ratio with the presence and grades of esophageal varices in patients with portal hypertension.

REVIEW OF LITERATURE

Portal hypertension, a brief description:

Portal hypertension (PHT) is a progressive condition of chronic liver disease and is a major cause of complications and death in patients with liver cirrhosis.[18] Gilbert and Villaret coined the term 'portal hypertension' in 1906.[19] It develops whenever resistance to portal blood flow increases because of hepatic (liver diseases), prehepatic (schistosomiasis), or posthepatic causes (Budd-Chiari syndrome). Cirrhosis of the liver (of any etiology) is by far the most common cause of portal hypertension. All other causes together represent only about 10% of cases.[1]

PPG elevation not reaching 10 mmHg is not associated with clinical complications or reduced survival probability, which is why this has been called ''mild'' or ''subclinical'' portal hypertension. However, once PPG crosses the 10mmHg threshold, complications of portal hypertension can begin to appear. Because of this, PPG elevations above 10 mmHg are defined as ''clinically significant portal hypertension'' (CSPH).[1]

The clinical relevance of portal hypertension is due to the fact that its complications represent the main cause of death and liver transplantation in patients with cirrhosis.[1] Portal hypertension is initially asymptomatic in the vast majority of patients (around 80–90%).[20] Once complications develop it may lead to gastric or esophageal varices, variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, portopulmonary hypertension, hepatopulmonary syndrome, hepatic encephalopathy, portal hypertensive gastropathy (PHG), enteropathy and colopathy and disturbances in the metabolism of endo- and xenobiotics normally metabolized by the liver.[21]

Portal hypertension- Pathophysiology

The portal pressure is estimated by the difference between the wedged hepatic venous pressure and the free hepatic venous pressure; the normal pressure is <5 mmHg.[22] It occurs secondary to both an increase in the intrahepatic vascular resistance and increased portal blood flow.

Intrahepatic vascular resistance: Increased intrahepatic vascular resistance occurs through mechanical and dynamic components. The mechanical component is related with intrahepatic fibrosis and regenerative nodules that lead to sinusoidal portal hypertension.[23-25] An additional response to liver injury is the hepatic stellate cells activation and transformation into myofibroblasts which contract around the newly formed sinusoidal vessels thereby increase the intrahepatic vascular resistance.[25] The dynamic component is related to an imbalance between vasoconstrictors and vasodilators leading to increased intrahepatic vascular tone.

Increased portal blood flow: It is mainly related to hyperdynamic circulation.[25] Splanchnic arterial vasodilation results from an excessive release of endogenous vasodilators such as nitric oxide, glucagon, endocannabinoids, and vasointestinal active peptide[23, 24] and decreased hepatic function which leads to decreased metabolism of these mediators.[3] Splanchnic vasodilation leads to increasing substantial blood volume which returns to the portal venous system leading to increased portal flow and pressure.[25] Peripheral vasodilation leads to decreased effective arterial volume and diminished blood flow to the kidney, and this causes activation of neurohormonal system (renin-angiotensin-aldosterone system, anti-diuretic hormone, and sympathetic nervous system) that leads to sodium and water retention, which in turn aggravates portal blood flow and pressure. Collateral supply usually exist between the portal venous system and the systemic veins. In fact these collaterals has higher resistance than the portal veins resulting in unidirectional blood flow from the systemic veins to the

portal system.[26] When portal hypertension develops, it leads to reversal of blood flow in these collaterals leading to the formation of gastroesophageal varices, rectal varices and caput medusa.[26] More collaterals develop by angiogenesis in an attempt to decompress the portal circulation

Common etiologies of portal hypertension:

Portal hypertension is a detrimental complication resulting from obstruction of portal blood flow, such as cirrhosis or portal vein thrombosis.[25] Portal hypertension has different etiological factors. portal hypertension etiology and incidence differs with respect to the age group and different socioeconomic status of the target population. [27]

Hepatic Causes:

a) pre sinusoidal: schistosomiasis, chronic viral hepatitis HBV, HCV, primary biliary cirrhosis, myeloproliferative disorders, sarcoidosis, tuberculosis, hemochromatosis, idiopathic portal hypertension Wilson disease, amyloidosis, polycystic liver disease, and benign and malignant neoplasms.

b) sinusoidal: Liver cirrhosis independent of etiology

c) post sinusoidal: venous occlusion disease, alcoholic hyaline sclerosis of central vein.

Portal hypertension is considered an advanced complication of cirrhosis. Once it has developed, the term "decompensated cirrhosis" is used. It is reported that intrahepatic vasoconstriction accounts for at least 25% of increased intrahepatic vascular resistance.[25]

Cirrhotic PHT is associated with an elevated hepatic venous pressure gradient (HVPG) predominantly due to raised sinusoidal resistance, while in the non-cirrhotic PHT (NCPH), HVPG is normal or only mildly elevated and is significantly lower than PV pressure. The diseases leading to NCPH are primarily vascular in nature and classified anatomically on the basis of site of resistance to blood flow, as prehepatic, hepatic, and post-hepatic – hepatic

causes are further subdivided into pre-sinusoidal, sinusoidal and post-sinusoidal. Most of the times, PHT is a late manifestation of the primary disease.[28]

Suprahepatic Causes: Suprahepatic abnormalities leading to portal hypertension include cardiac disease like chronic right ventricular failure, chronic constrictive pericarditis, tricuspid insufficiencies like regurgitation and stenosis of tricuspid valve, hepatic vein etiology, and inferior vena cava thrombosis or webs. Hepatic vein thrombosis, or Budd-Chiari syndrome, has multiple etiologies but is usually associated with hyper coagulable state and often treatable with anticoagulation. Liver fibrosis can result from suprahepatic disease, and cirrhosis can also develop late in the disease course.

Infrahepatic Causes: Alterations of portal venous blood flow can also lead to portal hypertension. Arteriovenous malformation of the splenic vasculature, splenomegaly and portal vein thrombosis are examples of infrahepatic causes of portal hypertension. Overall, these are not common conditions.

There had been a 46% increase in Chronic liver disease (CLD) death rate worldwide from 1980 to 2013, underscoring the emerging public health importance of CLD. Most of this increase in CLD mortality has been reported from the low and low-middle income (LMIC) countries of Asia and Africa. [29]The causes of portal hypertension in a country can vary over time. With increasing affluence, better standards of living as well as change to more sedentary lifestyle in India, metabolic syndrome leading to non-alcohol related fatty liver disease (NAFLD) as well as alcohol related cirrhosis are expected to increase in the coming years while hepatitis B or C virus related cirrhosis may be expected to decline.[27]

Portal hypertension and ascites

The pathological accumulation of fluid in the peritoneal cavity leads to ascites[30] It is mainly associated with cirrhosis and portal hypertension, because of the increase of the sinusoidal

hydrostatic pressure. Cirrhosis accounts for over 75% of episodes of ascites.[31] Conventionally, ascites has been classified as transudate or exudate with a cut-off value of ascitic fluid total protein (AFTP) of 2.5gm%.[32]

Pathophysiology

Portal hypertension leads to splanchnic arterial vasodilation in advanced cirrhosis. It ultimately results in impairment of systemic and splanchnic circulation. Further, systemic vasodilation leads to relative hypovolemia, with a decrease in effective blood volume and a fall in mean arterial pressure. States of homeostasis and antinatriuresis are activated to maintain arterial pressure, which results in sodium and fluid retention. Moreover, portal hypertension and splanchnic arterial vasodilation together alters splanchnic microcirculation and permeability of intestine, enabling the outflow of fluid into the abdominal cavity. [33]As cirrhosis progresses, the kidneys' ability to excrete sodium and free water is impaired; sodium retention and ascites develop when the amount of sodium excreted is less than the amount consumed. Decreased free water excretion leads to dilutional hyponatremia and eventually to impaired renal perfusion and hepatorenal syndrome.[23, 33] Severity of liver function reserve and presence of ascites are also important risk factors for variceal bleeding.[34]

Complications

Main complications of ascites are refractory ascites, hepatorenal syndrome and spontaneous bacterial peritonitis. Refractory ascites develops in about 10% of cases.[35] Hepatorenal syndrome occurs in up to 10% of patients with ascites[33] and can be described by a serum creatinine concentration greater than 1.5 mg/dL (> 133 μmol/L). Type 1 hepatorenal syndrome involves the rapid impairment of renal function resulting in increase in serum creatinine concentration to more than 2.5 mg/dL (> 221 μmol/L) within 2 weeks.[36] In type 2 hepatorenal syndrome, renal impairment is stable or progresses at a slower rate than that in

type 1.[23] Spontaneous bacterial peritonitis, an infection of the ascitic fluid, occurs in 10%–30% of patients with ascites.[37]

Diagnosis and Treatment

The diagnostic evaluation of ascites involves an assessment of its cause by determining the serum-ascites albumin gradient and the exclusion of complications eg, spontaneous bacterial peritonitis. Calculation of SAAG is performed by measuring albumin concentrations of serum and ascitic fluid on the same day and then subtracting the ascitic fluid albumin value from the serum albumin value. A SAAG value greater than or equal to 1.1 g/dL (11 g/L) predicts ascites due to PH with approximately 97% accuracy. Cell count, albumin, total protein concentration, and SAAG are tested in the initial testing of ascitic fluid if the ascites is believed to be likely uncomplicated on clinical grounds. [30]

Treatment of ascites includes diuretic therapy and dietary sodium reduction. In refractory ascites, repeated large-volume paracentesis (with volume expansion using albumin) and TIPS can be advised. In hepatorenal syndrome, the most serious complication is ascites, liver transplantation should be considered; vasoactive drug therapy in combination with albumin infusion can be given in the meantime. All patients with ascites must be screened for spontaneous bacterial peritonitis; if detected, treatment consists of antibiotics and albumin infusion to prevent hepatorenal syndrome.[23]

Portal hypertension and Esophageal Varices: pathophysisology:

Understanding of portal hypertension leading to variceal development improved slowly from 1928, when Wolf first demonstrated, in two patients, the occurrence of esophageal varices on thin barium Roentgenograms as small dilated luminal structures. Thereafter, studies in 1936 by Rousselot on patients with ‘Banti’s syndrome’ shed light on elevated portal pressures and, in 1937, Thomson and colleagues confirmed these findings by portal pressure measurement during celiotomy procedures[19] Portal hypertension leads to splanchnic and systemic arterial

vasodilation, contributing to increased splanchnic blood flow to the liver and increased portal pressure despite collateral formation. An excessive vasodilation of the mesenteric arteries facilitates this hyper dynamic circulation, and along with increasing blood flow to portosystemic collaterals results in clinically devastating complications including gastroesophageal varices and variceal hemorrhage, hepatic encephalopathy from the formation of portosystemic shunts, ascites, and renal failure due to the hepatorenal syndrome.[38]

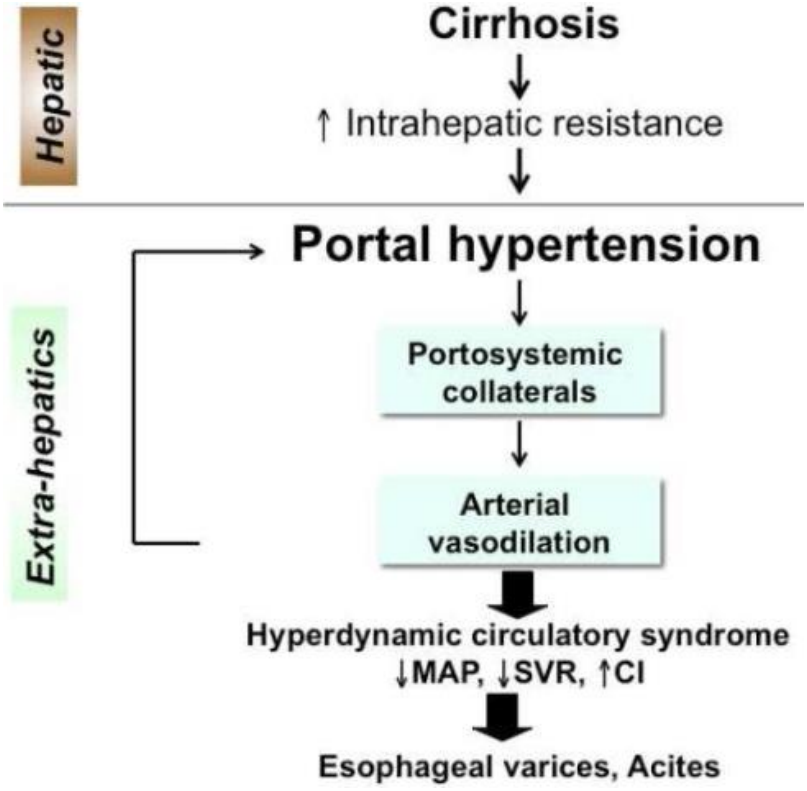


Figure 1:- Etiology of EV

Grading of EV

Subsequent to Butler's description about microvascular portal venous anatomy several classification and grading system for esophageal varices arosed. In 1955, Brick and Palmer first classified oesophageal varices. The first attempt at grading oesophageal varices by way of rigid oesophagoscopy was also made by Brick and Palmer in 1964. They graded varices as mild (<3 mm in diameter), moderate (3–6 mm) and severe (>6 mm) on direct visualization.

There are several gradding systems for esophageal varices

I. Conn’s classification
II. Dagradi classification
III. Soehendra classification
IV. Westaby classification
V. Paquet’s classification
VI. Cale`s classification

Conn’s classification: The Conn classification of oesophageal varices came into being in 1967. This classification dealt mostly with the presence and size of varices without mucosal descriptions. To improve the detection of varices, he had proposed the use of red filters and/or colour photography.

Grade I: Visible only during one phase of respiration/performance of Valsalva manoeuvre.

Grade II: Visible during both phases of respiration.

Grade III: 3–6mmin diameter.

Grade IV: >6mmin diameter.

After much complexity and multiple classification systems, the classification of oesophageal varices that is most comprehensively followed and universally endorsed is currently the one accepted by the Baveno consensus, endorsed by the American Association for Study of Liver Diseases (AASLD), the European Association for Study of the Liver (EASL) and the Asian-Pacific Association for Study of the Liver (APASL) societies, which classifies varices

(i) into small (<5 mm) and large (>5 mm)
(ii) the presence or absence of red colour signs.[19]

Mortality of due to EV

Variceal bleeding is a devastating complication of portal hypertension. The 6-week death rate among individuals with liver cirrhosis is between 17%-28% and rebleeding risk after acute

variceal hemorrhage (AVH) is highest within the first 6 week with a peak in the first 5 days.[6] Although mortality from a variceal bleeding episode has decreased with improved endoscopic and radiological techniques together with new pharmacologic therapies, a 15–20% mortality means that bleeding from oesophageal varices remains of significant clinical importance.[39] Approximately one-third of patients with varices develop acute bleeding, and each episode of variceal bleeding is associated with a 30 percent risk of mortality. The poor prognosis of bleeding from varices has led to an attempt to identify patients at high-risk for bleeding and attempts to prevent bleeding.[40]

Screening and diagnosis of EV: talk about upper GI endoscopy

Studies on primary prophylaxis of EV had shown that the risk of variceal hemorrhage can be reduced by 50% to about 15% for large esophageal varices. Hence early diagnosis of varices before the first bleed is essential.[39] Upper gastro intestinal endoscopy is the best available modality for screening. But it is associated with so many unwanted side effects. Endoscopic examination may require endotracheal intubation in patients who have significant alteration in mental status as a result of severe hepatic decompensation. Upper GI endoscopy may be performed with or without light sedation and should include a complete examination of the esophagus, stomach, and proximal duodenum, because portal-hypertension related lesions can be found in all 3 sites. Gastrointestinal endoscopy allows the physician to visualize and biopsy the mucosa of the upper gastrointestinal tract including the esophagus, stomach, and duodenum. The enteroscope allows visualization of at least 50% of the small intestine, including most of the jejunum and different degrees of the ileum. During endoscopic procedures, a pharyngeal topical anesthetic may be administered to help prevent gagging. Pain medication and a sedative may also be given priory. Left lateral position is the preferred posture. “All patients with cirrhosis should be screened for varices at diagnosis.” However, at a given point in time, a significant number of patients may not have varices; in fact, the

reported prevalence of esophageal varices is variable, ranging in different series between 24% and 80%. Thus, screening all cirrhotic patients with upper GI endoscopy to detect the presence of varices implies several unnecessary endoscopies, which increase the workload of endoscopy units. In addition, compliance with endoscopic screening recommendations may be suboptimal, because they require patients who are often totally asymptomatic to repeatedly undergo a procedure that is perceived as unpleasant.[41]

Role of non-invasive screening methods: a brief note on various methods

The Baveno IV Consensus Conference on PHT recommended that all patients with cirrhosis should be regularly screened for presence of varices. Endoscopy should be performed at 2-3 yearly intervals in patients without varices and at 1-2 yearly intervals in patients with small varices. [7]The widespread use of endoscopy as a clinical investigation method is hindered by the invasive nature and unavailability for large-scale and bedside use because it can only be performed in highly specialized centers. Moreover, such practice eventually places a significant burden on medical and economical resources.[40] Therefore several noninvasive markers that correlate with portal pressure, aand easy to test for had recently been evolved.[18] They provide quantifiable and immediate results, and help accurately stratify the risk of patients with chronic liver disease, thereby reducing the need of invasive tests only for selected cases.

Laboratory Tests: Laboratory tests assessing the degree of protein-synthetic function of the liver (albumin, international normalized ratio, bilirubin) correlate with the HVPG and the presence and grade of esophageal varices in patients with compensated as well as decompensated cirrhosis. However, the correlation is not good enough to allow these tests to be used for diagnosing PH or esophageal varices.

PSR: The PSR is calculated by dividing the platelet number per cubic millimeter by the maximum spleen bipolar diameter(mm) as assessed by abdominal ultrasonography. The ratio is higher in patients without than in those with varices.

Finometer: The Finometer® (Finapres Medical Systems, Amsterdam, The Netherlands) is a non-invasive device that allows continuous beat-to-beat blood pressure and haemodynamic monitoring over a number of hours. Utilising a volume-clamp method to provide a continuous measure of finger pressure with subsequent reconstruction of brachial pressure, it allows the computation of an aortic flow wave form and impedance from which HR, SV, peripheral vascular resistance and cardiac output can be derived. The Finometer therefore provides a non-invasive method of continuous beat-to-beat measurement of systemic haemodynamic variables with good positive correlation to portal pressure

SAAG: what is it? Pathophysiology? How is it useful in differential diagnosis of ascites

The serum ascites albumin gradient (SAAG), a minimally invasive method, which is based on the difference between the serum albumin level and albumin level of ascitic fluid is thought to reflect the colloid osmotic pressure gradient and the degree of portal hypertension. Portal hypertension results in a high hydrostatic pressure gradient between the portal bed and ascitic fluid. As a compensatory mechanism, a difference develops between the ascitic fluid and intravascular oncotic forces. Amongst all proteins, albumin exerts the maximum oncotic force per gram. Accordingly, the Serum-Ascites Albumin Gradient (SAAG), i.e. serum albumin minus ascitic albumin, reflects the changes in oncotic forces due to PHT and thus provides a useful tool in the differential diagnosis of ascites. [32]It is pointed out in the literature that the SAAG is an indicator of PHTN, and that a direct relationship probably exists between SAAG and different PHTN measurements, these parameters being obtained by invasive methods.[42] Patients with SAAG $\geq$ 1.1 gm/dL is considered as having high SAAG, indicating the presence of portal hypertension, while those with SAAG < 1.1 gm/dL are

considered as having low SAAG, indicating the absence of portal hypertension. [43] The SAAG correlates well with PH in cirrhotic patients. It is also of particular utility to differentiate between congestive heart failure and malignant ascites without liver metastases (both of them with elevated ascites fluid proteins -AFP-). [12] The SAAG appears to retain its predictive value despite diuresis, infusion of albumin, therapeutic paracentesis or infection in the ascitic fluid. [13]

Table 1: Classification of causes of serum-ascites albumin concentration gradient

High Gradient (> 1.1 gm/dl)	Low gradient (1.1 gm/dl)
Cirrhosis	Peritoneal carcinomatosis
Alchoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Mixed ascites	Bowel obstruction/infarction
Massive liver metastasis	Biliary ascites
Fulminant hepatic failure	Nephrotic syndrome
Budd-chiari syndrome	Postoperative lymphatic leak
Portal vein thrombosis	Serositis in connective tissue diseases
Veno occlusive disease	
Myxoedema	
Fatty liver of pregnancy	

Treatment of EV

Primary prophylaxis: In patients with no EV, no specific treatment is recommended.[22] For medium and large sized EV, either non-selective beta blockers (NSBB) or endoscopic band ligation (EBL) are recommended for primary prophylaxis.[44] The most commonly used beta-blockers are propranolol and nadolol. Multiple prior studies have shown EBL as better alternative for preventing variceal bleeding.[22] A recent meta- analysis has reported that there is no difference in bleeding-related and all-cause mortality rates between beta blockers and EBL.[45, 46]

Initial treatment: Acute variceal bleeding is a medical emergency that requires a multidisciplinary team of experienced staff.[47] The first step in treating variceal bleeding is the airway, breathing and circulation scheme (ABC). Patients with acute variceal bleeding, especially those with hepatic encephalopathy, are at a great risk of aspiration of blood and gastric contents, and the risk can increase with endoscopic procedures. All patients should have adequate intravenous access to allow volume expansion with crystalloids and transfusion of blood product. Patients with acute bleeding should be given fluids to maintain systolic blood pressure above 100 mmHg.[48-50] Hypotension and hypo perfusion should be carefully avoided to prevent infections and renal failure leading to increased risk of re-bleeding and mortality.[49, 51] Transfusion of blood should be administered to maintain hemoglobin between 7 and 8 g/dL.[47, 49, 51] It is also important to administer other blood products to achieve hemostasis because cirrhotic patients usually have thrombocytopenia and coagulopathy. Current guidelines suggest platelet transfusion if platelet count is less than 50 $\times 10^9$ /L,[47] fresh frozen plasma if international normalized ratio (INR) is greater than 1.5, and cryoprecipitate if fibrinogen is less than 150 mg/dL.

Pharmacotherapy: Vasoconstrictors like somatostatin, vasopressin,terlipressin should be administered as soon as possible when acute variceal bleeding is suspected.[48, 51]A meta-analysis showed that using vasoactive medications is associated with lower all-cause mortality, decreased transfusion requirements, improved control of bleeding and shorter hospital stay.[52] Prophylactic antibiotics are administered to prevent complication associated with bacterial infection in bleeding varices.

Endoscopic therapy: After initial resuscitation and stabilization, patients should undergo EGD for diagnosis and definitive treatment. In clinically significant bleeding, it is recommended that EGD should be performed within 12 hours of hospital admission.[44] In

stable patients, timing of endoscopy is controversial. Endoscopic options for treatment of EV include ligation and sclerotherapy.

Salvage therapy: In patients who are too unstable to have endoscopy or when endoscopic therapy fails to achieve hemostasis, balloon tamponade, mostly with a Sengstaken-Blakemore tube, offers another mean to stop bleeding with a success rate as high as 80%.[48, 53, 54] Self-expandable, esophageal covered metal stents offer an alternative to balloon tamponade for managing refractory bleeding. For patients with refractory bleeding or and/or failure to control bleeding with above mentioned modalities, transjugular intrahepatic portosystemic shunt (TIPS) represents the next step in management.[47]

Secondary prophylaxis: Patients are at increased risk of re-bleeding, after an acute episode of variceal bleeding.[55] The risk of re-bleeding after 1 year is 60%, with a mortality rate of 33%.[47, 55] Patients who underwent TIPS during the acute bleed should be considered for liver transplantation and should have ultrasound with Doppler's to assess for TIPS patency every 6 months.[47, 55]All other patients should receive nonselective beta blocker, in combination with surveillance EGDs to achieve obliteration of EV.[22]

REVIEW OF RELEVANT STUDIES:

A hospital based cross sectional study were done by Rahman A et al to evaluate the relation between serum ascitic albumin gradient and oesophageal varices in cirrhosis of liver disease patient among 50 cases of diagnosed cirrhosis of liver disease patients in department of medicine of Mymensingh medical college Hospital, Mymensingh, Bangladesh. Out of 50 patients, 38(76%) were male and 12(24%) were female patients. Twenty four (48%) patients had SAAG value 1.1-1.49, 21(42%) patients had SAAG value 1.5-1.99, 5(10%) patients had Serum Ascitic Albumin Gradient (SAAG) value >2.0 and 16(32%) patients had no oesophageal varices, 11(22%) patients had small straight varices (F1) esophageal varices, 18(36%) patients had less than one-third of the esophageal lumen (F2) oesophageal varices,

5(10%) patients had more than one-third of the esophageal lumen (F3) esophageal varices. The study reported that the degree of SAAG demonstrate significant statistical association with presence or absence of oesophageal varices (p=0.023) and stages of the EV in cirrhotic patients.[14]

A prospective study done by Shahed FHM et al involving 50 patients with cirrhosis of liver with ascites assessed whether the serum ascites albumin gradient (SAAG) (the difference between the albumin level of serum and of ascitic fluid) is endowed with clinical implications. Based on SAAG values, the patients were divided into three groups: Group 1 – SAAG value 1.1 to 1.49 gm/dL (n = 15); group 2 – SAAG value 1.5 to 1.99 gm/dL (n = 9); and group 3 – SAAG value 2.0 gm/dL (n = 26). In group 1, 14 patients had esophageal varices (93.3%) and 13 had gastropathy (86.6%). In group 2, all 9 patients had esophageal varices (100%), 7 (77.7%) had gastropathy, and 1 (11.1%) had gastric varices. In group 3, all 26 patients had esophageal varices (100%), 24 patients (92.3%) had gastropathy. Conclusion was that serum ascites albumin gradient value is weakly related to the extent of portal hypertension in patients with liver cirrhosis and its implication seems to be limited in clinics.[43]

Demirel U et al did a cross sectional study among 45 patients with non-alcoholic cirrhosis detected between January 2002 and June 2003 to evaluate whether a correlation exists between several parameters among non-alcoholic cirrhotic pateints. Albumin levels in the serum and ascites and esophageal varices were studied and the correlation between these parameters was assessed. Serum level of albumin was determined as 2.53+/-0.53 g/dl, ascites level of albumin as 0.42+/-0.31 g/dl and SAAG as 2.1+/-0.51. Endoscopic esophageal examination revealed first-degree esophageal varices in 15 patients, second-degree esophageal varices in 18 patients and third-degree esophageal varices in eight patients; no esophageal varices could be found in four patients. Furthermore, the patients were classified

by their SAAG values, and their varices were then assessed. Two of four patients with SAAG values between 1.1 and 1.49 had esophageal varices, as did 13 of 15 patients with SAAG values between 1.5 and 1.99. Findings from study was that, no correlation between the severity of the esophageal varices and serum levels of albumin (p=0.7) and SAAG (p=0.2).[16]

Gurubacharya DL et al conducted a cross sectional study to determine level of serum-ascites albumin concentration gradient among patients with portal hypertension. Low SAAG was found in 7 of 32 patients and high SAAG in 25 patients. The study found no association between the level of SAAG and size of oesophageal varices. Whereas high SAAG level and EV is related to level of SAAG.[15]

Das BB et al assessed SAAG level and its relation with oesophageal varices presence among childrens. The SAAG was measured in all 26 patients. 15.4% (4 of 26) had low SAAG (< 1.1 g/dl) ($p < 0.001$). EV was found in 91% and in 50% patients with high and low SSAG value respectively. The SAAG differentiated cirrhosis with EV from those without EV (sensitivity = 91%, specificity = 50%, positive predictive value = 91%, negative predictive value = 50% and efficacy = 85%). The study reported that high serum ascites albumin gradient can predict the presence of EV in children with ascites.[56]

A study by Mene A et al explored asoociation between SAAG measurements and the presence of gastrointestinal haemorrhage among patients with portal hypertension and ascites. Fifty-six consecutive patients of portal hypertension with ascites attending the GI surgery outpatients clinic were divided into two groups on the basis of history: (a) those who had no history of GI bleeding; and (b) those who had an episode of GI bleeding within the past 21 days. Groups (a) and (b) were compared and sensitivity, specificity, positive and negative predictive value of SAAG was assessed. SAAG values correlated significantly with bleeding and splenomegaly. For prediction of bleeding, SAAG is 100% sensitive and 33.33% specific. Estimation of SAAG is possible even in a small, modestly equipped laboratory, and

could provide a new means for the identification of high-risk patients for GI bleeding and define patients more accurately for future clinical studies.[57]

A hospital based cross sectional study was conducted by Suresh I et al [58]with an objectives to assess the correlation of level of "Serum-Ascites Albumin Concentration Gradient" (SAAG) and complications of "Portal hypertension" (PHTN), manifested by "Esophageal Varices" (EV) among 100 ascitic patients. SAAG was measured in all subjects. EV was assessed by endoscopy in all. Data was analyzed using proportions and appropriate statistical tests. Higher value of SAAG was seen in 79% of the patients. EV incidence was 84.5%.. The incidence of EV among patients with high "SAAG value of 1.1 to 1.44 g/dl" was 50%. The size of the EV was associated with SAAG level. Patients having ascites with EV were also having high levels of SAAG. SAAG more than or equal to 1.2±0.05 g/dl can be used as a predictor of EV presence among ascites patients.

Begum N et al undertook a cross sectional study to set up a diagnostic value of SAAG for the prediction of portal hypertensive changes (oesophageal and gastric varices, gastropathy) of uppergastrointestinal endoscopy in children.A total of 30 cases of portal hypertension were studied from November 2008 to February 2010. Oesophageal varices were found in 86.7% of cases. Significant association was found between high SAAG values and presence of oesophageal varices. Frequencies of oesophageal varices increased as the SAAG values increased. SAAG value was 1.55gm/dl for the occurrence of EV where sensitivity and specificity were found 84.6% and 100 % respectively. From this study, it can be concluded that SAAG value 1.6gm/dl is an indicator of portal hypertensive changes.[17]

Gokturk HS et al study among 142 patients with ascites evaluated the role of ascitic fluid viscosity in discriminating between ascites due to portal hypertension-related and nonportal hypertension-related causes, and to compare results with the serum-ascites albumin gradient (SAAG). Serum total protein, albumin, glucose, lactate dehydrogenase (LDH) levels and

complete blood count were obtained for all subjects. Of the 142 patients studied, 34 (24%) had an SAAG of 11 g/L or less, whereas 108 (76%) had an SAAG of greater than 11 g/L. Sex and mean age did not differ significantly between the two groups (P>0.05). Serum total protein, albumin, glucose, LDH levels, leukocyte count, ascitic fluid glucose levels and ascetic fluid leukocyte counts were similar in both groups, with no statistically significant relationship detected (P>0.05). However, the mean (±SD) ascitic fluid total protein (0.0172±0.1104 g/L versus 0.043±0.011 g/L), albumin (0.0104±0.0064 g/L versus 0.0276±0.0069 g/L) and LDH (102.76±80.95 U/L versus 885.71±199.93 U/L) was raised among individuals with SAAG of 11 g/L or less than in those with an SAAG of greater than 11 g/L (P<0.001). Regarding the cut-off value of 1.03 cP, ascitic fluid viscosity measurement had a high sensitivity, specificity (98% and 80%, respectively), and positive and negative predictive value (79% and 94%, respectively) for the etiological discrimination of ascites. The study concludes that the measurement of ascitic fluid viscosity correlates significantly with SAAG values.[59]

Jiang CF et al, retrospectively assessed 213 adult patients with ascites to define a new reasonable threshold of SAAG in Chinese ascetic patients. The mean value of SAAG in non-portal-hypertension-related ascites was significantly lower than that in portal-hypertension-related ascites. The SAAG cut-off value under 12.50 g/L predicted portal hypertension ascites with the sensitivity of 99.20%, specificity of 95.10% and accuracy of 97.65%. SAAG is useful to distinguish portal-hypertension-related ascites and non-portal-hypertension-related ascites, with a mean threshold of 12.50 g/L.[60]

Khandwalla HE et al assessed the predictive value of a low SAAG in patients with existing cirrhosis in whom the pretest probability of portal hypertension is high among 92 patients (76 with cirrhosis and 16 with no cirrhosis) with ascites. Patients with SAAG of <1.1 g/dl during a 5-year period was identified at a single large veterans affairs medical center. Cirrhosis was

defined by clinical, histological, and radiological features. Nonportal hypertension causes of low SAAG were identified, including bacterial peritonitis, peritoneal carcinomatosis, nephrogenous ascites, tuberculous peritonitis, chylous ascites, and pancreatic ascites. Of the 76 patients with cirrhosis, only 29 (38%) had an identifiable cause, most commonly primary bacterial peritonitis (11, 38%), followed by peritoneal carcinomatosis or malignant ascites (8, 28%) and nephrotic syndrome (5, 17%). There were 47 patients with cirrhosis and a low SAAG for whom no etiology was identified. Thirty-three patients underwent a repeat paracentesis, 24 (73%) of whom changed to a high SAAG. On the other hand, the 16 patients with no cirrhosis had significantly lower SAAG (0.66 vs. 0.81), and most (12, 75%) had an identifiable cause of ascites. Evaluation of a SAAG <1.1 g/dl in patients with known cirrhosis has low yield and is less likely to be helpful than that in patients without cirrhosis. A repeat paracentesis as part of the workup is recommended. Further studies of low SAAG cutoffs are needed. [61]

The objective of the prospective study conducted by Shanker Suman et al was to correlate serum ascites albumin gradient with ascitic fluid total protein in patients of ascites having portal hypertension. 100 cases of ascites are selected randomly. All the provisional diagnosis is confirmed with the help of different biochemical, pathological and radiological investigations. SAAG (≥1.1gm/dl) was more sensitive and specific (94% and 90% respectively) than ascitic fluid total protein concentration of <2.5g/dL (78% and 50% respectively) in detecting portal hypertension and had higher positive and negative predicative values (97% and 82% respectively) compared to AFTP concentration (85% and 38% respectively). SAAG has good predictive validity in diagnosis and classification of ascites. [62]

A study was conducted by Dewa Gde Agung Budiyasa YA et al aimed to recognize the correlation between albumin level and the degree of EV among cirrhotic patients. A

retrospective analysis was performed for 61 patients with liver cirrhosis who had EGD at Sanglah hospital between January and December 2008. There were 61 patients of 45 (73.8%) male and 16 (26.2%) female. Age was between 13–77 years (average 49.98 ± 1.62 years). Serum albumin level ranged between 1.10-3.60 mg/dL, the average value was 2.21 ± 0.451 mg/dL. We also found 8 (13.1%) patients without EV, 14 (23.0%) patients with EV grade I, 21 (34.4%) patients with grade II and 18 (29.5%) patients with grade III. serum albumin level and the degree of EV showed a negative correlation. Serum albumin level can predict the presence and the degree of EV in patients with liver cirrhosis.[11]

Thirty three cirrhotic patients with ascites were evaluated by Abdelhakam1 EADGS et al to assess the relation between SAAG and presence of EV and their grades in patients with portal hypertension. All patients were subjected to clinico-laboratory assessment, ascitic fluid analysis, calculation of SAAG, abdominal ultrasonography and upper gastrointestinal endoscopy. SAAG>1.4 predicted the presence of varices with a specificity the accuracy of this cutoff was 56.1%. However, it had a low sensitivity and a low negative predictive value. A cutoff ">1.2" for SAAG to discriminate between large and small varices yielded a specificity of 69.2% and a positive predictive value of 66.7%, the accuracy of this cutoff was 60%. However, it had a relatively low sensitivity and low negative predictive value. A cutoff ">1.4" for SAAG to predict the presence of varices yielded 100% specificity, the accuracy of this cutoff was 56.1%.[63]

A cross-sectional, analytical study was conducted by Sarwar S et al to identify hematological, biochemical and ultrasonographic predictors of esophageal varices in patients of cirrhosis in Department of Gastroenterology, Shaikh Zayed Postgraduate Medical Institute, Lahore, from September 2003 to March 2004. 101 cirrhotic patients underwent physical examination, hematological, biochemical tests and abdominal ultrasound examination. Presence of varices on EGD was correlated with hematological, biochemical and ultrasonographic variables by

regression analysis. Esophageal varices were seen in 65 patients while 36 patients had no varices. High grade varices were seen in 15 patients and 50 patients had low grade varices. Serum albumin less than 2.95 g/dl, platelet count less than 88 x 103/muL and portal vein diameter more than 11 mm were associated with presence of varices. High grade varices were predicted by serum albumin < 2.95 g/dl and portal vein diameter more than 11 mm. Patients with serum albumin < 2.95 g/dl, platelet count < 88 x 103/muL and portal vein diameter > 11 millimeter are highly likely to have high grade varices. These patients are candidates for surveillance endoscopy. [64]

A cross sectional was conducted by Santosh Kumar IAM et al on 100 cirrhotic patients with ascites to calculate SAAG level in serum and ascitis fluid the value of SAAG was examined (≥1.1 g/dl) and high SAAG was measured to be ≥1.1 g/dl and Low SAAG when it is <1.1g/dL to rank esophageal varices. From total 100 patients, male were 62 and female were 38. SAAG was 2.01 ± 0.52. Esophageal varices (EV) found in 87 patients and were absent in 13 patients. Grades of the esophageal varices highlighted significant correlation with degree of SAAG with r =0.55 ($p<0.01$) of pearson correlation coefficient. With uses of ROC curve a SAAG value i.e. ≥1.65 ± 0.014 g/dl was an correct marker of the occurrence of EV; cutoff points for the higher predictive value 98% were positive, and 96% were nagetive. In the cirrhotic patients having ascites, the occurrence of EV is related only with SAAG and size of EV are mainly associated to the degree of SAAG. A SAAG value of ≥1.65 ± 0.014 g/dl is a helpful mean to predict the occurrence of EV in cirrhotic patients with ascites.[65]

A study was conducted by Dittrich S et al[66] to evaluate the correlation between serum-ascites albumin gradient and portal pressure gradient in a population with ascites related to multiple conditions. Group 1: 30 patients with cirrhosis as the cause of ascites, and group 2: 7 patients with ascites due to other causes. All patients were submitted to paracentesis and blood examination to determine the serum-ascites albumin gradient and the hepatic venous pressure

gradient was measured. Mean serum-ascites albumin gradient was 2.0 g/dL in group 1 and 0.6 g/dL in group 2. Mean hepatic venous pressure gradient was 14.7 mm Hg in group 1 and 1.3 mm Hg in group. There was a significant relation between SAAG and the hepatic venous pressure gradient (r = 0.502), indicating the reliability of the serum-ascites albumin gradient in demonstrating the presence of portal hypertension and its relationship with the origin of ascites.

A study was conducted by Sartori M et al to assess the value of a serum to ascites albumin gradient and ascitic white blood cell counts among one hundred and fifty-three patient. 3 groups were formed 1) serum to ascites albumin gradient > = 11 g/L and white blood cells < 0.5 x 10(9)/L predicted cirrhosis (or liver carcinoma) without peritonitis with 83% efficacy, 96% positive predictive value and 65% negative predictive value; 2) serum to ascites albumin gradient > = 11 g/L and white blood cells > = 0.5 x 10(9)/L predicted cirrhosis (or liver carcinoma) with peritonitis with 86% efficacy, 45% positive predictive value and 99% negative predictive value; 3) serum to ascites albumin gradient < 11 g/L predicted the other diagnoses with 92% efficacy, 77% positive predictive value and 95% negative predictive value. As serum to ascites albumin gradient > = 11 g/L and white blood cells < 0.5 x 10(9)/L predicted cirrhosis (or liver carcinoma) without peritonitis in 96% of the cases and excluded peritonitis in 99% of the cases, further fluid ascitic analyses could be considered as a second step only in patients with serum to ascites albumin gradient < 11 g/L and/or white blood cells > = 0.5 x 10(9)/L. In a group of ascitic patients where the prevailing diagnosis is cirrhosis (or liver carcinoma) without peritonitis, this simplified approach could provide a favourable cost/benefit ratio.[67]

Torres E et al evaluated the SAAG value among patient with PH. The study included thirty-one ascitic patients demonstrated by ultrasonography, who had measurement of the SAAG. They reported that 80.6% and 19.4% pf the patients had high and low SAAG values.

Presence of EV was found in 68%. 14 of 14 (100%) had EV among patients with portal hypertension. Otherwise, in patients with nonALD, only three of 11 (27.3%) had EV ($p < 0.05$). Size of EV was not associated with high SAAG value among patients. Using the Receiver-Operating-Characteristic Curve a SAAG value of > or =1.435 +/- 0.015 g/dl indicated presence of EV. The study findings were that high SAAG score and EV is directly related to degree of SAAG[42]

One thirty two ascitic patients (96 males and 36 females, mean age 58.8+/-15.9 years) were studied by Al-Knawy BA et al for the various causes of ascites. They compared SAAG with the three usual parameters of ascitic fluid biochemical analysis used in the differential diagnoses of ascites. The nonliver disease group showed higher ascitic fluid total protein (aTP) concentration (4.77+/-2.05 versus 1.98+/-1.56 g/dL), ascitic to serum ratio of total protein (a/sTP) concentration (0.75+/-0.43 versus 0.26+/-0.19), ascitic fluid lactic dehydrogenase (aLDH) level (565.4+/-353.4 versus 254.1+/-205.03 U/L) and a lower SAAG (0.6+/-0.30 versus 1.71+/-0.61). P7lt;0.0001 for all parameters. The positive predictive values for aTP, a/sTP, aLDH and SAAG to detect ascites due to liver disease were 68%, 76%, 67%, and 80%, respectively, while the negative predictive values were 96%, 96%, 84%, and 98%, respectively. Liver causes accounted for 69.7% of cases, followed by peritoneal tuberculosis 10.6%, malignancy 9.1%, congestive heart failure 7.6%, and nephrotic syndrome 3.0%. SAAG is a useful diagnostic parameter which can be used to separate ascites of liver disease (nonalcoholic) from other causes of ascites, with an efficiency of 91%.[68]

To identify predictors of esophageal varices (EV) using available clinical, laboratory, and diagnostic imaging variable study Charts were reviewed by Madhotra R et al for 247 consecutive patients with cirrhosis who underwent screening esophagogastroduodenoscopy for varices. A total of 184 patients (68 women) were studied. Ninety-four patients (51% had varices; of whom, 90 had only EV (small, n = 66; large, n = 24), 13 had EV and gastric

varices, and 4 had isolated gastric varices. The distribution of EV according to the Child–Turcotte–Pugh class was as follows: A, 35%; B, 60%; and C, 69%, with roughly equal prevalence of large varices (29%, 24%, and 24%, respectively) in each class. Independent predictors of large varices were thrombocytopenia ($p = 0.02$) and splenomegaly ($p = 0.04$) seen using imaging. A platelet count of less than 68,000/mm 3 had the highest discriminative value for large EV with a sensitivity of 71% and a specificity of 73%. Splenomegaly had sensitivity and specificity of 75% and 58%, respectively. Using these two variables, they placed patients into one of four groups, with a risk for large varices ranging from 4% to 34%. Esophageal varices in cirrhosis increases with the severity of liver disease, Thrombocytopenia and splenomegaly are independent predictors of large EV in cirrhosis.[69]

A study was conducted by Chaurasia AK et al to study the SAAG and presence and grades of esophageal varices correlation in CLD a total of 51 patients were studied which included 29 Alcoholic and 22 non Alcoholic CLD. These patients were devided into 3 groups - Group A with SAAG = 1.1-1.49 (6 patients), Group B with SAAG = 1.5-1.99 (21 patients) and Group C with SAAG > 2.0 (24 patients). In group A, 33% patient had varices, In group B, 76.1% had varices while in group C all the 24 patients (100%) had varices ($p<0.05$). Among alcoholic 26 out of 29 patients had varices while among non- alcoholic 16 out of 22 patients had varices ($Z=1.70$)**.** We concluded in our study that there was significant correlation between SAAG value and endoscopic parameter of portal hypertension manifested by presence of varices. But the SAAG value has no significant correlation with severity of varices. This correlation exist in both alcoholic as well non- alcoholic liver disease, though there is proportionate difference among both these group and correlation is weaker in non-alcoholic liver disease.[70]

MATERIALS & METHODS

Study site: This study was carried out in the Department of General Medicine at R.L.Jalappa Hospital, Kolar.

Study population: All the patients attending the General Medicine Department(out patients/in patients) at R.L.Jalappa Hospital and who fulfill inclusion and exclusion criteria from outpatients and inpatients were considered as study population.

Study design: The current study was a Case series study

Sample size: The sample size was calculated to assess one sample and sensitivity.

Numeric Results for testing H0: Se = Se0 vs. H1: Se ≠ Se0 and H0: Sp = Sp0 vs. H1: Sp ≠ Sp0

Test Statistic: Binomial Test

--- Sensitivity ---			**--- Specificity ----------**		**Alpha -------**	**Prevalence-----**	**Power -----**
Sample Size	**H0 Sens.**	**H1 Sens.**	**H0 Spec.**	**H1 Spec.**	**N1 and N**	**Se0**	**Se1**
			Sp0	**Sp1**		**Target**	**Actual**
			Actual		**P**		
0.9723			0.9362		24 48	0.5000	0.1000
			0.5000		0.8780	0.0100	0.0066
			0.0066		0.5000		

A total sample size of 48 (which includes 27 subjects with the disease) achieves 98% power to detect a change in sensitivity from 0.5 to 0.1 using a two-sided binomial test and 94% power to detect a change in specificity from 0.5 to 0.878 using a two-sided binomial test. The target significance level is 0.01. The actual significance level achieved by the sensitivity test is 0.1250 and achieved by the specificity test is 0.0066. The prevalence of the disease is 0.1.

Sampling method: All the eligible subjects were recruited into the study consecutively till the sample size is reached.

Study duration: The data collection for the study was done between from January 2017 to may 2018for a period of 1.5 years.

Inclusion Criteria:

- All patients aged above 18 years with chronic liver disease and portal hypertension
- Presence of chronic liver disease as evidenced by: abdominal ultrasound and liver profile derangement.
- Presence of portal hypertension as evidenced by the presence of splenomegaly, portal vein diameter > 13 mm.
- Presence of ascites detected by clinical examination and confirmed by abdominal ultrasound

Exclusion criteria:

- Patients with congestive heart failure.
- Patients with renal failure.
- Patients with tuberculosis.
- Patients with Hepatocellular carcinoma.

Ethical considerations: Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Study participants confidentiality was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

Patients attending R.L. Jalappa Hospital who satisfied the inclusion/exclusion criteria were included in the study after obtaining a written informed consent. A detailed clinical case

history of study participants including demographic data, history, clinical examination and details of investigation were recorded in study proforma. Under aseptic condition 10 ml of blood was drawn from the brachial vein and subjected to the investigations including CBC, RFT, LFT, RBS, serum albumin.

Under strict aseptic precautions 20 ml of ascitic fluied was taken (paracentecis) and sent for measuring ascitic fluid albumin concentration by using Bromocresol green dry binding method in vitrose 5.1fs dry chemistry analyser.

Serum Ascitic Albumin Gradient (SAAG) was calculated by subtracting the ascitic albumin concentration from serum albumin concentration (SAAG=serum albumin – ascitic albumin) g/dl.

The patients were subjected to upper gastro-intestinal endoscopy to determine presence/absence of the oesophageal varices and its grades.

The grades of oesophageal varices and its presence were correlated with SAAG ratio.

Investigations:

1) Liver function tests
2) Upper gastro intestinal endoscopy
3) Renal function tests
4) Hepatitis viral marker (HBsAg and anti HCV)
5) Ascitic fluid analysis-cell type, cell count, albumin, sugar
6) Abdominal ultrasonography
7) Complete blood count.
8) ECG

Statistical Methods:

Presence and grading of Esophageal varices was considered as primary outcome variable SAAG was considered as explanatory variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

The association between SAAG and Esophageal varices was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. Independent sample t-test was used to assess statistical significance.

RECEIVER OPERATIVE CURVE (ROC) analysis:

Predictive validity of SAAG in Esophageal varices was assessed by Receiver Operative curve (ROC) analysis. Area under the ROC curve along with it's 95% CI and p value are presented. Basing on the ROC analysis, it was decided to consider x, y, z as the cut off values. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test with the decided cut off values along with their 95% CI were presented.

P value < 0.05 was considered statistically significant. IBM SPSS version 22[71] was used for statistical analysis.

OBSERVATIONS AND RESULTS

RESULTS

A total of 50 people were included in the final analysis

Table 2: Descriptive analysis of Age in study population (N=50)

Parameter	Mean ± SD	Median	Min	Max	95% C.I	
					Lower	Upper
Age	50.26 ± 14.42	48.50	27.00	80.00	46.16	54.36

In study population, the mean age was 50.26 ± 14.42 years. Minimum age was 27 and maximum age was 80 years (95% CI 46.16 to 54.36). (Table 2)

Table 3: Descriptive analysis of gender in study population (N=50)

Gender	Frequency	Percentage
Male	48	96.00%
Female	2	4.00%

Among the study population 48(96%) were males and remaining 2(4%) were females. (Table 3 & figure 2)

Figure 2: Bar chart of Gender distribution in study population (N=50)

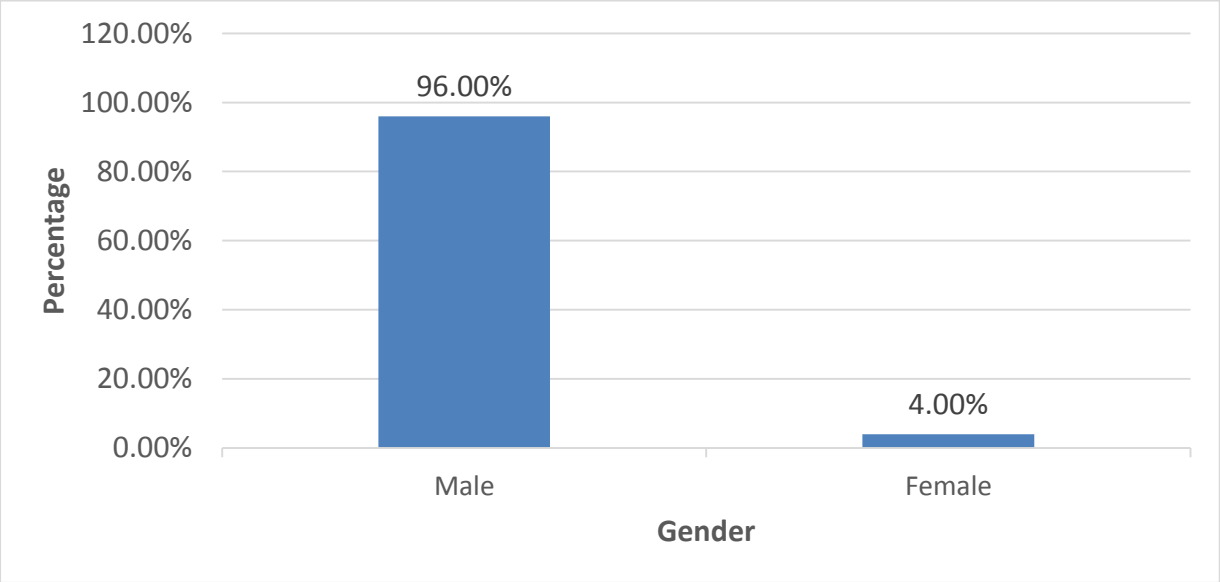


Table 4: Descriptive analysis of hematemesis in study population (N=50)

Hematemesis	Frequency	Percentage
Yes	14	28.00%
No	36	72.00%

Among the study population 14(28%) participants had Hematemesis. (Table 4 & figure 3)

Figure 3: Pie chart of hematemesis distribution in study population (N=50)

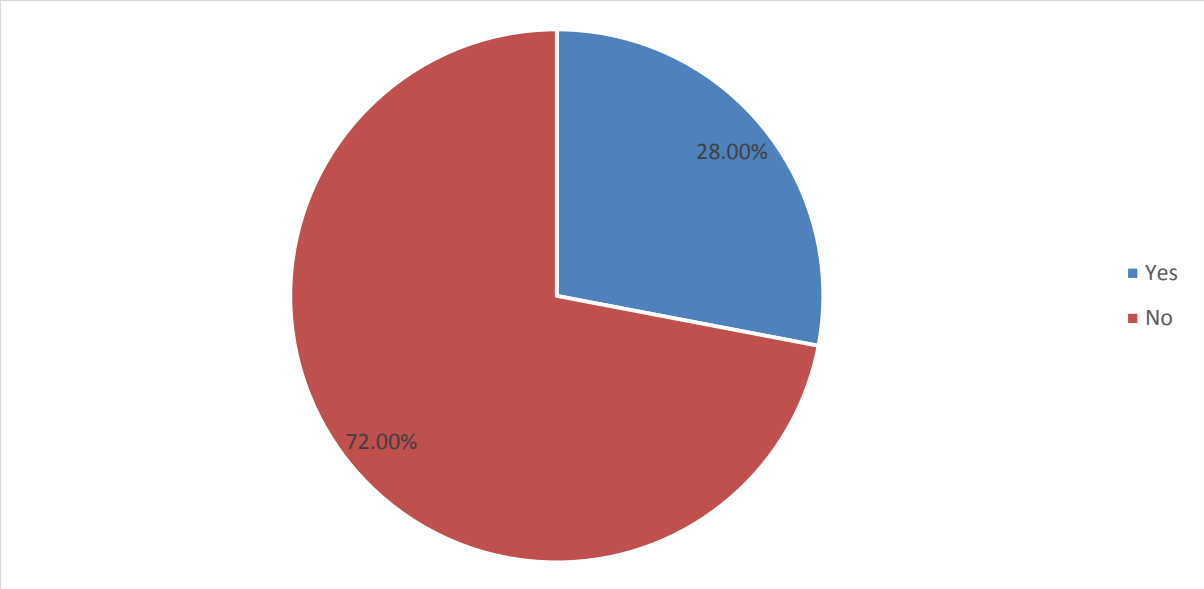


Table 5: Descriptive analysis of hepatic encephalopathy in study population (N=50)

Hepatic encephalopathy	Frequency	Percentage
Yes	15	30.00%
No	35	70.00%

Among the study population 15(30%) participants had hepatic encephalopathy (Table 5 & figure 4)

Figure 4: Bar chart of hepatic encephalopathy distribution in study population (N=50)

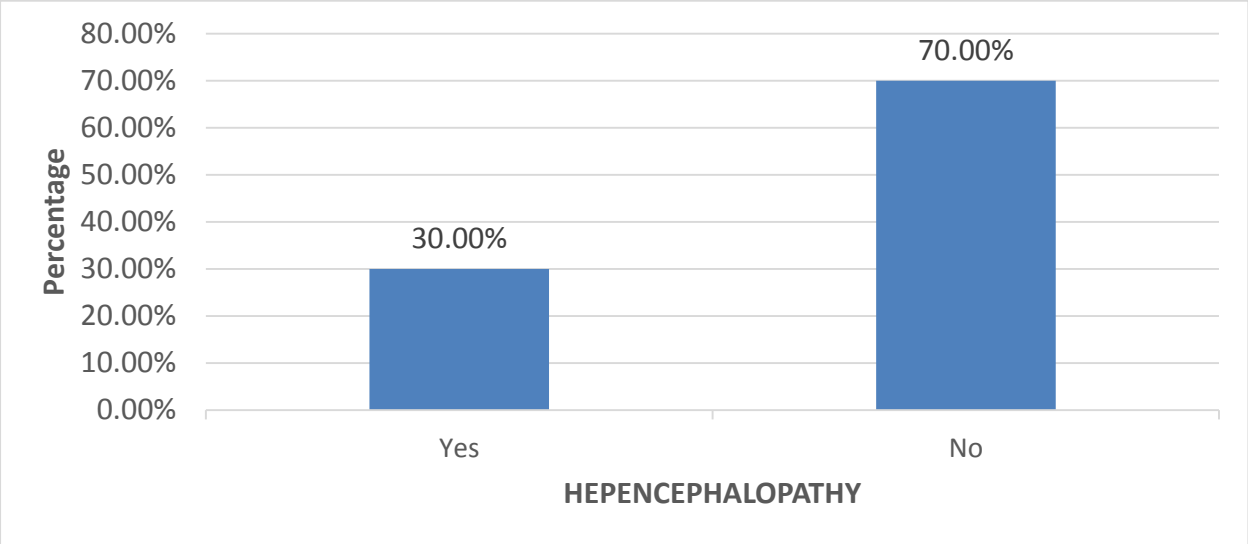


Table 6: Descriptive analysis of ASCITES in study population (N=50)

ASCITES	Frequency	Percentages
GRADE1	1	2.00%
GRADE2	33	66.00%
GRADE3	16	32.00%

Among the study population only 1(2%) had grade 1 ascites, 33(66%) had grade 2 and 16(32%) had grade 3 ascites. (Table 6& figure 5)

Figure 5: Pie chart of ASCITES distribution in study population (N=50)

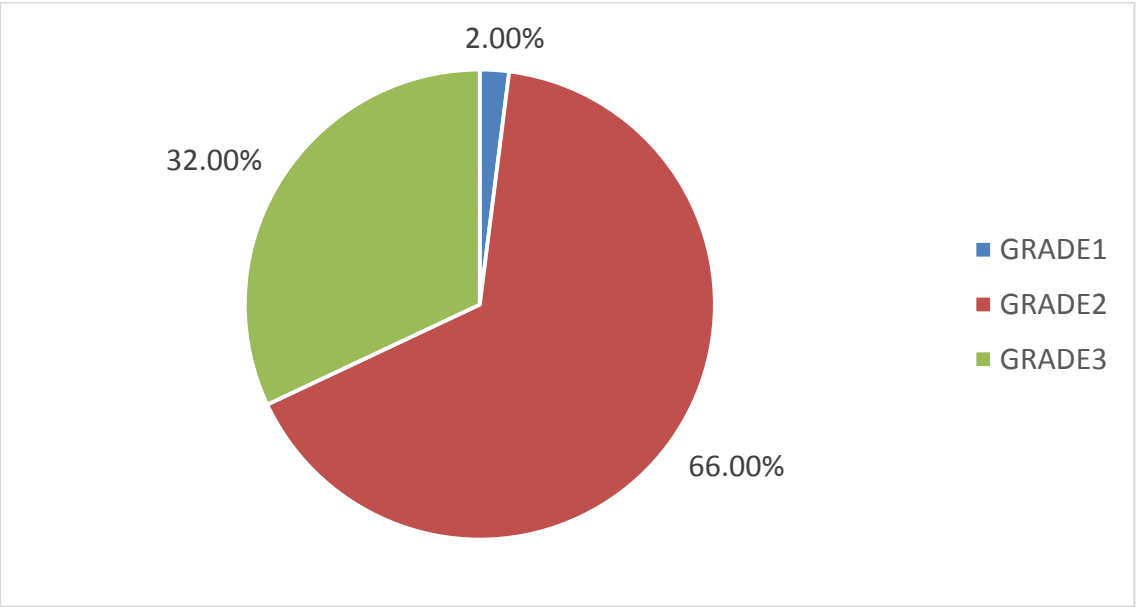


Table 7: Descriptive analysis of HBsAg in study population (N=50)

HBsAg	Frequency	Percentage
Yes	7	14.00%
No	43	86.00%

Among the study population only 7(14%) participants were seropositive for HBsAg. (Table 7 & figure 6)

Figure 6: Bar chart of HBsAg distribution in study population (N=50)

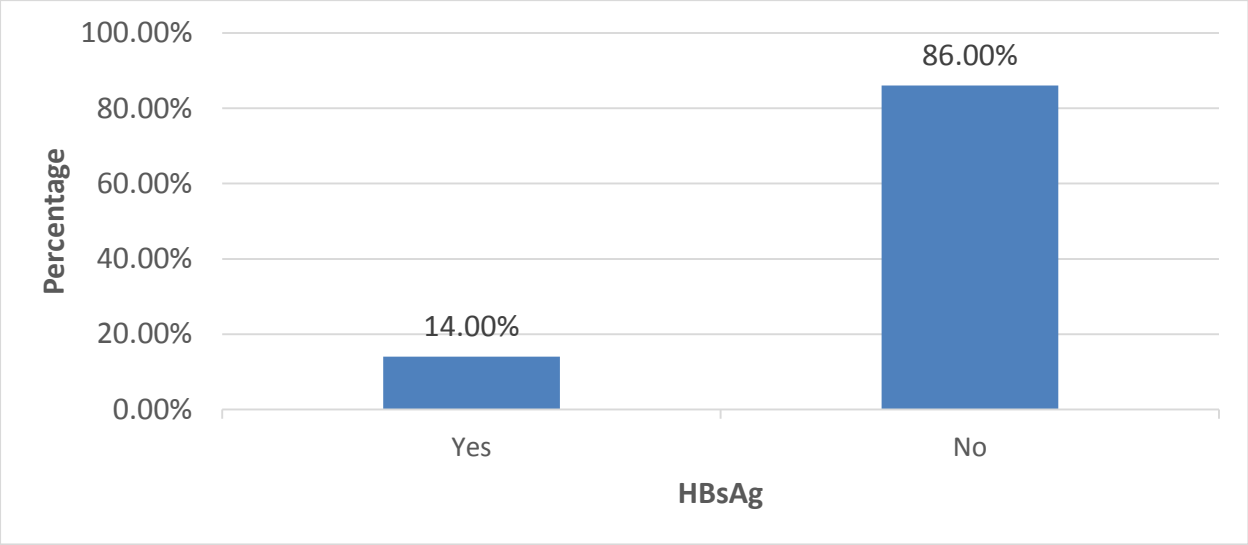


Table 8: Descriptive analysis of HCV in study population (N=50)

HCV	Frequency	Percentage
Yes	3	6.00%
No	47	94.00%

Among the study population only 3(6%) participants were seropositive for HCV. (Table 8 & figure 7)

Figure 7: Bar chart of HCV distribution in study population (N=50)

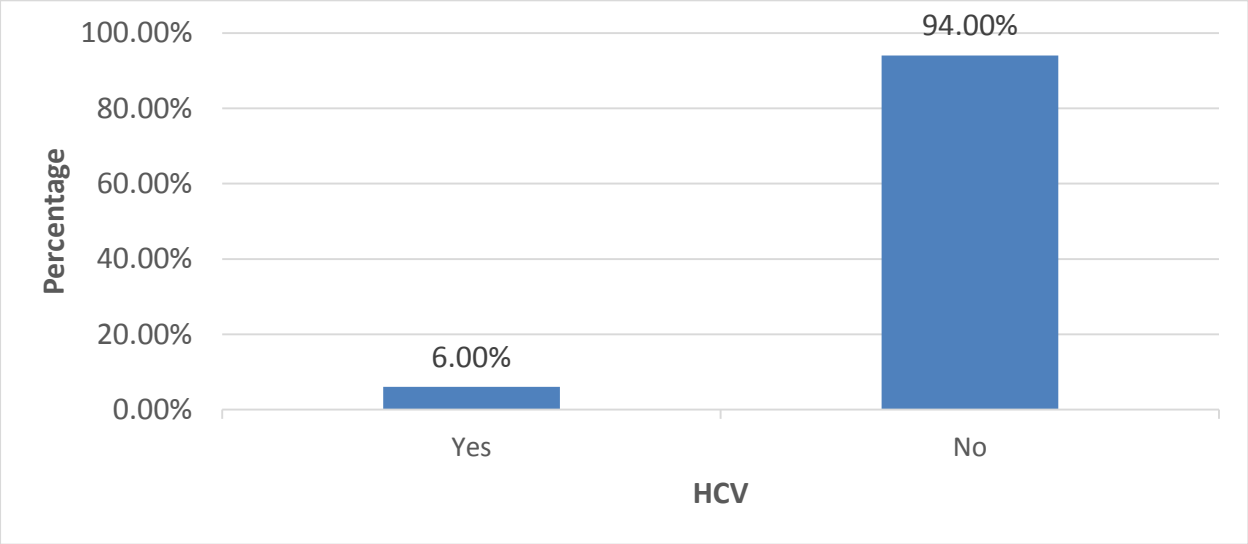


Table 9: Descriptive analysis of etiology of liver disease/portal hypertension (N=50)

Other	Frequency	Percentage
Alcoholic	40	80.00%
Alcoholic+HBsAg	3	6.00%
HBsAg	4	8.00%
HCV	3	6.00%

Among the study population 40(80%) were alcoholic, 3(6%) were alcoholic with HBsAg, 4(8%) had HBsAg and remaining 3(6%) had HCV. (Table 9& figure 8)

Figure 8: Pie chart of other distribution in study population (N=50)

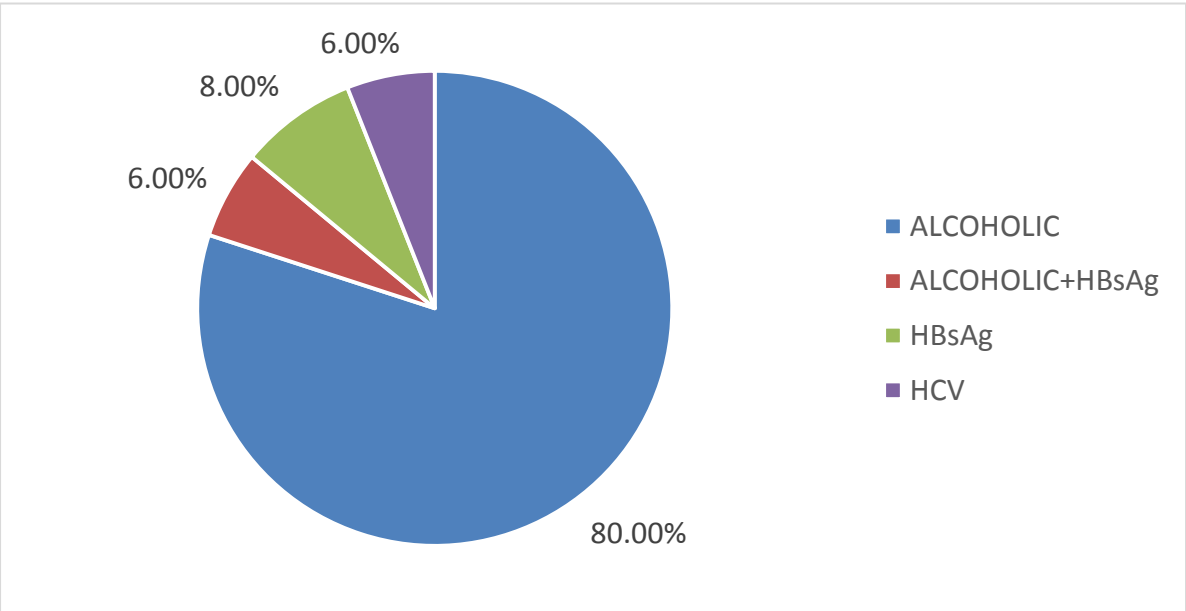


Table 10: Summary of laboratory parameters (N=50)

Parameter	Mean ± SD	Median	Min	Max	95% C.I	
					Lower	Upper
Platelet (Cells/cumm)	140479.17 ± 67897.29	135000	15000	37600	120763.85	160194.48
Total Bilirubin(gm/dl))	4.92 ± 5.97	2.55	0.00	25.0	3.18	6.65
Direct Bilirubin (gm/dl))	2.26 ± 2.67	1.20	0.10	12.0	1.49	3.04
Serum albumin (gm/dl))	2.2 ± 0.42	2.15	1.40	3.8	2.08	2.32
AST(IU/L)	138.46 ± 158.77	105.00	18.00	109	92.36	184.56
ALT(IU/L)	90.25 ± 162.71	53.00	7.00	1100	43.0	137.5
INR (IU/L)	1.63 ± 0.95	1.30	0.90	5.6	1.35	1.90
Asciticfluid albumin ()	0.34 ± 0.25	0.20	0.10	1.0	0.27	0.41

The mean of platelets was 140479.17 ± 67897.29. Minimum level was 15000 and maximum level was 376000. The mean of total bilirubin was 4.92 ± 5.97. Minimum level was 0 and maximum level was 25 in study population. The mean of direct bilirubin was 2.26 ± 2.67. Minimum level was 0.10 and maximum level was 12 in study population. The mean of serum albumin was 2.2 ± 0.42. Minimum level was 1.40 and maximum level was 3.80 in study population. The mean of AST was 138.46 ± 158.77. Minimum level was 18and maximum level was 1100 in study population. The mean of ALT was 90.25 ± 162.71. Minimum level was 7 and maximum level was 1100 in study population. The mean of INR was 1.63 ± 0.95. Minimum level was 0.90 and maximum level was 5.60 in study population. The mean of Asciticalbumin was 0.34 ± 0.25. Minimum level was 0.10 and maximum level was 1 in study population. (Table 10)

Table 11: Descriptive analysis of SAAG in study population (N=50)

Parameter	Mean ± SD	Median	Min	Max	95% C.I	
					Lower	Upper
SAAG(g/L)	1.86 ± 0.52	1.95	1.10	3.70	1.72	2.01

The mean of SAAG was 1.86 ± 0.52. Minimum level was 1.10 and maximum level was 3.70 in study population. (95% CI 1.72 to 2.01) (Table 11)

Table 12: Descriptive analysis of esophageal varices in study population (N=50)

Esophageal varices	Frequency	Percentage
Yes	38	76.00%
No	12	24.00%

Among the study population 38(76%) had Esophageal varices. (Table 12& figure 9)

Figure 9: Pie chart of esophageal varices distribution in study population (N=50)

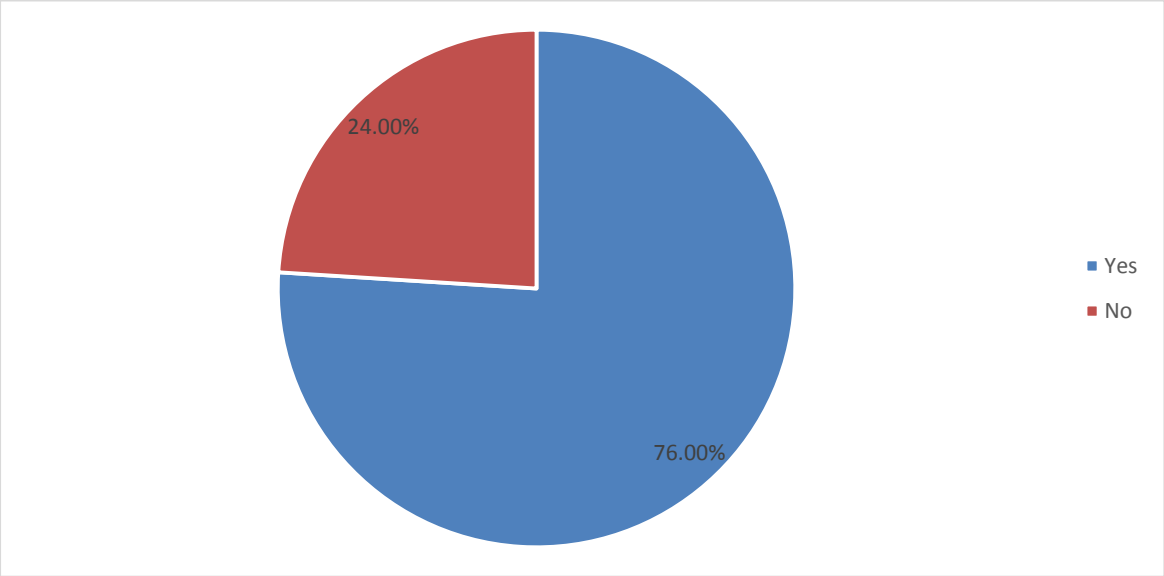


Table 13: Descriptive analysis of esophageal varices in study population (N=50)

Esophageal Varices	Frequency	Percentage
GRADE1	9	18.00%
GRADE2	14	28.00%
GRADE3	15	30.00%
NO	12	24.00%

Among the study population 9(18%) had grade 1 Esophageal Varices, 14(28%) had grade2, 15(30%) had grade 3 and 12(24%) had no Esophageal Varices. (Table 13 & figure 10)

Figure 10: Bar chart of esophageal varices distribution in study population (N=50)

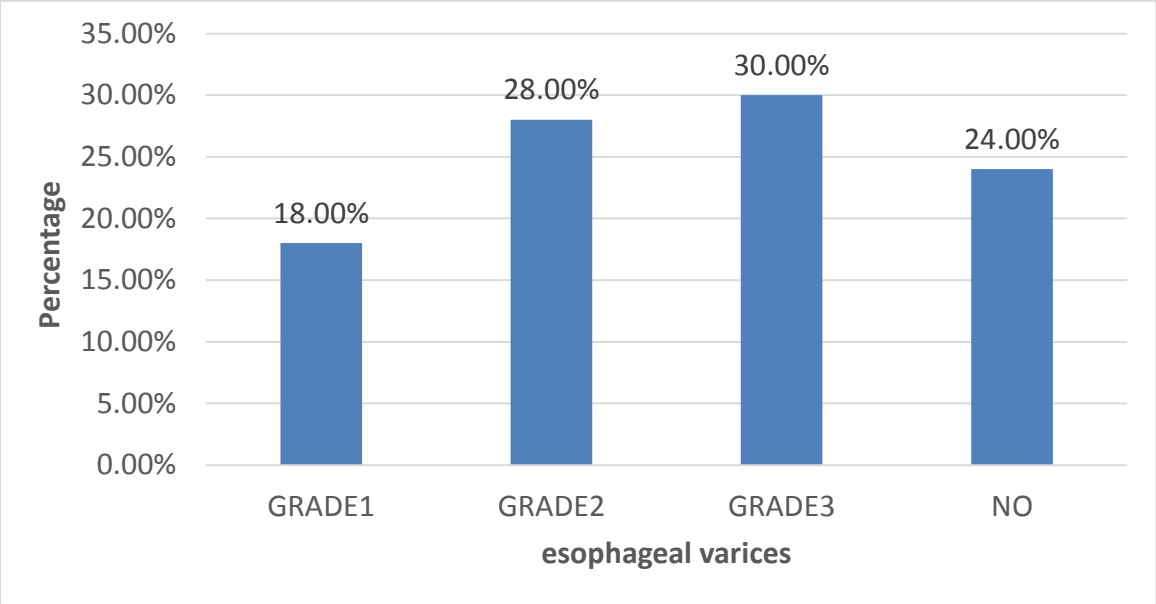


Table 14: Comparison of mean SAAG between study groups (N=50)

Esophageal varices	SAAG Mean± STD	Mean difference	95% CI		P value
			Lower	Upper	
Yes	2.04 ± 0.46	0.74	0.47	1.02	*<0.001*
No	1.3 ± 0.2				

The mean of SAAG in people with Esophageal varices was 2.04 ± 0.46, it was 1.3 ± 0.2 people without Esophageal varices. There was a statistically significant difference in the proportion of SAAG between Esophageal varices. (P value <0.001) (Table 14 & figure 11)

Figure 11: Error bar graph for comparison of mean SAAG between study groups (N=50)

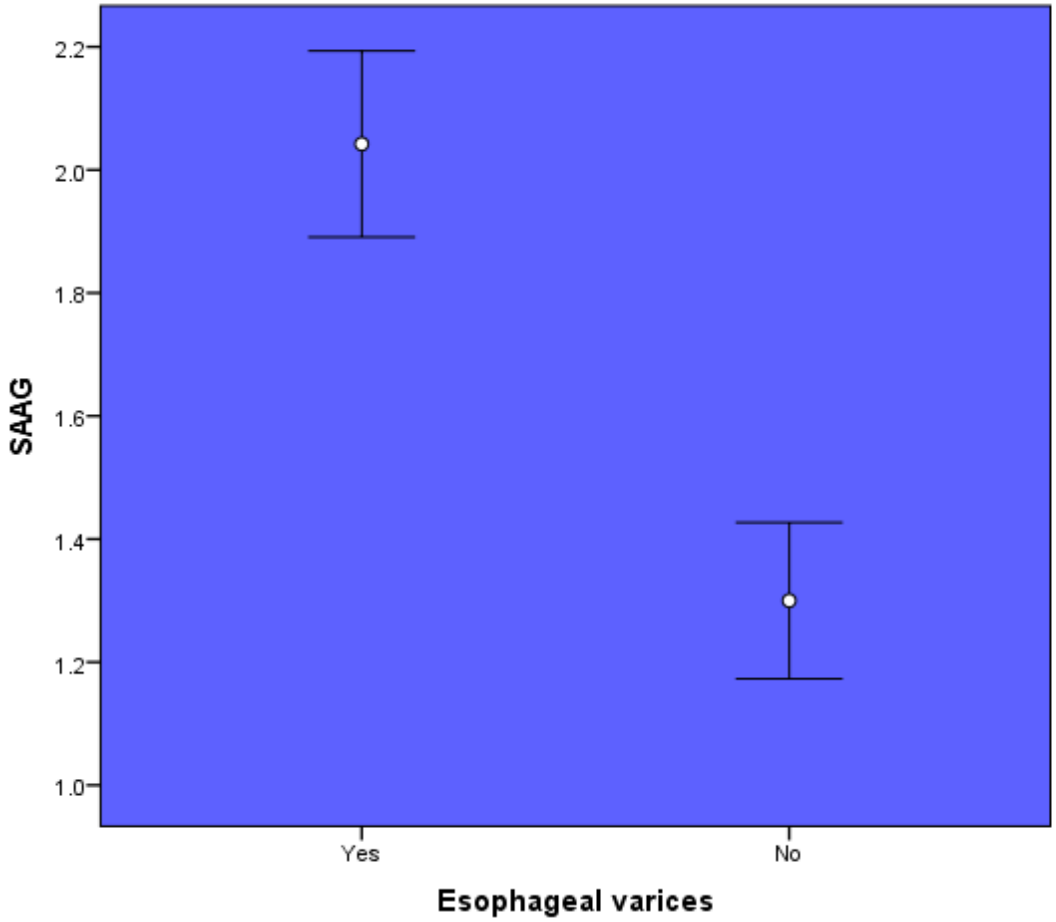


Table 15: Predictive validity of SAAG in predicting Esophageal varices (ROC analysis)

Test Result Variable(s): SAAG				
Area Under the Curve	Std. Error	95% Confidence Interval of AUC		P value
		Lower Bound	Upper Bound	<0.001
0.932	0.035	0.863	1.00	

The SAAG had excellent predictive validity in predicting Esophageal varices**,**as indicated by area under the curve of 0.932 (95% CI 0.863 to 1.00, P value <0.001) (Table 16 & Figure 12)

Figure 12: Predictive validity of SAAG in predicting Esophageal varices (ROC analysis)

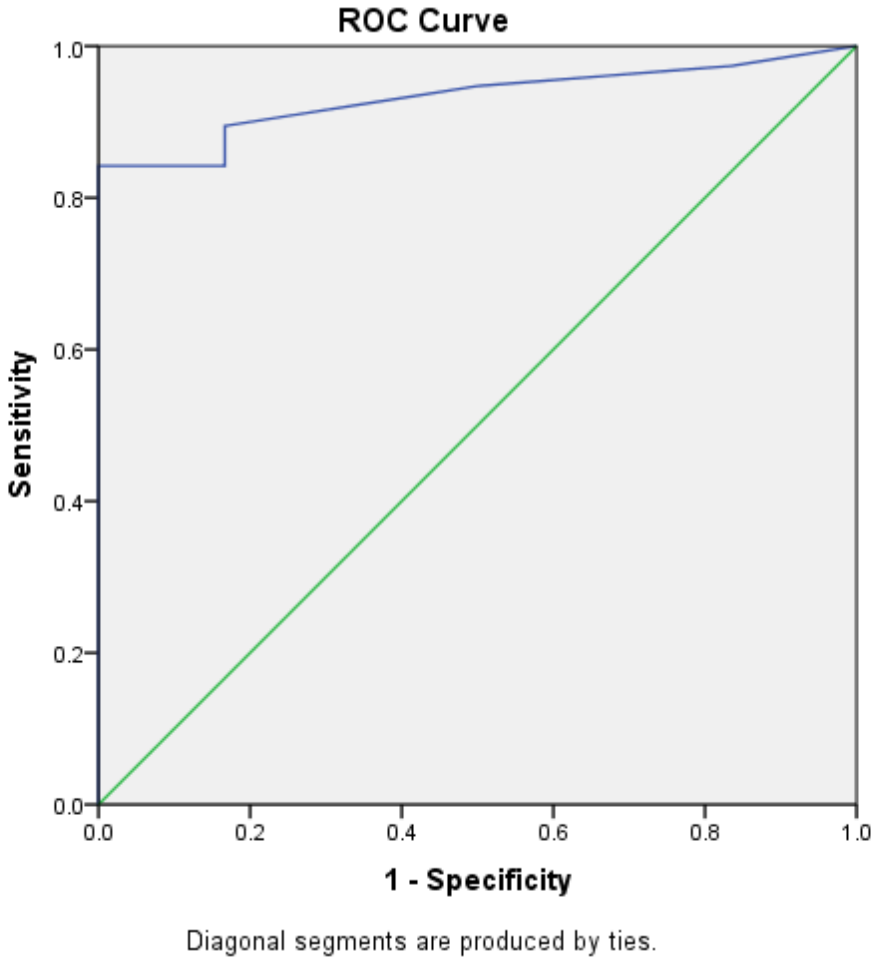


Table 16: Comparison of esophageal varices between high and low SAAG (N=50)

SAAG category	Esophageal varices	
	Yes	**No**
High	32 (84.21%)	0 (0%)
Low	6 (15.79%)	12 (100%)

**No statistical test was performed due to 0 subjects in the cells*

Among the people with Esophageal varices 32 (84.21%) had high SAAG and only 6 (15.79%) had low SAAG. Among the people without Esophageal varices 12 (100%) had low SAAG. (Table15)

Table 17: Predictive validity of SAAG value (>1.75) in predicting esophageal varices (N=50)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	84.21%	68.75%	93.98%
Specificity	100.00%	73.54%	100.00%
False positive rate	0.00%	0.00%	26.46%
False negative rate	15.79%	6.02%	31.25%
Positive predictive value	100.00%	89.11%	100.00%
Negative predictive value	66.67%	40.99%	86.66%
Diagnostic accuracy	88.00%	75.69%	95.47%

High and low SAAG had sensitivity of 84.21% (95% CI 68.75% to 93.98%) in predicting Esophageal varices, specificity was 100.00% (95 CI 73.54% to 100.00%), False positive ratewas 0.00% (95 CI 0.00% to 26.46%), False negative ratewas 15.79% 95 CI 6.02% to 31.25%), Positive predictive value was 100.00% (95 CI 89.11% to 100.00%), Negative predictive valuewas 66.67% (95 CI 40.99% to 86.66%), and the total diagnostic accuracy was 88.00% (95 CI 75.69% to 95.47%).(Table16)

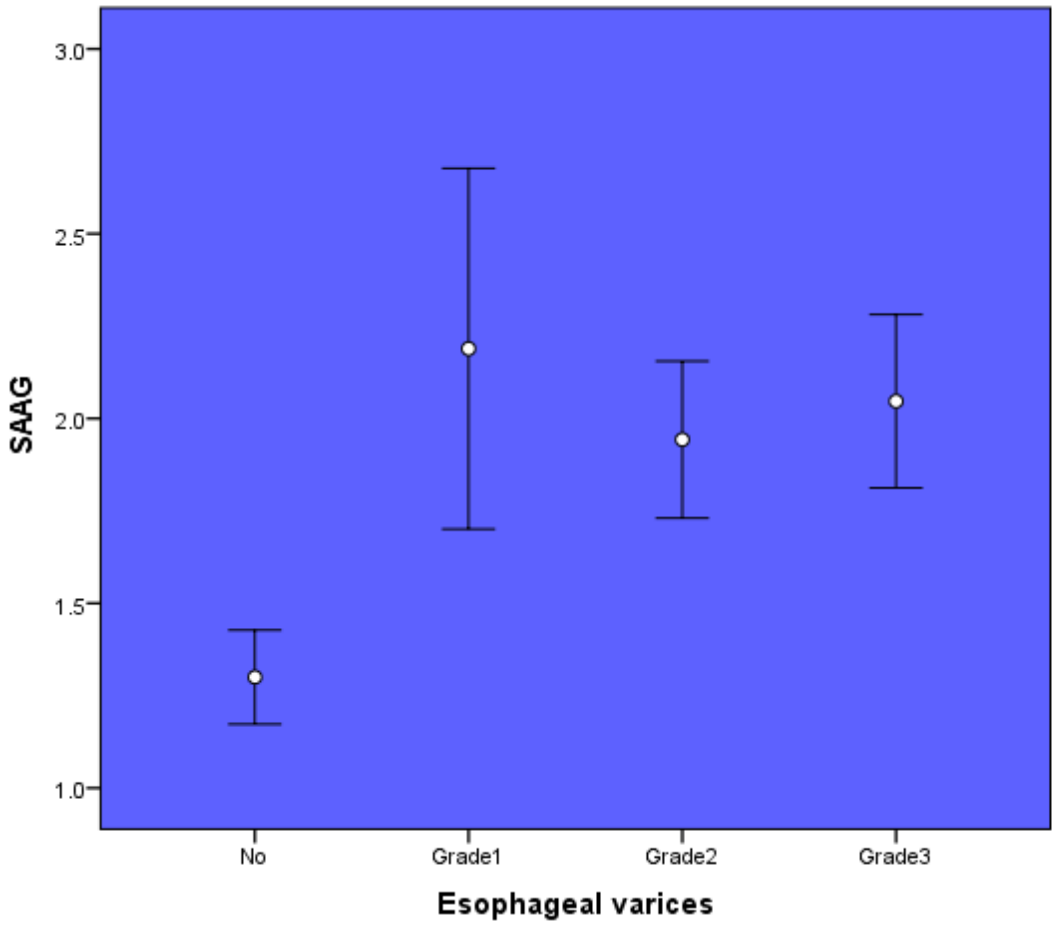
Table 18: Comparison of mean SAAG across the study groups (N=50

Esophageal varices	SAAG Mean ± Std. Dev	Mean difference	95% Confidence Interval for Mean		P value
			Lower Bound	Upper Bound	
No	1.3 ± 0.2				
Grade1	2.19 ± 0.64	-.88889*	-1.26	-0.52	*<0.001*
Grade2	1.94 ± 0.37	-.64286*	-0.97	-0.31	*<0.001*
Grade3	2.05 ± 0.42	-.74667*	-1.07	-0.42	*<0.001*

The mean of SAAG in grade 1 Esophageal varices was 2.19 ± 0.64, it was 1.94 ± 0.37 for Grade2 and it was 2.05 ± 0.42 for grade 3. The difference in the proportion of SAAG

between Esophageal varices was statistically significant. (P value <0.001). (Table17 & figure 13)

Figure 13: Error bar for Comparison of mean SAAG across the study groups (N=50



DISCUSSION

DISCUSSION

Current guidelines recommend performance of oesophago-gastro-duodenoscopy at the time of diagnosis of hepatic cirrhosis to screen for oesophageal varices.[72] These guidelines require people to undergo an unpleasant invasive procedure repeatedly with its attendant risks, despite the fact that half of the people do not have identifiable oesophageal varices 10 years after the initial diagnosis of cirrhosis. Hence the aim of the current study was to correlates the SAAG ratio, a non-invasive method with the presence and grades of esophageal varices in patients with portal hypertension.

A total of 50 people were included in the final analysis. The mean age of the study participants was 50.26 ± 14.42 years with a minimum age of 27 years and maximum age of 80 years. Prabakaran et al[73] reported that the minimum and maximum age of the participants were 19 years and 76 years respectively. (Table:1). A systematic review had reported the median age was 54 (44-67) for the onset of portal hypertension and two thirds were male. Portal hypertension prevalence is most common among old age people due to persistent chronic alcohol consumption and other deleterious habits.

Table 19: Comparison of the mean age of the study participants

Studies	Mean age in years
Current study	50.2 ± 14.4
Suresh I et al[58]	44.5 ± 11.8
Chaurasia et al[70]	45.3 ± 11.5
Demirel U et al[16]	56.3± 12.5

Among the study population majority of the participants were males 48(96%) in the current study. Simialrly Suresh I et al[58] (80%), Chaurasia et al[70] (83.3%), Demirel U et al[16](71%) were also reported a higher prevalance of males in their study.

Portal hypertension is contributing mechanism for the development of ascites and encephalopathy, and a direct cause for variceal bleeding. Among the study population 14(28%) participants had Hematemesis and 15(30%) participants had hepatic encephalopathy. It is in line with study results by Suresh I et al[58] were the author reported that 29% and 10% of the participants presented with hematemesis and encephalopathy respectively. But Suresh I et al[58] could not find any association with hepatic encephalopathy and esophageal varices. Moreover, comparison of prevalence of hepatic encephalopathy with other studies were limited because most studies excluded participants with hepatic encephalopathy in their study population. Majority of the study population had grade 2 33(66%)ascites followed by 16(32%) grade 3 ascites and 1(2%) had grade 1 ascites.

When the etiological factors for portal hypertension was assessed among the study group, only 7(14%) participants were seropositive for HBsAg. Among the study population 40(80%) were alcoholic, 3(6%) were alcoholic with HBsAg, 7(14%) had HBsAg and remaining 3(6%) had HCV. Demirel U et al[16] reported that the causative agents were found to be hepatitis B virus in 35 patients and hepatitis C virus in six patients, whereas no etiology could be determined in the remaining four patients. Kajani et al[74] established that the different causes of intrahepatic PHTN produces different structural changes in microcirculation according to the cause of portal hypertension. Thereby changes in intravascular resistance and hemodynamic changes depending on causes of PHTN. (Table: 2).

Table 20: Prevalence of various etiological factor of liver disease/portal hypertension

Studies	Alcoholic	HBsAg	Alcoholic+HBsAg	HCV
Current study	40(80%)	7(14%)	3(6%)	3(6%)
Suresh I et al[58]	75 (75%)	10 (10%)	-	14(14%)
Torres et al[42]	14(56%)	-	-	-
Chaurasia et al[70]	29(56.81%)	-	-	-
Demirel U et al[16]	35(77%)	-	-	6(13%)

Among the study participants the mean platelets count was 140479.17 ± 67897.29 cells/mm^3. The mean of total bilirubin and direct bilirubin was 4.92 ± 5.97g/dl and 2.26 ± 2.67g/dl. The mean serum albumin was 2.2 ± 0.42. The mean of ALT was 90.25 ± 162.71. Demirel U et al[16] reported that the serum level of albumin was 2.53±0.53 (1.8-3.6 g/dl), ascites level of albumin was 0.47±0.34 (0.1- 1.8 g/dl), and SAAG was 2.1±0.53 (1.1-3.2), bilirubin level was 3.6±6.5 mg/dl (6-37 mg/dl).

In the current study EV was present in 76% of the study subjects. This reported prevalence was slightly higher compared with the studies done by Torres et al[42] who reported that EV were present in 68% of the participants and Suresh I et al[58] were the author reported the presence of EV in 67% of the study subjects. Among the study population 18% had grade 1 Esophageal Varices, 30% had grade 3. This was consistent to that reported by Suresh I et al [58]. Whereas the prevalence of grade 2 EV (28%) was comparatively more in the current study compared to Suresh I et al.[58] Depending on the classification used grading of EV changes. Several studies classifying EV based on same 'Japanese classification' used in the current study, were compared with the present study. (Table:3)

Table 21: Grades of esophageal varices

Studies	No EV	Grade 1	Grade 2	Grade 3
Current study	12(24)	9(18)	14(28)	15(30)
Suresh I et al[58]	33(33%)	18(18)	19(19)	30(30)
Torres et al[42]	8(32%)	-	-	-

The mean of SAAG value in the current study was 1.86 ± 0.52. The difference in SAAG ratio between presence and absence of esophageal varices was statistically significant (p value<0.01). Similarly, Suresh I et al[58] documented that 84.5 % of the study population had varices when SAAG value was more than 1.1 g/dl (P < 0.001) and there is very highly significant relation found between high SAAG and presence of esophageal varices. The mean

of SAAG in grade 1 esophageal varices was 2.19 ± 0.64 and it was 1.94 ± 0.37 for grade 2 EV and it was 2.05 ± 0.42 for grade 3. Similarly, the difference of SAAG between grades of esophageal varices was also statistically significant (P value<0.01). Our result is in line with the studies done by Suresh I et al[58], Chaurasia et al.[70] Suresh I et al[58] reported that when the value of SAAG was < 1.1 g/dl it was noted that Grade II and III varices were absent. When the SAAG values increased more than 1.1 g/dl, there was significant increase in grading of varices. The association between SAAG values and grade of varices were highly significant.

Torres et al[42] reported that 25% each had grade 1 and 2 esophageal varices and remaining 50% had EV of grade 3 whereas Prabakaran et al[73] reported 14.29% had grade 1 EV and 71.4% had grade 1-2 EV and 17.86% hah grade 2 esophageal varices, when the SAAG value was considered between 1 and 1.49g/dl. When the estimated SAAG value was between 1.99g/dl and 1.50 g/dl, 50% patients each had grade 1 and grade 2 EV and Prabakaran et al[73] reported 3.57% had grade 1-2 EV and 3.57% had grade 2 EV. Prabakaran et al[73] found that when the SAAG value varies, the degree of EV also varies significantly. Similarly, a significant correlation between SAAG value and occurrence of EV was reported by Chaurasia et al[70]. But this significant difference was not found between SAAG value and severity of esophageal varices. However Torres et al[42] found that the EV size showed a poor correlation (R 5 0.54) with severity of EV among patients with high SAAG value. Demirel et al[16] also reported a significant correlation (p=0.001, r=0.54). Gurubacharya et al[15] reported that SAAG value and severity of EV were not significantly clorrelated. Al-Knawy et al[68] in a study among 87 non alcoholic cirrhotic patients found that there is no linear relation between SAAG value and portal hypertension.

In the current study SAAG value>1.75g/dl was considered for predicting EV based on the ROC curve. The predictive validity of SAAG differs depending on the SAAG value identified for predicting. The current study found that SAAG value >1.75 g/dl were 100%

specific whereas 84.21% sensitive in predicting EV. So far various studies[56, 58, 65, 70] have found various predictive validity for different SAAG value in predicting esophageal varices. Demirel et al[16] reported that even though SAAG value >1.1 was found to have a low specificity and sensitivity, it appeared to be a highly reliable guide for esophageal varices. (Table:4)

Table 22: Predictive validity of SAAG value

Parameter	**Current study**	**Suresh I et al[58]**	**Chaurasia et al[70]**		**Das BB et al[56]**	**Prabakaran et al[73]**	**Kumar S et al[65]**
SAAG value (g/dl)	>1.75	**>1.1**	**>1.5**	**>2.0**	**>1.1**	**1.45**	**-**
Sensitivity	84.21%	81%	95.2%	57%	91%	90%	-
Specificity	100.00%	100%	44.4%	100%	50%	82%	-
False positive rate	0.00%	0	-	-	-	-	-
False negative rate	15.79%	19%	-	-	-	-	-
Positive predictive value	100.00%	100%	88.8%	100%	91%	-	98%
Negative predictive value	66.67%	64%	66.6%	33%	50%	-	85%
Diagnostic accuracy	88.00%	-	-	-	85%	89%	-

There are scant studies in the literature to evaluate SAAG and esophageal varices in the patients with portal hypertension. The current study found a significant association (P value<0.01) between SAAG value and degree of esophageal varices. But these findings should be considered under studies limitation.

CONCLUSION

A non-invasive test could play the role of a triage test it is able to detect people with very low probability of having oesophageal varices accurately and hence reduce the use of endoscopy, reserving it only for people with positive results. The current study was done to correlates the SAAG ratio, a non-invasive method with the presence and grades of esophageal varices in patients with portal hypertension. A total of 50 people were included in the final analysis. The following conclusions were established from the study. The mean age of the study participants was 50.26 ± 14.42 years with the majority being males (96%) Among the study population 40(80%) were alcoholic, 3(6%) were alcoholic with HBsAg, 4(8%) had HBsAg and remaining 3(6%) had HCV infection. Among the study population only 1(2%) had grade 1 ascites, 33(66%) had grade 2 and 16(32%) had grade 3 ascites and 38(76%) had EV. The mean of SAAG was 1.86 ± 0.52. Minimum level was 1.10 and maximum level was 3.70 in study population. (95% CI 1.72 to 2.01). Among the study population 9(18%) had grade 1 Esophageal Varices, 14(28%) had grade2, 15(30%) had grade 3 and 12(24%) had no Esophageal Varices. The mean of SAAG among participants with EV was 2.04 ± 0.46 and without EV was 1.3 ± 0.2 people. The difference in SAAG value between presence and absence of EV was statistically significant. The mean of SAAG in grade 1 EV was 2.19 ± 0.64; Grade 2 was 1.94 ± 0.37; grade 3 was 2.05 ± 0.42. The difference in the proportion of SAAG between EV was statistically significant.

The current study found that there is a statistically significant association between both presence and severity of EV and SAAG value. However, for a non-invasive test to replace oesophago-gastro-duodenoscopy as the preferred diagnostic test for varices, it should accurately demonstrate the presence of varices and also provide the other information that can be gained from endoscopy. Importantly, it should be able to predict the risk of variceal bleeding with as much or greater accuracy as oesophagogastro-duodenoscopy.[72] Hence

further longitudinal studies with large sample size are recommended to accurately determine the predictive validity of SAAG in relation to EV.

LIMITATION

1. This was a case series; thus, the observed association cannot be interpreted as causal inferences.
2. It was a single center study. Hence the study cannot be generalized to the rest of the population.
3. Purposive sampling technique was employed for the study which is not a true representation of the general population.

RECOMMENDATION

Larger cross-sectional studies and longitudinal studies are needed for a more precise estimation of sensitivity and specificity.

Since we totally lack data in paediatric populations and in people with portal thrombosis further studies includes those patients are recommended.

BIBLIOGRAPHY

REFERENCE:

1. Bosch J, Iwakiri Y. The portal hypertension syndrome: etiology, classification, relevance, and animal models. Hepatol Int. 2018;12(Suppl 1):1-10.
2. Kang SH, Kim MY, Baik SK. Novelties in the pathophysiology and management of portal hypertension: new treatments on the horizon. Hepatol Int. 2018;12(Suppl 1):112-21.
3. Maruyama H, Yokosuka O. Pathophysiology of portal hypertension and esophageal varices. Int J Hepatol. 2012;2012:895787.
4. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Non-invasive predictors of esophageal varices. Saudi J Gastroenterol. 2011;17(1):64-8.
5. Hegab AM, Luketic VA. Bleeding esophageal varices. How to treat this dreaded complication of portal hypertension. Postgrad Med. 2001;109(2):75-6, 81-6, 9.
6. Mohammed SE, Abdo AE, Mudawi HM. Mortality and rebleeding following variceal haemorrhage in liver cirrhosis and periportal fibrosis. World J Hepatol. 2016;8(31):1336-42.
7. Eslam M, Ampuero J, Jover M, Abd-Elhalim H, Rincon D, Shatat M, et al. Predicting portal hypertension and variceal bleeding using non-invasive measurements of metabolic variables. Ann Hepatol. 2013;12(4):588-98.
8. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. Noninvasive prediction of large esophageal varices in chronic liver disease patients. Saudi J Gastroenterol. 2010;16(1):38-42.
9. Fagundes ED, Ferreira AR, Roquete ML, Penna FJ, Goulart EM, Figueiredo Filho PP, et al. Clinical and laboratory predictors of esophageal varices in children and adolescents with portal hypertension syndrome. J Pediatr Gastroenterol Nutr. 2008;46(2):178-83.
10. Kraja B, Mone I, Akshija I, Kocollari A, Prifti S, Burazeri G. Predictors of esophageal varices and first variceal bleeding in liver cirrhosis patients. World J Gastroenterol. 2017;23(26):4806-14.
11. Dewa Gde Agung Budiyasa YA, I Ketut Mariadi,. Correlation between Serum Albumin Level and

Degree of Esophageal Varices in Patients

with Liver Cirrhosis. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy. 2011;12(1).

12. Alba D, Torres E, Vazquez JJ. [Sero-ascitic gradient of albumin: usefulness and diagnostic limitations]. An Med Interna. 1995;12(8):404-7.
13. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic fluid protein concentration in patients with chronic liver disease. J Lab Clin Med. 1983;102(2):260-73.
14. Rahman A, Sumon SM, Sutradhar SR, Chowdhury M, Khan NA, Rozana FK, et al. Prediction of oesophageal varices in cirrhosis of liver patients by serum ascitic albumin gradient. Mymensingh Med J. 2013;22(4):669-75.
15. Gurubacharya DL, Mathura KC, Karki DB. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Kathmandu Univ Med J (KUMJ). 2005;3(4):327-33.
16. Demirel U, Karincaoglu M, Harputluoglu M, Ates M, Seckin Y, Yildirim B, et al. Two findings of portal hypertension: evaluation of correlation between serum-ascites albumin gradient and esophageal varices in non-alcoholic cirrhosis. Turk J Gastroenterol. 2003;14(4):219-22.
17. Begum N, Afroza A, Karim BM. Evaluation of correlation between high serum-ascites albumin gradient and the upper gastrointestinal endoscopic parameters in children presenting with portal hypertension with ascites. Mymensingh Med J. 2014;23(4):703-8.
18. de Oliveira AC. Short article: Noninvasive assessment of portal hypertension and detection of esophageal varices in cirrhosis: state-of-the-art. Eur J Gastroenterol Hepatol. 2017;29(5):531-4.
19. Abby Philips C, Sahney A. Oesophageal and gastric varices: historical aspects, classification and grading: everything in one place. Gastroenterol Rep (Oxf). 2016;4(3):186-95.
20. Ravaioli F, Montagnani M, Lisotti A, Festi D, Mazzella G, Azzaroli F. Noninvasive Assessment of Portal Hypertension in Advanced Chronic Liver Disease: An Update. Gastroenterol Res Pract. 2018;2018:4202091.
21. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol. 2013;7(2):141-55.
22. Tayyem O, Bilal M, Samuel R, Merwat SK. Evaluation and management of variceal bleeding. Dis Mon. 2018;64(7):312-20.
23. Dib N, Oberti F, Cales P. Current management of the complications of portal hypertension: variceal bleeding and ascites. CMAJ. 2006;174(10):1433-43.

24. Shibayama Y, Nakata K. Localization of increased hepatic vascular resistance in liver cirrhosis. Hepatology. 1985;5(4):643-8.
25. Iwakiri Y. Pathophysiology of portal hypertension. Clin Liver Dis. 2014;18(2):281-91.
26. Al-Busafi SA, McNabb-Baltar J, Farag A, Hilzenrat N. Clinical manifestations of portal hypertension. Int J Hepatol. 2012;2012:203794.
27. Goel A, Madhu K, Zachariah U, Sajith KG, Ramachandran J, Ramakrishna B, et al. A study of aetiology of portal hypertension in adults (including the elderly) at a tertiary centre in southern India. Indian J Med Res. 2013;137(5):922-7.
28. Khanna R, Sarin SK. Non-cirrhotic portal hypertension - diagnosis and management. J Hepatol. 2014;60(2):421-41.
29. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, Chawla YK, et al. Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. PLoS One. 2017;12(10):e0187033.
30. Hou W, Sanyal AJ. Ascites: diagnosis and management. Med Clin North Am. 2009;93(4):801-17, vii.
31. Salerno F, Guevara M, Bernardi M, Moreau R, Wong F, Angeli P, et al. Refractory ascites: pathogenesis, definition and therapy of a severe complication in patients with cirrhosis. Liver Int. 2010;30(7):937-47.
32. Seth AK, Rangarao R, Pakhetra R, Baskaran V, Rana P, Rajamani S. Accuracy of Serum - Ascites Albumin Gradient in the Aetiological Diagnosis of Ascites. Med J Armed Forces India. 2002;58(2):124-6.
33. Arroyo V, Colmenero J. Ascites and hepatorenal syndrome in cirrhosis: pathophysiological basis of therapy and current management. J Hepatol. 2003;38 Suppl 1:S69-89.
34. Merkel C, Zoli M, Siringo S, van Buuren H, Magalotti D, Angeli P, et al. Prognostic indicators of risk for first variceal bleeding in cirrhosis: a multicenter study in 711 patients to validate and improve the North Italian Endoscopic Club (NIEC) index. Am J Gastroenterol. 2000;95(10):2915-20.
35. Suzuki H, Stanley AJ. Current management and novel therapeutic strategies for refractory ascites and hepatorenal syndrome. QJM. 2001;94(6):293-300.
36. Arroyo V, Gines P, Gerbes AL, Dudley FJ, Gentilini P, Laffi G, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International Ascites Club. Hepatology. 1996;23(1):164-76.

37. Rimola A, Garcia-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. J Hepatol. 2000;32(1):142-53.
38. McConnell M, Iwakiri Y. Biology of portal hypertension. Hepatol Int. 2018;12(Suppl 1):11-23.
39. Rye K, Mortimore G, Austin A, Freeman J. Non-invasive Diagnosis of Oesophageal Varices Using Systemic Haemodynamic Measurements by Finometry: Comparison with Other Non-invasive Predictive Scores. J Clin Exp Hepatol. 2016;6(3):195-202.
40. Min YW, Bae SY, Gwak GY, Paik YH, Choi MS, Lee JH, et al. A clinical predictor of varices and portal hypertensive gastropathy in patients with chronic liver disease. Clin Mol Hepatol. 2012;18(2):178-84.
41. de Franchis R, Dell'Era A. Invasive and noninvasive methods to diagnose portal hypertension and esophageal varices. Clin Liver Dis. 2014;18(2):293-302.
42. Torres E, Barros P, Calmet F. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Am J Gastroenterol. 1998;93(11):2172-8.
43. Shahed FHM, Mamun Al M, Rahman S. The Evaluation of Serum Ascites Albumin Gradient and Portal Hypertensive changes in Cirrhotic Patients with Ascites. Euroasian J Hepatogastroenterol. 2016;6(1):8-9.
44. de Franchis R. 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(1):167-76.
45. Imperiale TF, Chalasani N. A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. Hepatology. 2001;33(4):802-7.
46. Khuroo MS, Khuroo NS, Farahat KL, Khuroo YS, Sofi AA, Dahab ST. Meta-analysis: endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleeding. Aliment Pharmacol Ther. 2005;21(4):347-61.
47. Haq I, Tripathi D. Recent advances in the management of variceal bleeding.. Gastroenterol Rep (Oxf). 2017;5(2):113-26.
48. YD K. Management of acute variceal bleeding. Clin Endosc. 2014;47(308-314).
49. Kim DH, Park JY. Prevention and management of variceal hemorrhage. Int J Hepatol. 2013;2013:434609.
50. Cremers I, Ribeiro S. Management of variceal and nonvariceal upper gastrointestinal bleeding in patients with cirrhosis.. Therap Adv Gastroenterol. 2014;7(5):206-16.

51. Augustin S, Gonzalez A, Genesca J. Acute esophageal variceal bleeding: Current strategies and new perspectives. World J Hepatol. 2010;2(7):261-74.
52. Wells M1, Chande N, Adams P, Beaton M, Levstik M, Boyce E, et al. Wells M, Chande N, Adams P, et al. Meta-analysis: vasoactive medications for the management of acute variceal bleeds. Aliment Pharmacol Ther. 2012;35(11):1267–1278.
53. Tripathi D, Ferguson JW, Therapondos G, Plevris JN, Hayes PC. Review article: recent advances in the management of bleeding gastric varices. Aliment Pharmacol Ther. 2006;24(1):1–17.

.

54. Avgerinos A, Armonis A. Balloon tamponade technique and efficacy in variceal haemorrhage. Scand J Gastroenterol Suppl. 1994;207:11–16.
55. Bari K, Garcia-Tsao G. Treatment of portal hypertension. World J Gastroenterol. 2012;18(11):1166–1175.
56. Das BB, Purohit A, Acharya U, Treskova E. Serum-ascites albumin gradient: a predictor of esophageal varices with ascites. Indian J Pediatr. 2001;68(6):511-4.
57. Mene A, Sharma D, Raina VK. Correlation between serum-ascites albumin concentration gradient with gastrointestinal bleeding in patients of portal hypertension. Trop Doct. 2003;33(1):39-41.
58. Suresh I JS. Correlation of serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension in chronic liver disease. Int J Adv Med. 2018;5(1):159-63.
59. Gokturk HS, Demir M, Ozturk NA, Unler GK, Kulaksizoglu S, Kozanoglu I, et al. The role of ascitic fluid viscosity in the differential diagnosis of ascites. Can J Gastroenterol. 2010;24(4):255-9.
60. Jiang CF, Shi B, Shi J, Yuan ZL, Xie WF. New proposal for the serum ascites albumin gradient cut-off value in Chinese ascitic patients. Diagn Pathol. 2013;8:143.
61. Khandwalla HE, Fasakin Y, El-Serag HB. The utility of evaluating low serum albumin gradient ascites in patients with cirrhosis. Am J Gastroenterol. 2009;104(6):1401-5.
62. Shanker Suman1* DJ, PKA, BKB. Clinicopathological correlation of serum ascites albumin gradient with

ascitic fluid total protein in patients of ascites with portal hypertension

attending a tertiary care hospital in Eastern Bihar, India. Int J Adv Med 2017;4(3):842-6.
63. Abdelhakam1 EADGS, Ibrahim. aWA. Correlation between Serum-Ascites Albumin Gradient and Esophageal Varices in Patients with Portal

Hypertension Report and Opinion 2011;3(8):39-49.

64. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, et al. Non-endoscopic prediction of presence of esophageal varices in cirrhosis. J Coll Physicians Surg Pak. 2005;15(9):528-31.
65. Santosh Kumar IAM, Mohammad Kaleem, Suhail A. Alamani Prediction of Esophageal Varices in Cirrhotic Patients with

Serum - Ascites Albumin Gradient. HLUMHS. 2013;12(3).

66. Dittrich S, Yordi LM, de Mattos AA. The value of serum-ascites albumin gradient for the determination of portal hypertension in the diagnosis of ascites. Hepatogastroenterology. 2001;48(37):166-8.
67. Sartori M, Andorno S, Gambaro M, Leone F, Molinari GL, Pontiroli L, et al. Diagnostic paracentesis. A two-step approach. Ital J Gastroenterol. 1996;28(2):81-5.
68. Al-Knawy BA. Etiology of ascites and the diagnostic value of serum-ascites albumin gradient in non-alcohol liver disease. Ann Saudi Med. 1997;17(1):26-8.
69. Madhotra R, Mulcahy HE, Willner I, Reuben A. Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol. 2002;34(1):81-5.
70. Chaurasia AK MB. Correlation between Serum Ascites Albumin Gradient and Esophageal

Varices in Patients of Chronic Liver Disease. 2016;4(2):9392-7.

71. IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.
72. Colli A, Gana JC, Turner D, Yap J, Adams-Webber T, Ling SC, et al. Capsule endoscopy for the diagnosis of oesophageal varices in people with chronic liver disease or portal vein thrombosis. Cochrane Database Syst Rev. 2014(10):CD008760.
73. Prabakaran B, Gowri T. Correlation Between Serum Ascites Albumin Gradient And Esophageal Varices In Portal Hypertension. IOSR-JDMS 2016;15(8):48-50.
74. Kajani MA, Yoo YK, Alexander JA, et al. Serum-ascites albumin gradients in nonalcoholic liver disease. Dig Dis Sci 1990;35:33–7.

ANNEXURES

PROFORMA

STUDY TO CORRELATE THE SERUM –ASCITES ALBUMIN GRADIENT (SAAG) WITH THE ESOPHAGEAL VARICES AND ITS GRDES IN PATIENTS WITH PORTAL HYPERTENSION

Name: DOA:

Age/sex: IP NO:

Occupation:

Address:

Date:

Presenting complaints:	Yes	No
Lower limb swelling		
Abdominal distension		
Jaundice		
Bleeding (hematemesis/malaena)		
Fever		
Abdominal pain		
Altered sensorium		
Others		

Past history:

Personal history:

Smoking

Alcohol

General physical examination

Pulse: RR:

BP: Temp:

Pallor: Icterus: Cyanosis:

Clubbing: Lymphadenopathy: Pedal edema:

S/O liver cell failure

Systemic examination

Per abdomen: Abdominal distension

Distended veins

Liver

Spleen

Shifting dullness/fluid thrill

Bowel sounds

RS:

CVS:

CNS: Sensorium

Asterexis

Investigations

HB TC PLT RBS

Urea Creatinine

LFT

TB/DB HBsAG

TP Anti HCV

ALB	Ascitic fluid analysis:
GLB	Cell count
AST	Cell type
ALT	Albumin
ALP	Sugar
	Gram stain

USG ABDOMEN:

OGD: Esophageal varices-

Present/absent

Grade

Serum albumin:	Ascitic albumin:
SAAG:	Esophageal varices:

INFORMED CONSENT FORM

STUDY TITLE: A STUDY TO CORRELATE THE SERUM ASCITIS ALBUMIN GRADIENT (SAAG) WITH THE ESOPHAGEAL VARICES IN PATIENTS WITH PORTAL HYPERTENSION.

SUBJECT'S NAME: **HOSPITAL NUMBER:**

AGE:

Objectives:

1) To determine the SAAG gradient in patients with portal hypertension.

2) To determine the presence and grades of esophageal varices in patients with portal hypertension.

3) To correlate the SAAG gradient with the presence and grades of esophageal varices in patients with portal hypertension

If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. We will collect the treatment and relevant details from your hospital record. This information collected will be used for only dissertation and publication. This study has been reviewed by the institutional ethical committee. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

I understand that I remain free to withdraw from the study at any time and this will not change my future care. I have read or have been read to me and understood the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of information that will be collected and disclosed during the study. I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction. I, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information for dissertation.

Subject name

(Parents / Guardians name)

DATE: SIGNATURE /THUMB IMPRESSION

For any further clarification you can contact the study investigator:

Dr. Raghvendar Reddy Mobile no: 8105903722

E-mail id: raghu.reddy12333@gmail.com

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿಯ ನಮೂನೆ

ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಸನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ ಮತ್ತು ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್ ನಡುವೆ ಸಾಂಗತ್ಯದ ಅಧ್ಯಯನ

ಅಧ್ಯಯನದ ಉದ್ದೇಶ:

1) ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಸನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ.
2) ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಸನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್‌ನ ವ್ಯಾಪ್ತಿ ಪಡೆಸುವ ಅಧ್ಯಯನ.
3) ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಸನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ ಹಾಗೂ ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್‌ನ ಸಾಂಗತ್ಯ.

ಇದು ಸೂಕ್ತ ಪೂರ್ವಸೂಚಕ ಅಂಶಗಳಲ್ಲಿ ಜ್ಞಾನ ತೀವ್ರ ನಿಗಾ ಚಿಕಿತ್ಸೆಯ ಅಗತ್ಯ ಹೆಚ್ಚಿನ ಅಪಾಯ ರೋಗಿಗಳ ಆರಂಭಿಕ ಗುರುತಿನ ಉಪಯುಕ್ತ ಇರಬಹುದು ಭರವಸೆಯಿದೆ . ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ವೇಳೆ ನೀವು ಅಥವಾ ನೀವು ಅಥವಾ ಎರಡೂ ಜವಾಬ್ದಾರಿ ವ್ಯಕ್ತಿಯಿಂದ ಮಾಹಿತಿ (ಪ್ರತಿ proforma ಮಾಹಿತಿ) ಸಂಗ್ರಹಿಸುತ್ತದೆ . ನಿಮ್ಮ ಆಸ್ಪತ್ರೆ ದಾಖಲೆಯಿಂದ ಚಿಕಿತ್ಸೆ ಮತ್ತು ಸೂಕ್ತ ವಿವರಗಳನ್ನು ಸಂಗ್ರಹಿಸುತ್ತದೆ . ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿ ಮಾತ್ರ ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ಮತ್ತು ಪ್ರಕಟಣೆ ಬಳಸಲಾಗುತ್ತದೆ . ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ವಿಮರ್ಶಿಸುತ್ತದೆ ಮಾಡಲಾಗಿದೆ . ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುತ್ತಾನೆ ಆರೈಕೆ ಬದಲಾಗುವುದಿಲ್ಲ . ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಕೊಂಡಲ್ಲಿ ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಸೈನ್ / ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ .

ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂತೆಗೆದುಕೊಳ್ಳುವಂತೆ ಮತ್ತು ಈ ನನ್ನ ಮುಂದಿನ ಆರೈಕೆ ಬದಲಾಗುವುದಿಲ್ಲ ಉಚಿತ ಉಳಿಯಲು ಎಂದು ಅರ್ಥ . ನಾನು ಓದಲು ಅಥವಾ ನನಗೆ ಓದಲು ಮಾಡಲಾಗಿದೆ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶ , ಬಳಸಲಾಗುವ ವಿಧಾನ , ಅಧ್ಯಯನ ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗ ನಡೆಯಲಿದೆ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕೃತಿಯಲ್ಲಿ ನನ್ನ ಒಳಗೊಳ್ಳುವಿಕೆ ಸಂಬಂಧಿಸಿದ ಅಪಾಯ ಮತ್ತು ಲಾಭಗಳನ್ನು ಅರ್ಥ . ನಾನು ಅಧ್ಯಯನ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ವಿವಿಧ ಅಂಶಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿ ಉತ್ತರಿಸುವ ಬಗ್ಗೆ ನನ್ನ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ಅವಕಾಶ ಹೊಂದಿದ್ದರು . ನಾನು , ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಮತ್ತು ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಡಿಸ್ಕ್ಲೋಸರ್ ಅಧಿಕೃತಗೊಳಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ರುಜುಮಾಡಿರುವ .

ವಿಷಯದ ಹೆಸರು

(ಪಾಲಕರು / ಗಾರ್ಡಿಯನ್ಸ್ ಹೆಸರು)

ಡಾ. ರಾಘವೆಂಡೆರ್ ಮೊಬೈಲ್ ಸಂಕೆ: 8105903722 ಮೇಲ್ ಐಡಿ: raghu.reddy12333@gmail.com

DATE : ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಒಪ್ಪಿಗೆ ತೆಗೆದುಕೊಳ್ಳುವ ವ್ಯಕ್ತಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

PATIENT INFORMATION SHEET

Study Title: **A STUDY TO CORRELATE THE SERUM ASCITIS ALBUMIN GRADIENT (SAAG) WITH THE ESOPHAGEAL VARICES IN PATIENTS WITH PORTAL HYPERTENSION.**

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Objectives:

1) To determine the SAAG gradient in patients with portal hypertension.

2) To determine the presence and grades of esophageal varices in patients with portal hypertension.

3) To correlate the SAAG gradient with the presence and grades of esophageal varices in patients with portal hypertension

This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr. Raghvendar Reddy

Mobile no: 8105903722

E-mail id: raghu.reddy12333@gmail.com

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಸ್ಟಡಿ ಶೀರ್ಷಿಕೆ: **ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಷನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ ಮತ್ತು ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್ ನಡುವೆ ಸಾಂಗತ್ಯದ ಅಧ್ಯಯನ**

ಸ್ಟಡಿ ಸೈಟ್: ಆರ್. ಎಲ್. ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ, ತಮಕ, ಕೋಲಾರ

ಅಧ್ಯಯನದ ಉದ್ದೇಶ:

1)ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಷನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ.

2)ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಷನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್‌ನ ವ್ಯಾಪ್ತಿ ಪಡೆಸುವ ಅಧ್ಯಯನ.

3)ಪೋರ್ಟಲ್ ಹೈಪರ್‌ಟೆನ್ಷನ್ ಇರುವ ರೋಗಿಗಳಲ್ಲಿ SAAG ಅನುಪಾತ ಹಾಗೂ ಎಸೋಫಾಕಲ್ ವರಿಸೀಸ್‌ನ ಸಾಂಗತ್ಯ.

ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಲು ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರು ಚರ್ಚಿಸಬೇಕು ದಯವಿಟ್ಟು. ನೀವು ಅಧ್ಯಯನ ಬಗ್ಗೆ ಯಾವುದೇ ಪ್ರಶ್ನೆ ಕೇಳಬಹುದು. ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ವೇಳೆ ನಿಮ್ಮಿಂದ (ಪ್ರೋಫಾರ್ಮ ಪ್ರಕಾರ) ಮಾಹಿತಿ ಸಂಗ್ರಹಿಸುತ್ತದೆ. . ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಬಳಸಲಾಗುತ್ತದೆ.

ನೀವು ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರ ಬಹಿರಂಗ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ತೋರಿಸಲಾಗುವುದಿಲ್ಲ. ಮೇಲೆ ತನಿಖೆ ಅಗತ್ಯವಿದೆ ವೆಚ್ಚಗಳು ಅಧ್ಯಯನ ಸಂಶೋಧಕ ಹಣಕಾಸು ಒದಗಿಸುವುದಾಗಿತ್ತು. ಈ ಅಧ್ಯಯನವು ನೈತಿಕ ಸಮಿತಿಯ ವಿಮರ್ಶೆ ಮತ್ತು ನೀವು ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯ ಸಂಪರ್ಕಿಸಲು ಉಚಿತ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಕಡ್ಡಾಯ ಇಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುತ್ತಾನೆ ರಕ್ಷಣೆ ಬದಲಾಗುವುದಿಲ್ಲ. ನೀವು / ಸೈನ್ ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ಮಾತ್ರ ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ.

ಯಾವುದೇ ಸ್ಪಷ್ಟೀಕರಣ ನೀವು ಅಧ್ಯಯನ ಸಂಶೋಧಕ ಸಂಪರ್ಕಿಸಬಹುದು:

ಡಾ. ರಾಘವೆಂಡೆರ್ ಮೊಬೈಲ್ ಸಂಕೆ: 8105903722 ಮೇಲ್ ಐಡಿ: raghu.reddy12333@gmail.com

MASTERSHEET

Sino	Age	Sex	Ipnumber	Hematemesis	Hepencephalopathy	Ascites	Hbsag	Hcv	Other	Platelets	Tb	Db	Serum albumin	Ast	Alt	Inr	Asciticalbumin	Ev	Saag
1	65	Male	618522	Yes	Yes	grade2	No	No	alcoholic	15000	2	0.40	2.5	18	7	1.50	0.7	Grade3	1.80
2	49	Male	626066	No	No	grade2	No	No	alcoholic	173000	3	1.10	1.9	49	12	1.10	0.6	No	1.30
3	40	Male	626070	Yes	Yes	grade3	No	No	alcoholic	140000	6	3.60	2.2	120	39	2.10	0.2	Grade3	2.00
4	50	Male	620563	Yes	No	grade2	No	No	alcoholic	54000	10	2.70	3.6	1,090	1,100	3.00	1.0	Grade3	2.60
5	60	Male	624505	No	No	grade1	No	No	alcoholic	164000	25	11.00	1.9	186	27	1.46	0.7	No	1.20
6	80	Male	624277	Yes	Yes	grade3	Yes	No	alcoholic+hbsag	193000	23	12.00	1.9	190	80	2.19	0.1	Grade3	1.80
7	80	Male	623577	No	No	grade2	No	No	alcoholic	175000	15	8.00	2.3	190	67	1.60	0.1	Grade2	2.20
8	48	Male	622067	No	No	grade3	No	No	alcoholic	120000	5	2.40	2.1	180	13	5.20	0.2	Grade2	1.90
9	38	Male	619521	Yes	Yes	grade3	No	No	alcoholic	95000	4	1.40	2.3	112	27	1.64	0.1	Grade3	2.20
10	50	Male	618483	No	No	grade2	No	No	alcoholic	78000	9	3.70	2.4	147	24	2.40	0.5	Grade2	1.90
11	45	Female	420255	No	No	grade2	No	No	alcoholic	120000	3	1.50	2.3	122	53	1.90	0.2	Grade2	2.10
12	27	Male	612442	No	No	grade2	No	Yes	hcv	120000	2	1.10	2.5	45	56	1.30	0.3	Grade1	2.20
13	47	Male	615393	No	Yes	grade3	No	No	alcoholic	180000	16	8.00	1.8	168	145	1.40	0.7	No	1.10
14	64	Male	614307	Yes	No	grade2	Yes	No	alcoholic+hbsag	150000	3	1.40	2.1	90	20	1.10	0.1	Grade1	2.00
15	52	Male	611949	No	No	grade3	No	No	alcoholic	43000	3	2.10	2.3	132	45	1.20	0.2	Grade2	2.10
16	30	Male	612834	Yes	No	grade2	No	No	alcoholic	114000	4	1.80	2.2	78	31	1.04	0.3	Grade1	1.90
17	59	Female	475094	No	No	grade3	Yes	No	hbsag	143000	2	1.40	2.1	92	23	1.31	0.1	Grade2	2.00
18	38	Male	608508	Yes	Yes	grade2	No	No	alcoholic	82000	2	1.20	2.4	56	55	1.88	0.2	Grade3	2.20
19	52	Male	611949	No	No	grade2	No	No	alcoholic	95000	23	1.00	1.9	270	63	5.60	0.7	No	1.20
20	60	Male	610171	No	No	grade2	No	No	alcoholic	82000	2	1.10	2.7	98	41	0.96	0.2	Grade3	2.50
21	34	Male	610060	No	No	grade2	No	No	alcoholic	100000	0	0.10	2.3	30	12	1.10	0.2	Grade2	2.10
22	47	Male	460285	No	No	grade2	No	Yes	hcv	65000	4	1.20	1.9	66	28	1.98	0.4	Grade3	1.50
23	68	Male	460854	No	Yes	grade2	No	No	alcoholic	272000	25	11.00	2.0	273	146	1.33	0.7	No	1.30
24	68	Male	457554	No	No	grade3	No	No	alcoholic	198000	3	2.00	2.0	214	111	2.10	0.9	No	1.10
25	47	Male	465868	No	No	grade2	No	No	alcoholic	376000	1	0.10	3.8	19	20	1.21	0.1	Grade1	3.70

26	35	Male	459938	No	No	grade3	Yes	No	hbsag	80000	1	0.20	2.8	20	17	1.10	0.1	Grade3	2.70
27	65	Male	470051	Yes	Yes	grade2	No	No	alcoholic	150000	2	1.20	2.0	124	54	1.50	0.5	Grade3	1.50
28	35	Male	474321	Yes	Yes	grade2	No	No	alcoholic	173000	3	2.60	2.0	72	48	1.30	0.1	Grade2	1.90
29	35	Male	476758	No	No	grade2	No	No	alcoholic	95000	1	0.60	1.9	35	45	1.00	0.6	Grade1	1.30
30	75	Male	478043	No	No	grade2	No	No	alcoholic	39000	3	1.20	1.9	189	255	2.10	0.2	No	1.70
31	40	Male	485061	No	No	grade3	No	No	alcoholic	245000	1	0.50	2.3	144	155	1.10	0.1	Grade1	2.20
32	61	Male	486251	No	No	grade2	No	No	alcoholic	240000	1	0.50	1.4	20	22	1.00	0.2	No	1.20
33	70	Male	487411	No	No	grade2	No	Yes	hcv	160000	2	1.10	2.3	166	222	1.90	0.3	Grade2	2.00
34	29	Male	489604	Yes	Yes	grade2	No	No	alcoholic	120000	12	6.90	2.4	199	99	2.50	0.2	Grade1	2.20
35	40	Male	489494	No	No	grade3	No	No	alcoholic	99000	2	1.10	2.5	155	145	1.30	0.1	Grade3	2.40
36	34	Male	490788	No	Yes	grade3	Yes	No	alcoholic+hbsag	210000	3	1.20	1.8	144	101	0.90	0.5	No	1.30
37	58	Male	493885	No	No	grade2	No	No	alcoholic	147000	2	0.70	1.9	32	15	0.90	0.7	No	1.20
38	29	Male	489604	No	Yes	grade2	Yes	No	hbsag	245000	2	1.10	2.4	25	22	0.90	0.1	Grade3	2.30
39	63	Male	498528	Yes	Yes	grade3	No	No	alcoholic	120000	4	2.10	2.2	145	45	1.50	0.2	Grade2	2.30
40	50	Male	498528	No	No	grade2	Yes	No	hbsag	190000	1	0.30	1.9	74	54	1.10	0.1	Grade3	1.80
41	46	Male	504430	No	No	grade2	No	No	alcoholic	155000	4	2.60	2.4	266	122	1.00	0.2	Grade1	2.20
42	55	Male	508123	No	Yes	grade3	No	No	alcoholic	123000	1	0.20	1.8	96	45	1.10	0.7	Grade2	1.10
43	55	Male	509321	No	No	grade2	No	No	alcoholic	240000	8	5.10	2.0	300	158	2.50	0.3	No	1.70
44	30	Male	509940	Yes	No	grade2	No	No	alcoholic	130000	5	2.90	2.3	255	120	2.10	0.2	Grade3	2.10
45	40	Male	517610	No	No	grade2	No	No	alcoholic	78000	1	0.30	1.8	56	54	1.00	0.6	Grade2	1.20
46	40	Male	518384	No	Yes	grade3	No	No	alcoholic	142000	5	2.60	2.4	255	324	1.20	0.4	Grade1	2.00
47	62	Male	525044	No	No	grade2	No	No	alcoholic	193000	2	1.90	1.5	54	53	0.90	0.2	No	1.30
48	44	Male	528493	No	No	grade2	No	No	alcoholic	54000	1	0.60	1.9	85	57	1.00	0.6	Grade3	1.30
49	80	Male	530099	Yes	No	grade3	No	No	alcoholic	198000	2	0.50	2.1	89	54	1.10	0.1	Grade2	2.00
50	44	Male	440742	No	No	grade2	No	No	alcoholic	240000	4	2.30	2.6	98	58	1.90	0.2	Grade2	2.40

CLINICAL IMAGES

Image 1: GRADE 1 ESOPHAGEAL VARICES

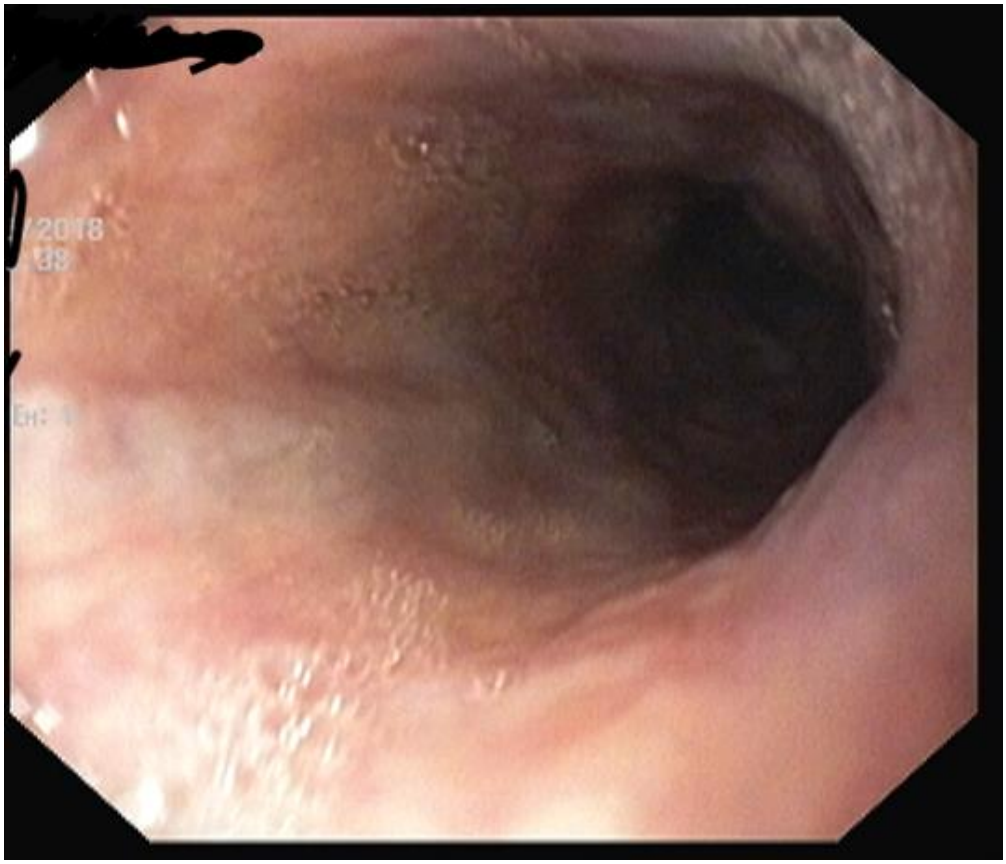


Image 1: ESOPHAGEAL VARICES GRADE I

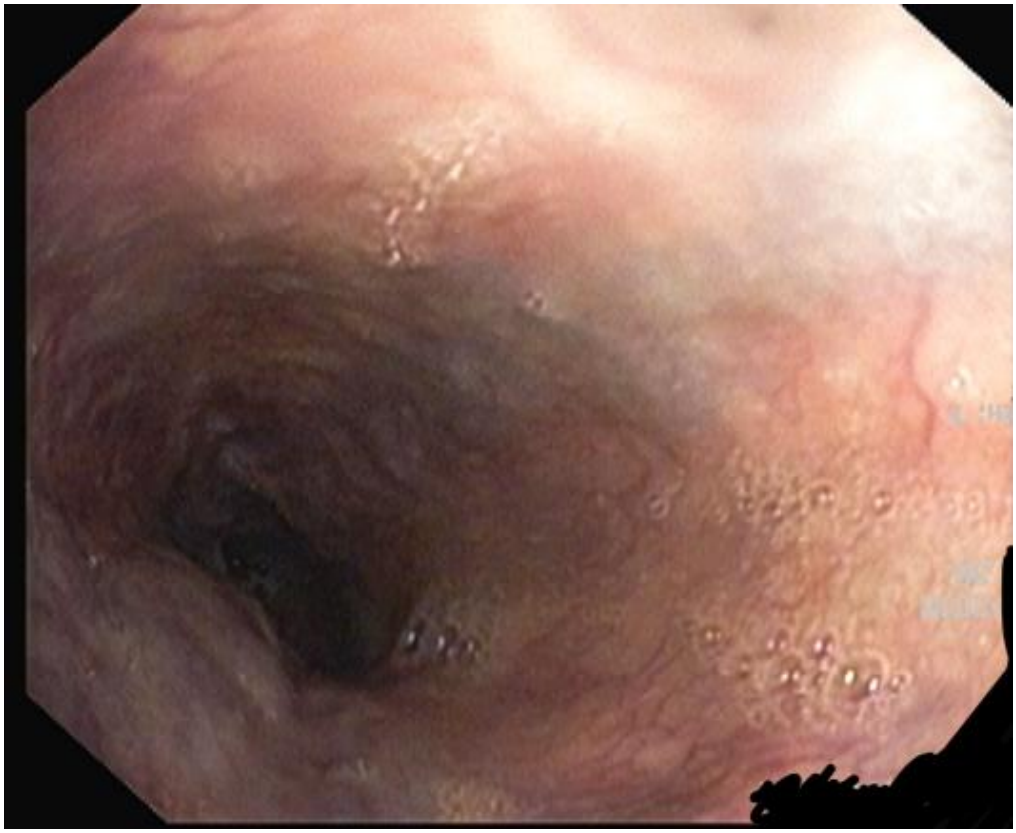


Image 1: GRADE I ESOPHAGEAL VARICES

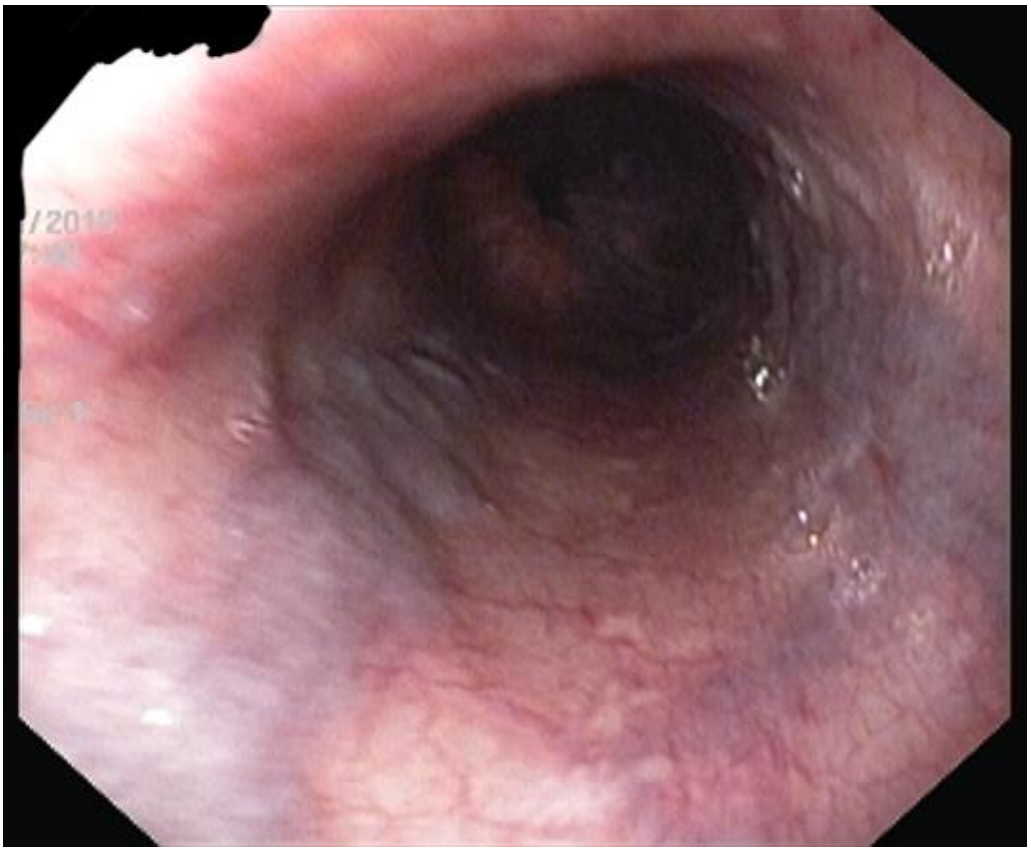
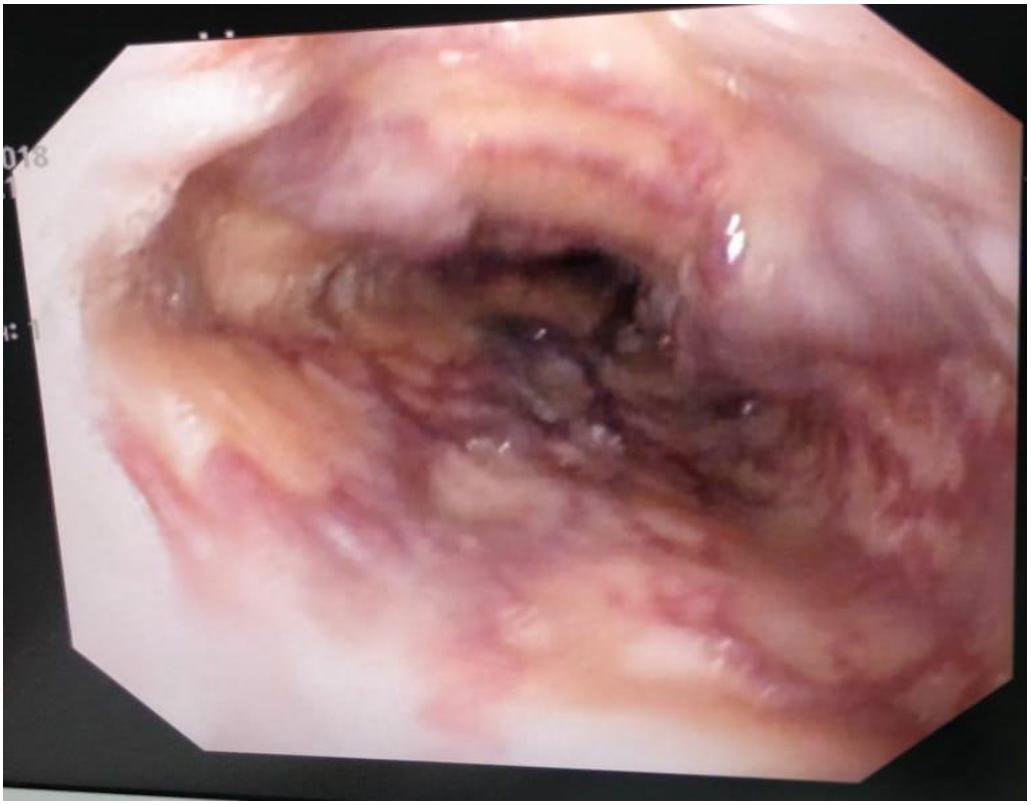


Image 1: GRADE II ESOPHAGEAL VARICES



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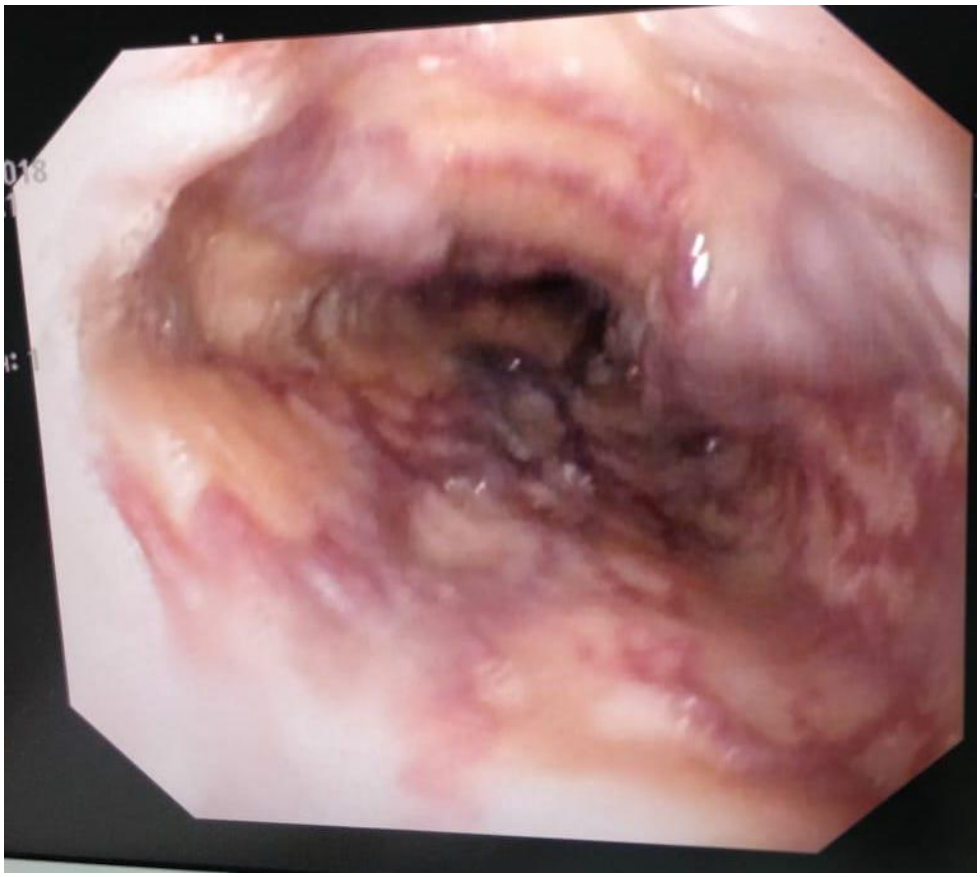

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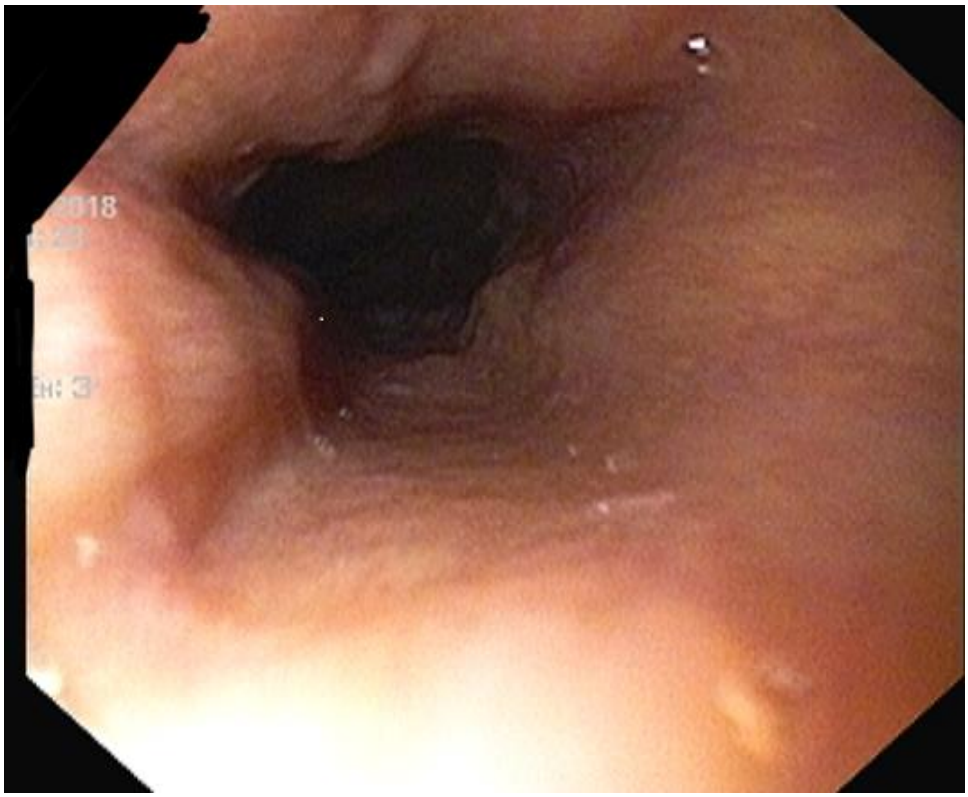

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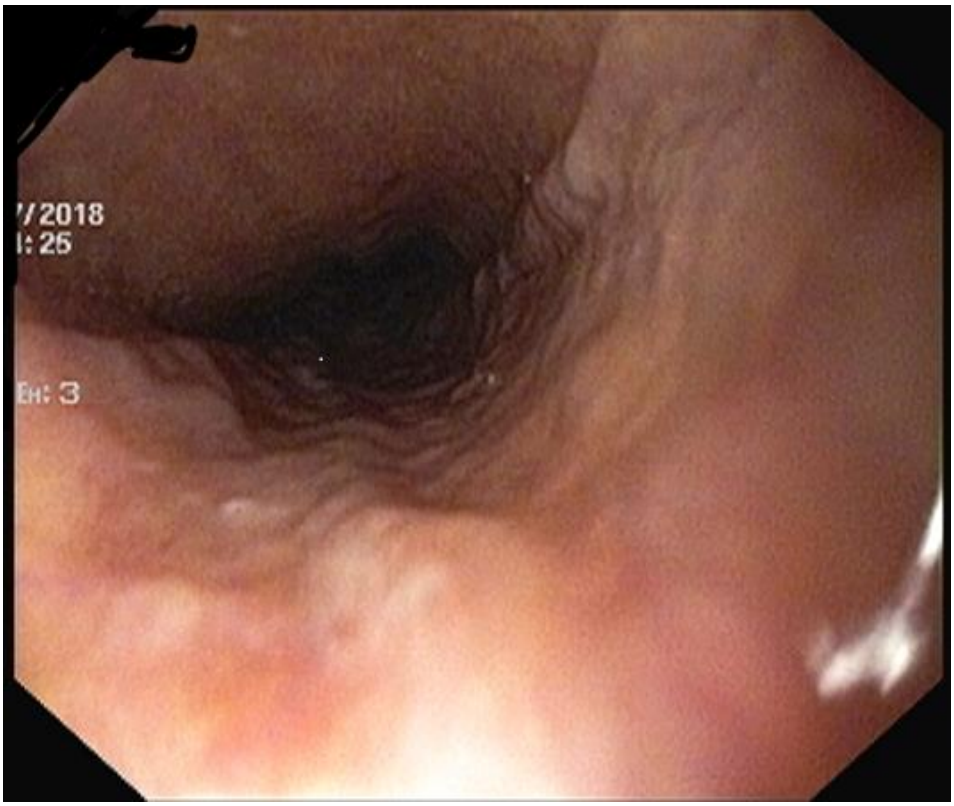

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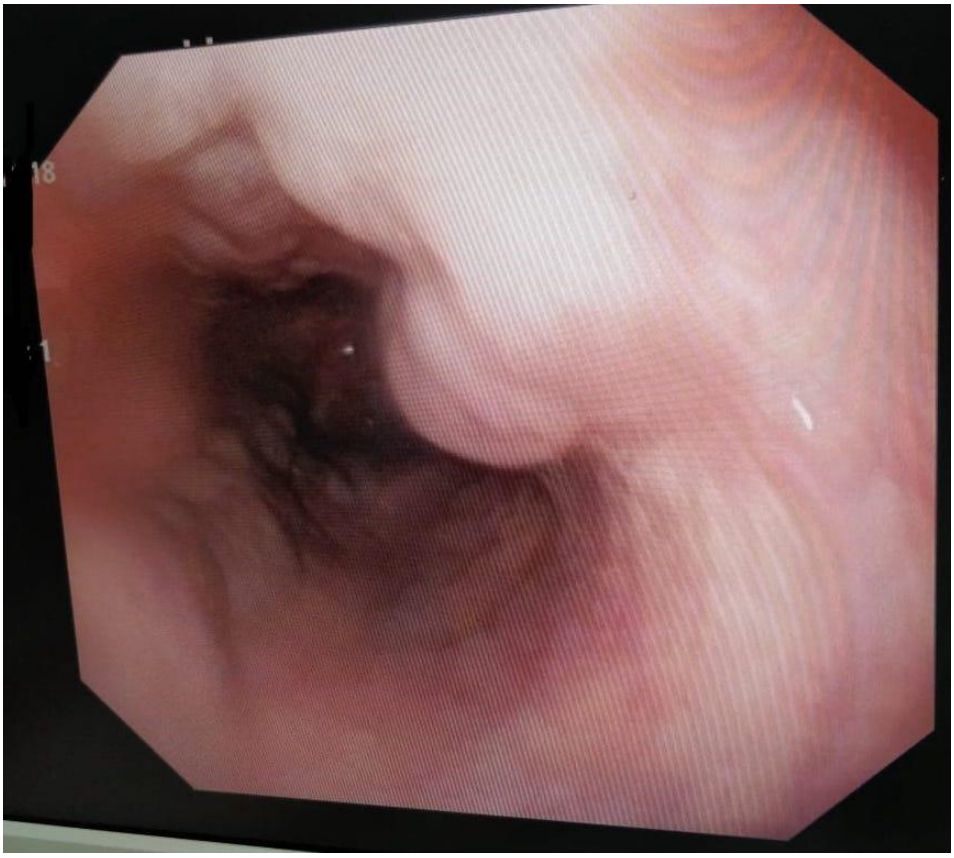
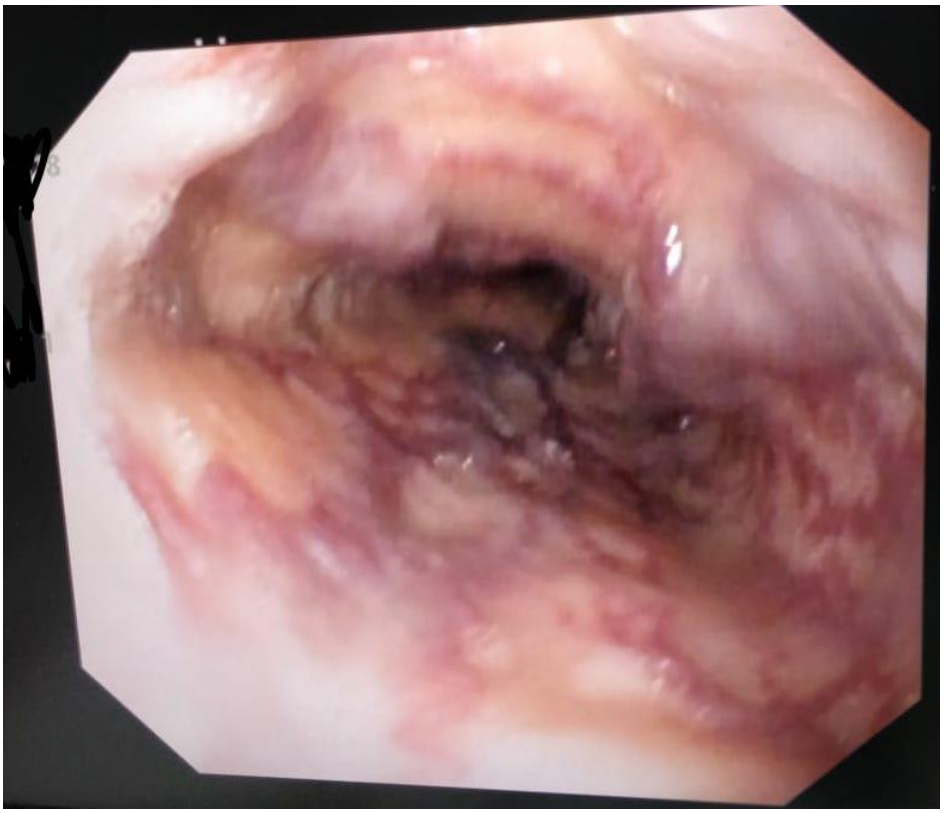


Image 1: GRADE III ESOPHAGEAL VARICES



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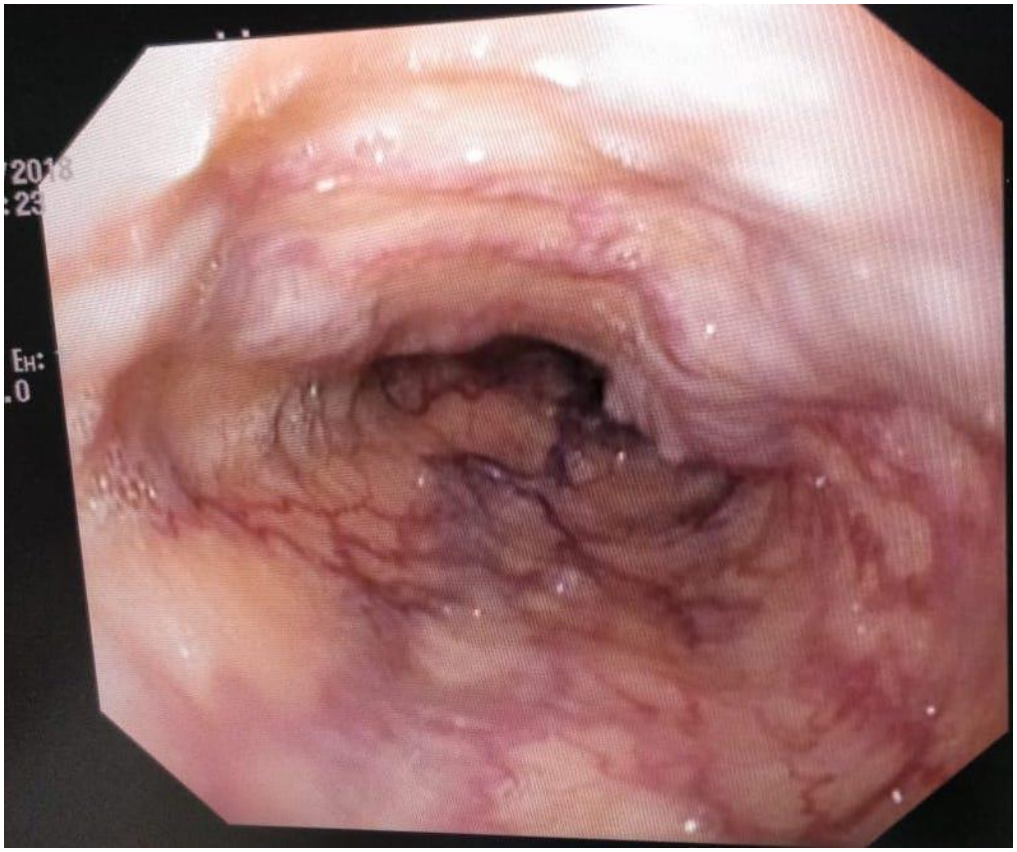


Image 1: GRADE III ESOPHAGEAL VARICES

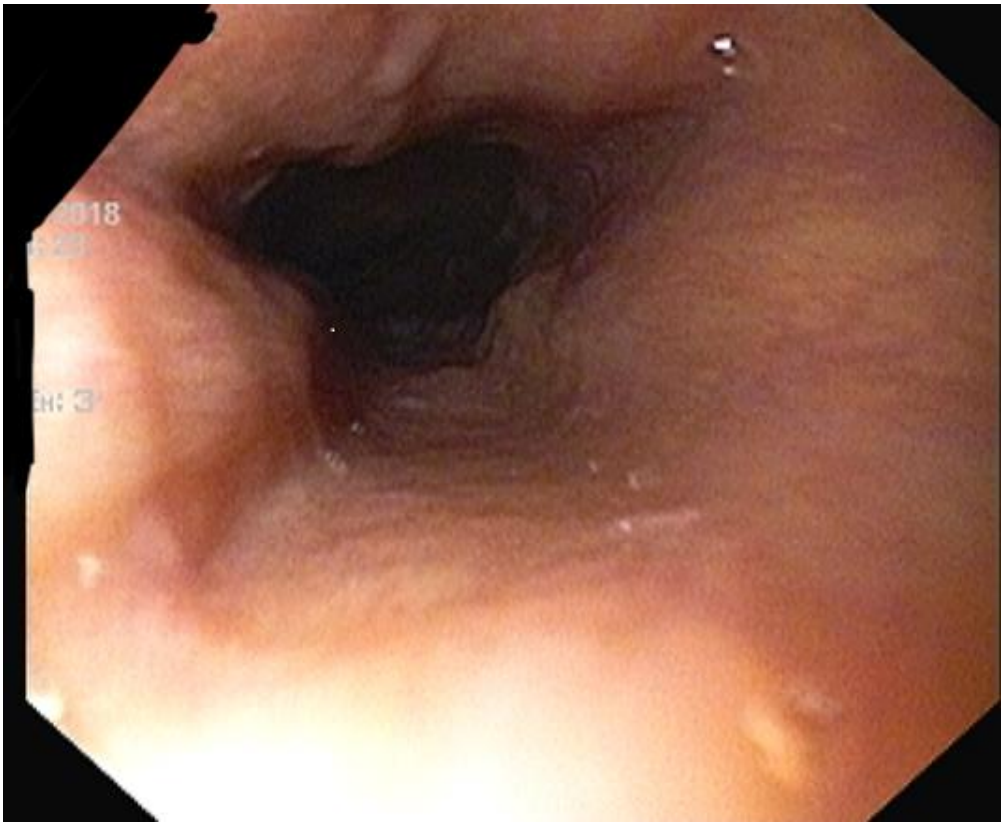


Image 1: GRADE II ESOPHAGA

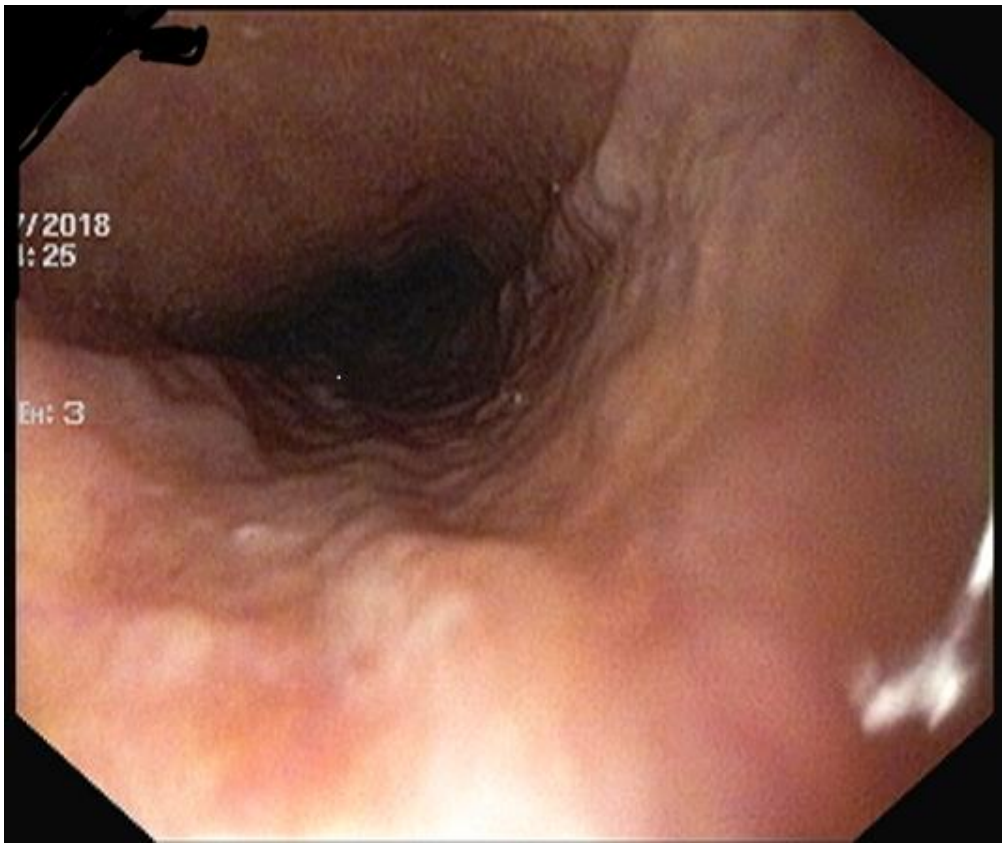


Image 1: GRADE III ESOPHAGEAL VARICES

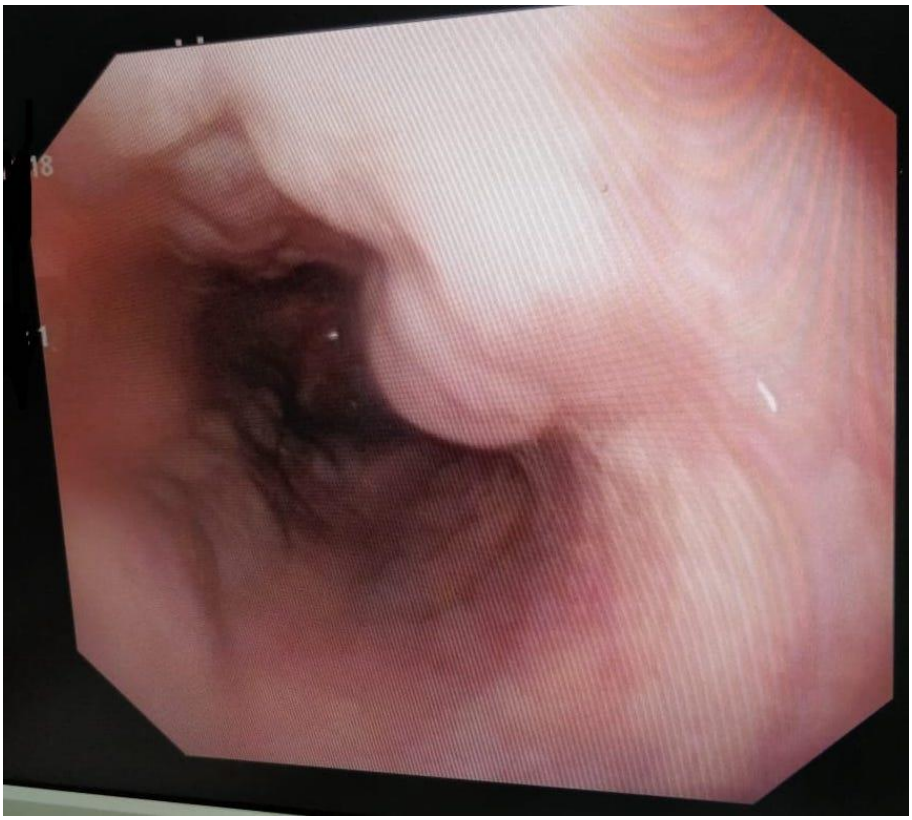


Image 1: GRADE III ESOPHAGEAL VARICES

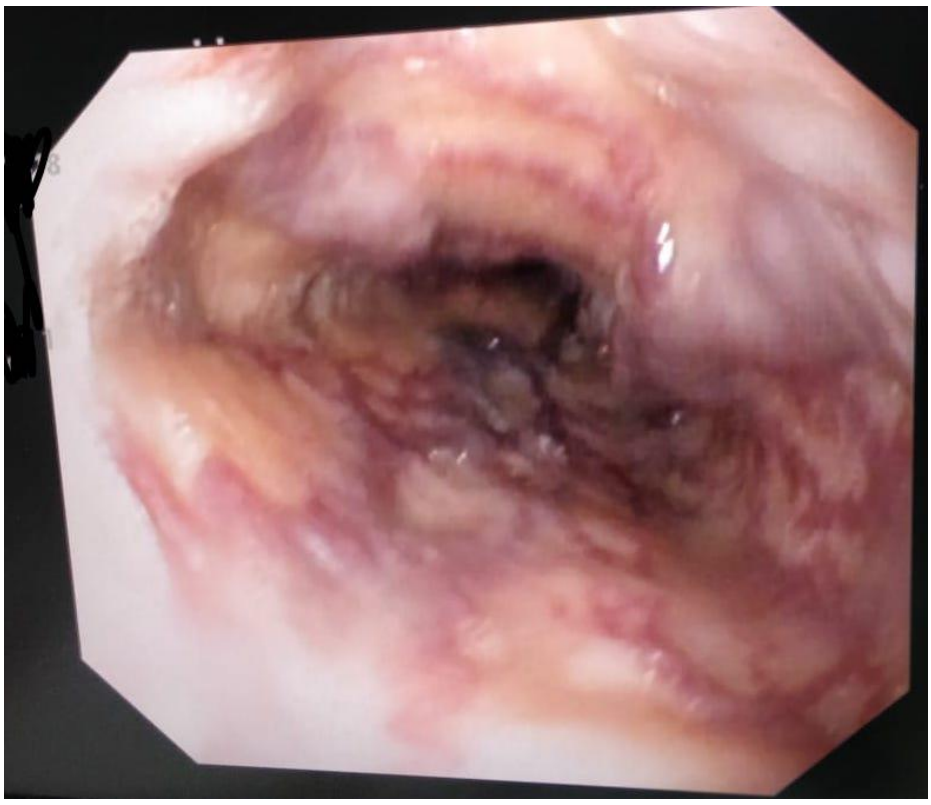


Image 1: GRADE III ESOPHAGEAL VARICES

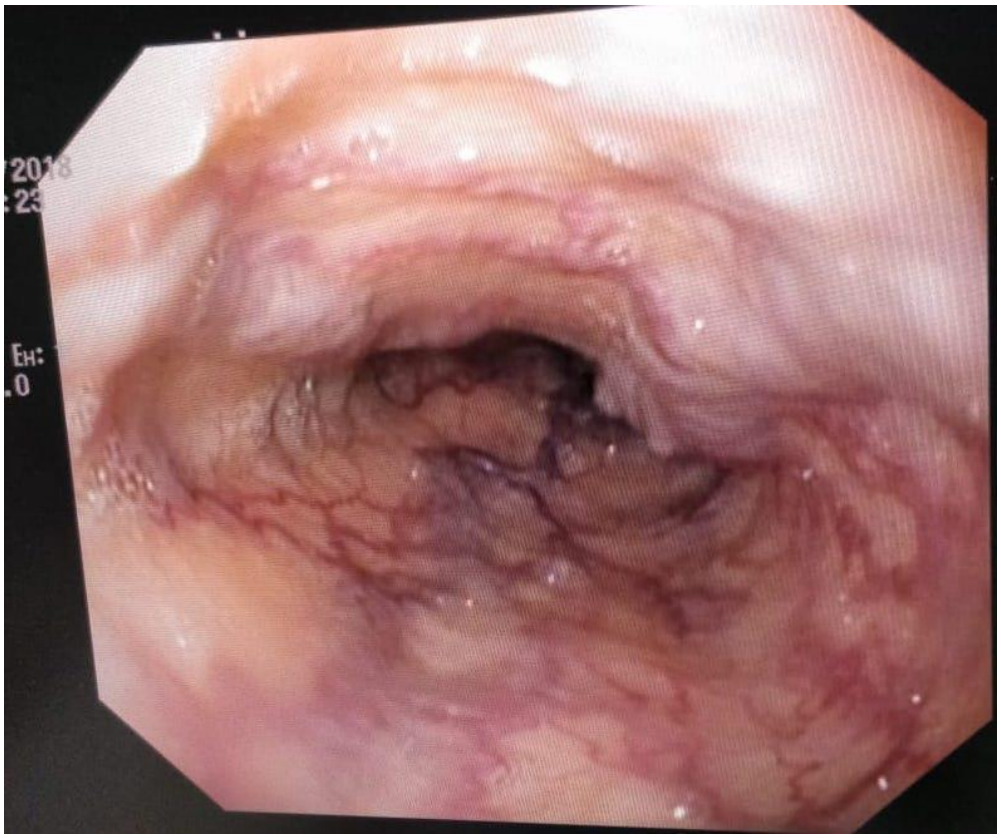


Image 1: GRADE III ESOPHAGEAL VARICES

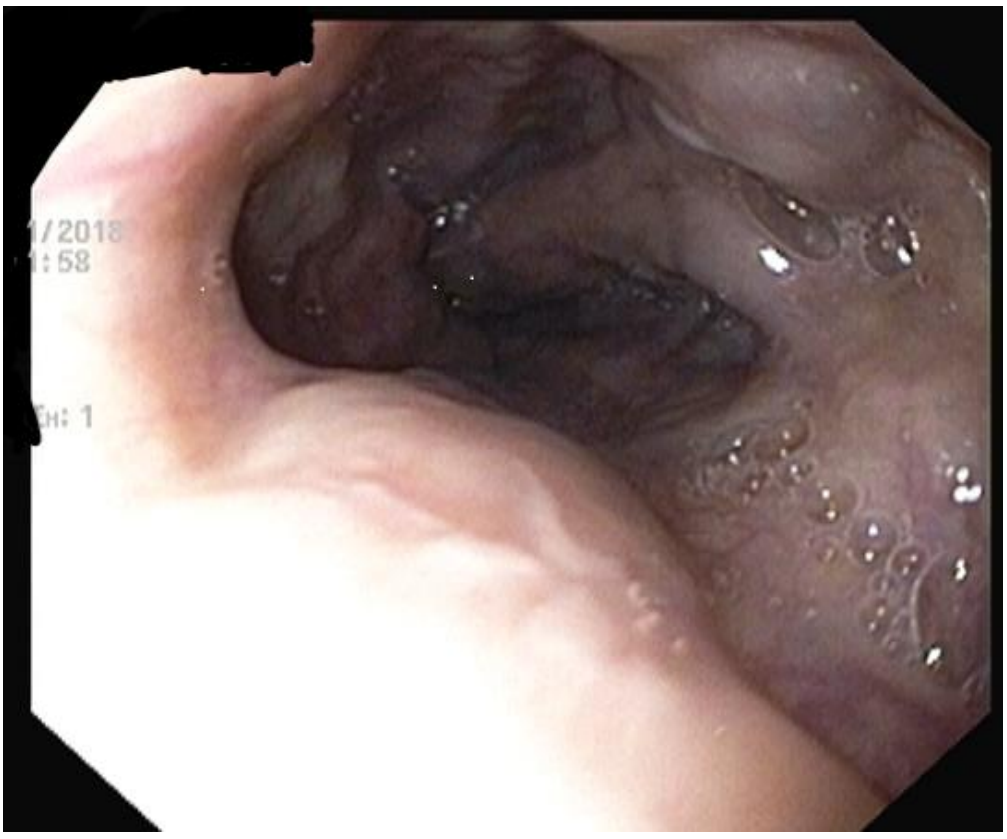


Image 1: GRADE III ESOPHAGEAL VARICES

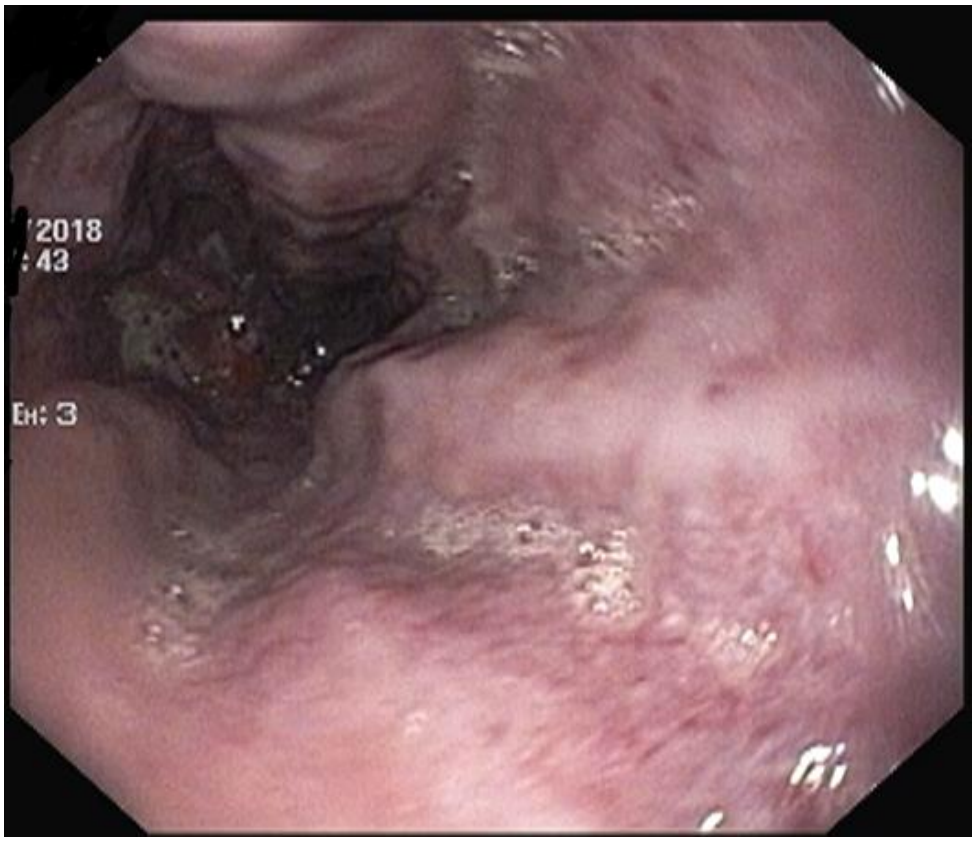


Image 1: GRADE III ESOPHAGEAL VARICES

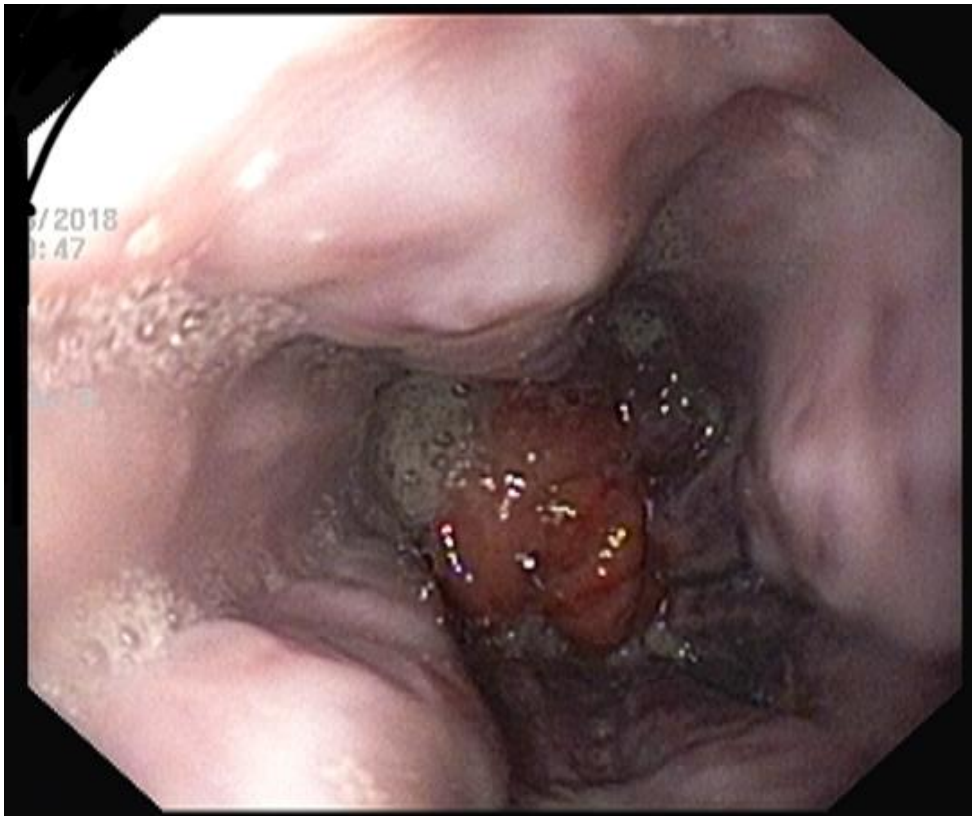
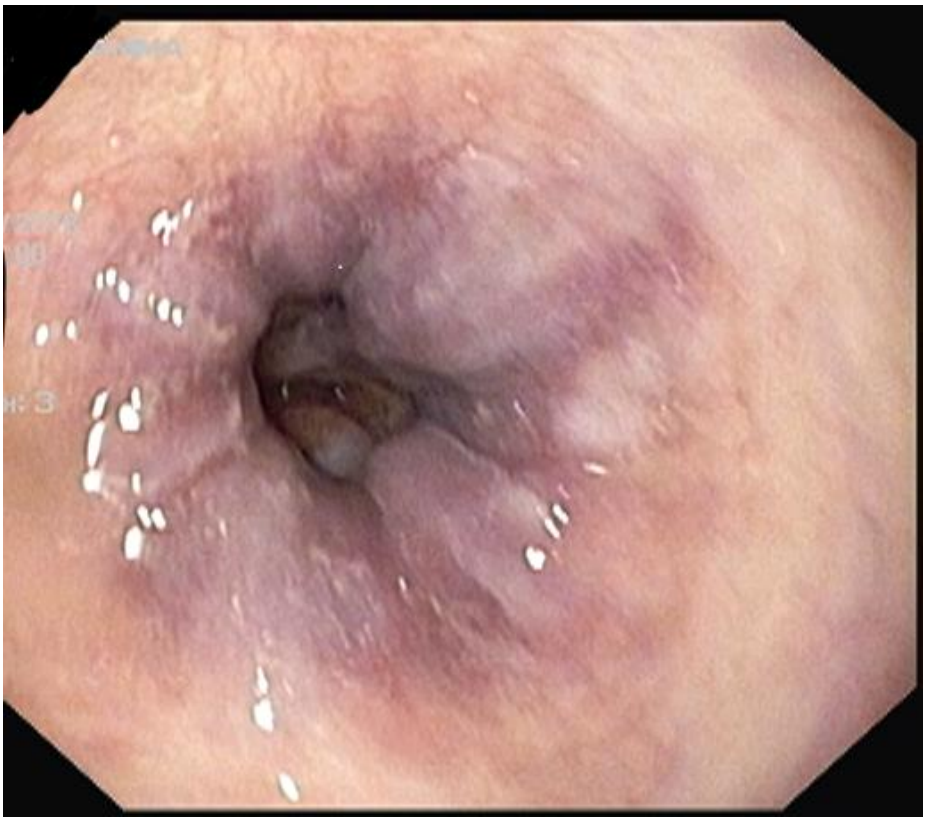


Image 1: GRADE III ESOPHAGEAL VARICES



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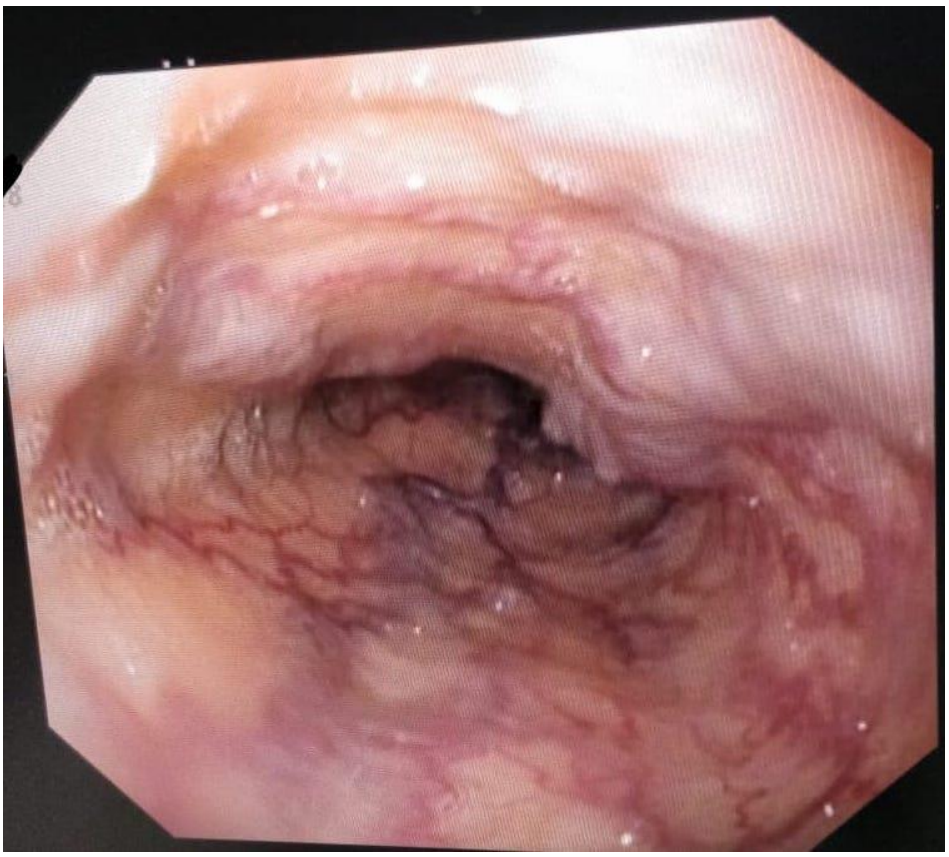

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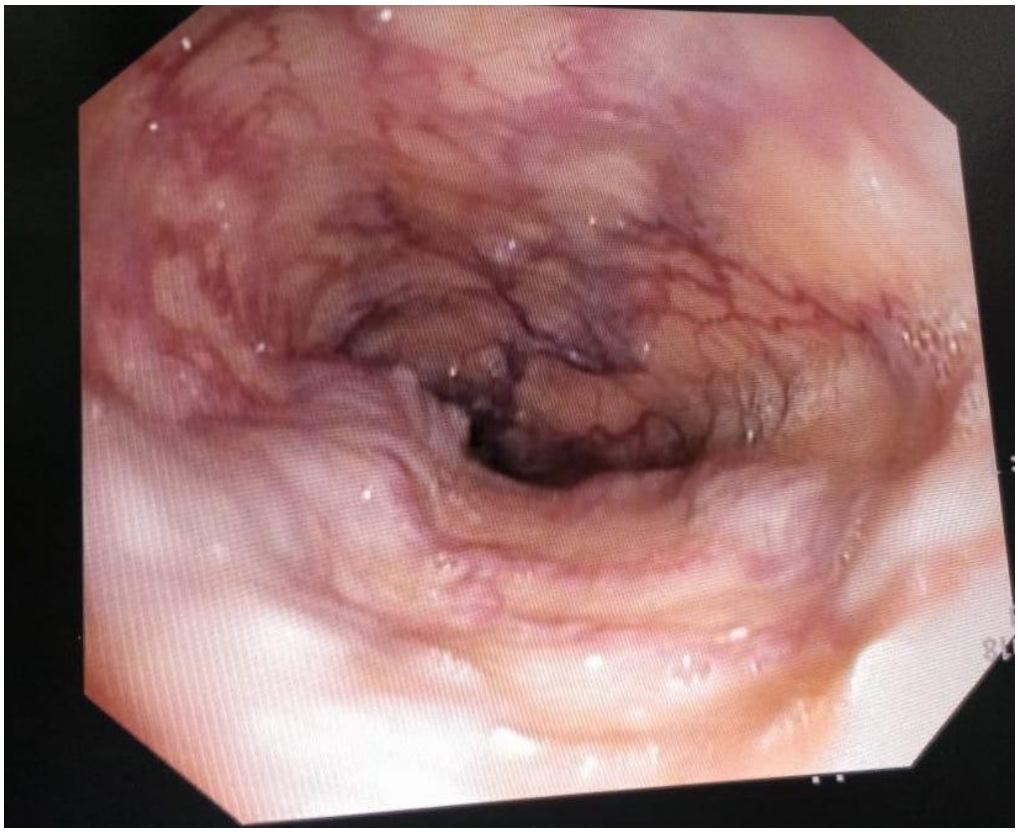

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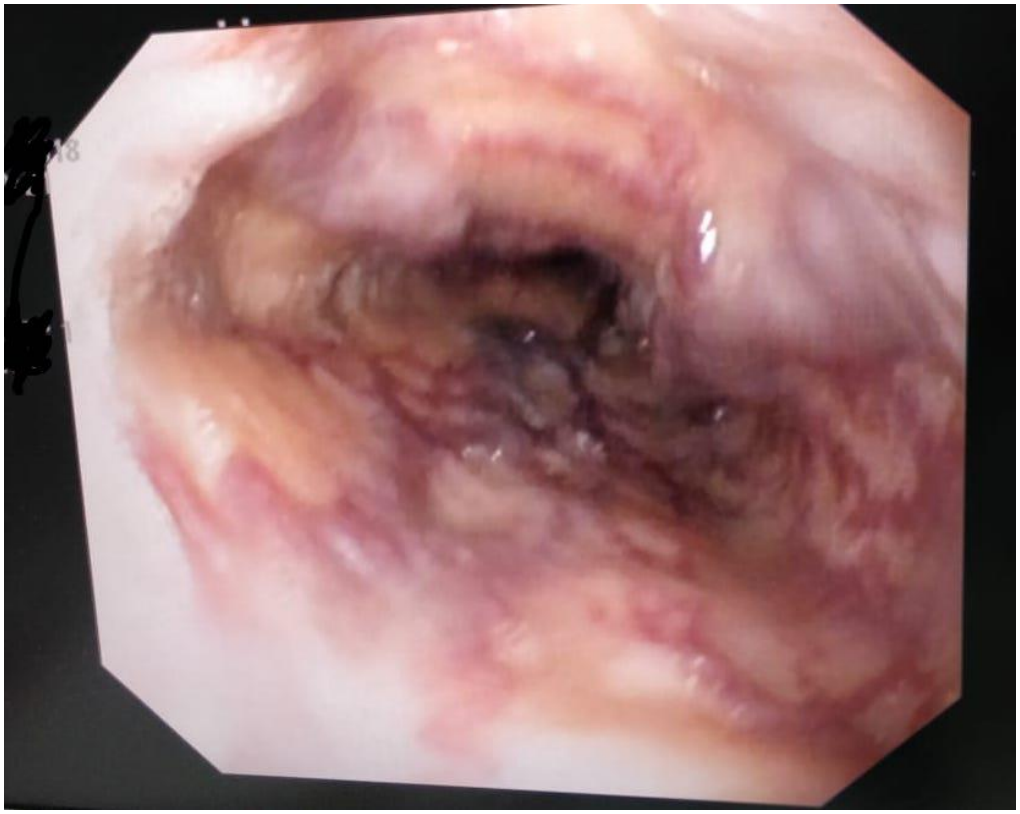

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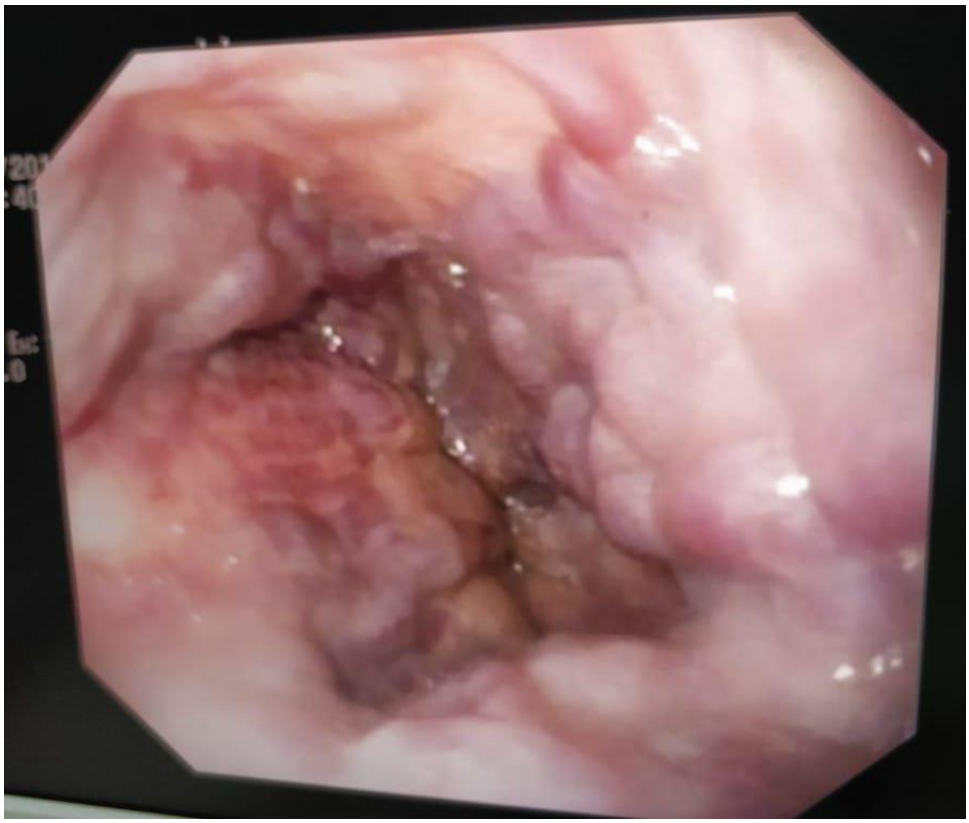

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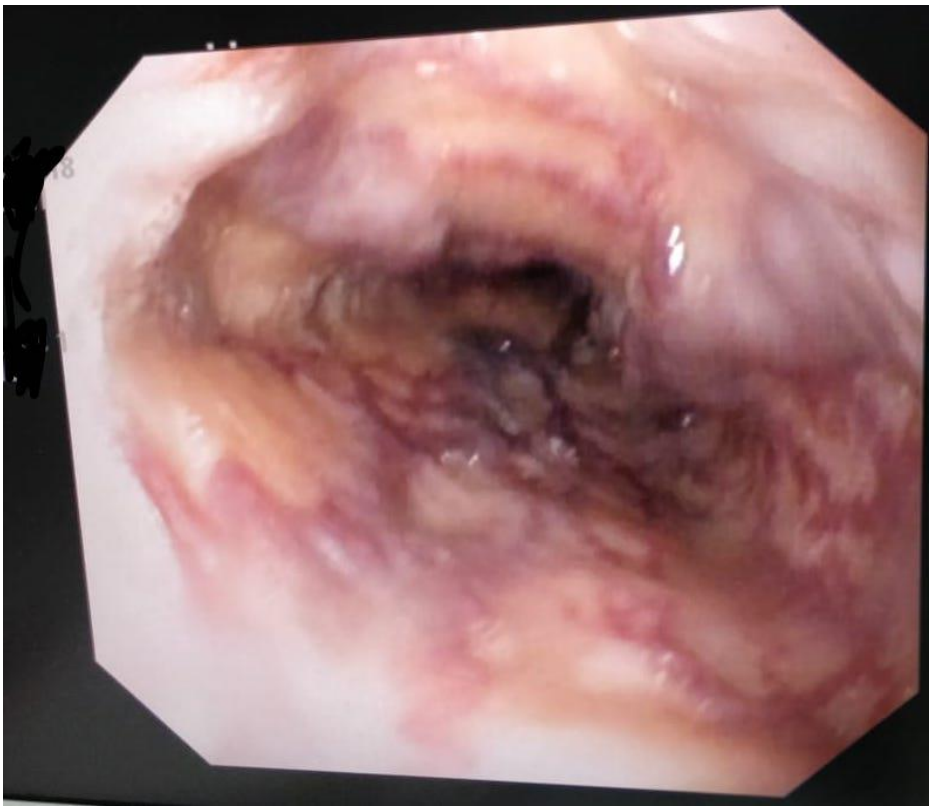

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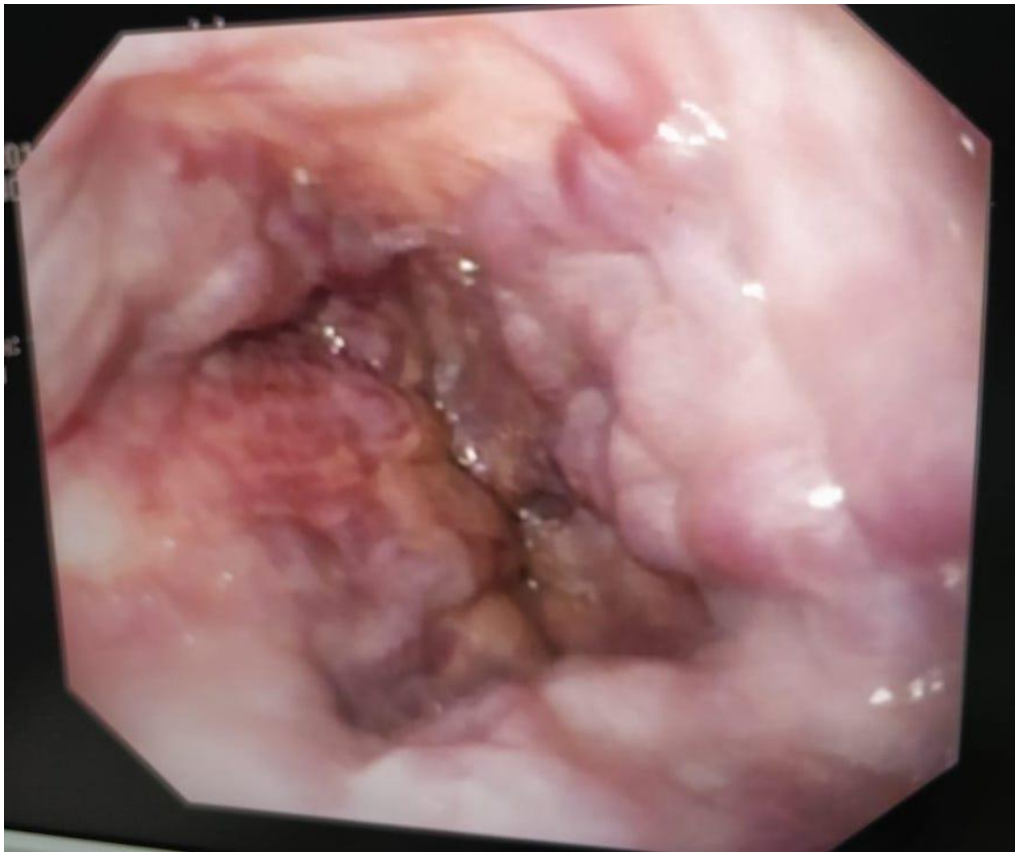

Image 1: