"CORRELATION OF PLATELET COUNT/SPLENIC DIAMETER RATIO FOR THE DIAGNOSIS OF ESOPHAGEAL VARICES IN PATIENTS OF CIRRHOSIS OF LIVER"

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LIST OF ABBREVATIONS USED

ALD- ALCHOLIC LIVER DISEASE

CLD-CHRONIC LIVER DISEASE

EGD : ESOPHAGOGASTRODUODENOSCOPY

EGV : ESOPHAGOGASTRIC VARICES

EV : ESOPHGEAL VARICES

EVL : ENDOSCOPIC VARICEAL LIGATION

FHVP : FREE HEPATIC VENOUS PRESSURE GRADIENT

HBV : HEPATITIS B VIRUS

HCC : HEPATOCELLULAR CARCINOMA

HCV : HEPATITIS C VIRUS

HREV : HIGH RISK ESOPHAGEAL VARICES

HVPG : HEPATIC VENOUS PRESSURE GRADIENT

LEV : LARGE ESOPHGEAL VARICES

MELD : MODEL FOR END STAGE LIVER DISEASE

MCV : MEAN CORPUSCULAR VOLUME

MCHC : MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION

NO : NITRIC OXIDE

NPV : NEGATIVE PREDICTIVE VALUE

NSAIDs : NONSTEROIDAL ANTIINFLAMMATORY AGENTS

PCV : PACKED CELL VOLUME

PC/SD : PLATELET COUNT TO SPLEEN DIAMETER RATIO

PLT : PLATELET

PPV : POSITIVE PREDICTIVE VALUE

RBC : RED BLOOD CELL

SAAG : SERUM ASCITES ALBUMIN GRADIENT

SD :STANDARD DEVIATION

SGOT : SERUM GLUTAMATE OXALOACETATE TRANSAMINASE

SGPT : SERUM GLUTAMATE PYRUVATE TRANSAMINASE

SV : SMALL VARICES

TIPS : TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

TPO : THROMBOPOIETIN

WHVP : WEDGED HEPATIC VENOUS PRESSURE GRADIENT

ABSTRACT

BACKGROUND AND OBJECTIVES

In patients with cirrhotics, Endoscopic screening for esophageal varices is currently recommended as a gold standard tool in all the patients at the time of diagnosis of cirrhosis and to institute prophylactic measures in patients with large esophageal varices. In order to reduce the increasing burden that endoscopy units will have to bear, new methods have been proposed as alternatives to conventional endoscopy for the non-invasive or minimally invasive diagnosis of esophageal varices. In this study we aimed at identifying non invasive parameters especially platelet count, splenic diameter and platelet count/spleen diameter ratio that could predict the presence of esophageal varices.

METHODOLOGY

The present one year observational study was done in the Department of General Medicine at KLES Dr Prabhakar kore Hospital and Medical Research Centre Belagavi. A total of 70 patients with cirrhosis of liver were included in the study. Patients were subjected to relevant clinical examination, laboratory workup like complete blood count, liver function test, ultrasound abdomen and all patients underwent screening upper gastrointestinal endoscopy. Platelet count to spleen diameter ratio was calculated for all patients.

RESULTS

Among 70 patients of cirrhosis 54(77.14%) had varices. Males predominated with 64(91%). Majority patients ranged in between 31-50 years. Evidence of esophageal varices was more common with cirrhosis secondary to alcoholism as compared to HBV, HCV. The Child Pugh score, platelet count,

spleen size, platelet count/spleen diameter ratio in patients with varices was significantly different from patients without varices. Platelet count spleen diameter ratio cutoff value of 909 was obtained with sensitivity of 77% and specificity of 79%. The positive predictive value was 88% and negative predictive value was 62%.

CONCLUSION AND INTERPRETATION

There is strong evidence of correlation between platelet count, spleen diameter and platelet count/spleen diameter ratio for predicting esophageal varices in patients of cirrhosis. But platelet count/spleen diameter ratio with cut-off value of 909 may not be sufficiently accurate. The platelet count to spleen diameter ratio may be useful inexpensive tool for diagnosing esophageal varices in liver cirrhosis noninvasively when endoscopy facilities are not available.

KEYWORDS

Endoscopy, Esophageal varices, Liver cirrhosis, Platelet count to spleen diameter ratio, endoscopic screening.

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INTRODUCTION

The term portal hypertension was coined by Gilbert in 1902. However, it was not until 1937 that Thompson could verify the increase in portal pressure directly during laparotomy that portal hypertension was confirmed. It was way back in 1650 that Glisson at a dissection in London, established the portal vein as the vessel by which blood was collected from the gastrointestinal tract and returned to the systemic circulation. As early as 1543, Vesalius drew an anatomical picture of the portal venous system.

Portal hypertension is the consequence of an increase in the splanchnic blood flow secondary to vasodilation and increased resistance to the passage of blood through the cirrhotic liver.[1] Development of esophageal varices is one of the major complications of portal hypertension.[2] Its prevalence varies from 50-60% in patients with cirrhosis of the liver.[3] After varices have developed, about one-third of patients die of bleeding gastroesophageal varices[4]. The risk of initial bleeding from varices is 25-35% within two years with most first bleeding episodes occurring within one year after detection of varices[5]. The reported mortality from first episode of variceal bleeding ranges from 40-70%. In patients with cirrhosis the incidence of esophageal varices increases by nearly 5% per year, and the rate of progression from small to large varices is approximately 5 to10 % per year. The risk of variceal rupture is greatest in the 2 years following diagnosis.

In 1996, The American Association for the study of liver disease stated that all cirrhotic patients should be screened for the presence of oesophageal varices when portal hypertension is diagnosed. Recently, the Baveno III consensus conference on

portal hypertension recommended that all cirrhotic patients should be screened for the presence of oesophageal varices when liver cirrhosis is diagnosed[6]. Repeat endoscopy is recommended at 2-3 years intervals in patients without varices and at 1-2 years interval inpatients with small varices to evaluate the development or progression of varices[7].

However, this approach has two major limitations. Endoscopy is an invasive procedure and secondly the cost effectiveness of this approach is also questionable[8].As only 9-36% patients with cirrhosis are found to have varices on screening endoscopy.It may therefore be more cost effective to routinely screen patients at high risk for the presence of varices, so as to reduce the increasing burden and procedure costs of endoscopy units. Certain biochemical, clinical and ultrasonographic parameters alone or together have good predictive power for non-invasively assessing the risk of bleeding from varices. However, the factors that predict the presence of varices are not as well-defined. Identification of non-invasive predictors of oesophageal varices will enable us to carry out upper GI endoscopy in selected groups of patients, thus avoiding unnecessary intervention and at the same time not missing the patients at risk of bleeding.

Currently many non invasive methods have been used to predict the presenceof esophageal varices and hence decrease the burden on the endoscopic units and also the social burden the patients. Overall, the most common result of these studies was that parameters directly or indirectly linked to portal hypertension, such as splenomegaly and decreased platelet count, were predictors of the presence of esophageal varices.

In a study by Thomopoulos et al (2003) seventeen variables consideredrelevant to the presence of esophageal varices were tested and they came to theconclusion that thrombocytopenia, splenomegaly and ascites are independentpredictors of large esophageal varices in cirrhotic patients. The authors suggest thatendoscopy could be avoided safely in cirrhotic patients with none of these predictive factors, as large varices are absent in this group of patients.

However, in patients with chronic liver disease the presence of decreasedplatelet count may depend on several factors other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses. On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension. With this in mind, according to Gianni et al (2003), their study used the platelet count/spleen diameter ratio as a parameter linking thrombocytopenia to spleen size in order to introduce a variable that takes into consideration the decrease in platelet count, which most likely depends on hypersplenism.

Three of these non invasive methods (the platelet count/spleen diameter ratio, Fibrotest and Fibroscan) are truly non-invasive. Of these, the former is promising and needs a proper validation[9].

OBJECTIVE OF THE STUDY

- To Identify the correlation of platelet count, splenic diameter and their ratio with presence of esophageal varices in patients of cirrhosis of liver without any previous evidence of GI bleeding.

- To Assess the ability of these parameters as non invasive tool to diagnose the presence of oesophageal varices

REVIEW OF LITERATURE

Cirrhosis is a pathologically defined entity that is associated with a spectrum of characteristic clinical manifestations[10]. The cardinal pathologic features reflect irreversible chronic injury of the hepatic parenchyma and extensive fibrosis in association with the formation of regenerative nodules.

CLINICAL FEATURES OF HEPATIC CIRRHOSIS

- Hepatomegaly (although liver may also be small)
- Jaundice
- Ascites
- Circulatory changes
  - Spider telangiectasia, palmar erythema, cyanosis
- Endocrine changes
  - Loss of libido, hair loss
  - Men: gynaecomastia, testicular atrophy, impotence
  - Women: breast atrophy, irregular menses, amenorrhoea
  - Hemorrhagic tendencies
  - Bruises, purpura, epistaxis, menorrhagia
- Portal hypertension
- Splenomegaly, collateral vessels, variceal bleeding, fetor hepaticus
- Hepatic (portosystemic) encephalopathy
- Other features
  - Pigmentation, digital clubbing, low-grade fever

Definition

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. Although the causes are many, the end results are the same[11].

Evolution of cirrhosis[10]

The cardinal pathological features reflect irreversible chronic injury of thehepatic parenchyma and include extensive fibrosis in association with formation of regenerative nodules. These features result from hepatocyte necrosis, collapse of supporting reticulin network with subsequent connective tissue deposition, distortion of vascular bed, and nodular regeneration of remaining liver parenchyma. The pathologic process should be viewed as a final common pathway of many types of chronic liver injury. Clinical features of cirrhosis derive from the morphological alterations and often reflect the severity of hepatic damage rather than the etiology of the underlying liver disease. Loss of functioning hepatocellular mass may lead to jaundice, edema, coagulopathy, and a variety of metabolic abnormalities; fibrosis and distorted vasculature lead to portal hypertension and its sequelae, including gastroesophageal varices and splenomegaly. Ascites and hepatic encephalopathyresult from both hepatocellular insufficiency and portal hypertension.

Classification of cirrhosis[12]

Micronodular cirrhosis is characterized by thick, regular septa, byregenerating small nodules varying little in size, and by involvement of every lobule. The micronodular liver may represent impaired capacity for regrowth as in alcoholism, malnutrition, old age or anemia.

Macronodular cirrhosis is characterized by septa and nodules of variable sizes and by normal lobules in larger nodules. Previous collapse is shown by juxtaposition in the fibrous scars of three or more portal tracts. Regeneration is reflected by large cells with large nuclei and by cell plates of varying thickness.

Regeneration in a micronodular cirrhosis results in a macronodular or mixed appearance. With time, micronodular cirrhosis often converts to macronodular.

Aetiology:

1. Alcohol.

2. Viral hepatitis types B ± delta; type C.

3. Metabolic, e.g. haemochromatosis, Wilson's disease, α1 antitrypsin deficiency, type IV glycogenosis, galactosaemia, congenital tyrosinosis and non-alcoholic steatohepatitis.

4. Prolonged cholestasis, intra-and extra-hepatic.

5. Hepatic venous outflow obstruction, e.g. venoocclusive disease, Budd-Chiari

syndrome, constrictive pericarditis.

6. Disturbed immunity (autoimmune hepatitis).

7. Toxins and therapeutic agents, e.g. methotrexate, amiodarone.

8. Indian childhood cirrhosis.

9. Others: Malnutrition, infections, granulomatous lesions, cryptogenic cirrhosis

Compensated cirrhosis[11]

The disease may be discovered at a routine examination or biochemicalscreen, or at operation undertaken for some other condition. Cirrhosis may besuspected if the patient has mild pyrexia, vascular spiders, palmar erythema, or unexplained epistaxis or edema of the ankles. Firm enlargement of the liver andsplenomegaly are helpful diagnostic signs. Vague morning indigestion and flatulent dyspepsia may be early features in the alcoholic cirrhotic. Confirmation should be sought by biochemical tests, scanning and if necessary, by liver biopsy. Biochemical tests may be quite normal in this group. The most frequent changes are a slight increase in the serum transaminase or γ-GT level. Diagnosis is confirmed by needle liver biopsy.

Decompensated cirrhosis

The patient usually seeks medical advice because of ascites and or jaundice. General health fails with weakness, muscle wasting and weight loss. Continuous mild fever (37.5-38°C) is often due to gram-negative bacteremia, to continuing hepatic cell necrosis or to liver cell carcinoma. A liver flap may be present. The deeper the jaundice, the greater the liver cell dysfunction. Pigmentation of the skin and clubbing of the fingers are occasionally seen. Purpura over the arms, shoulders and shins may be associated with a low platelet count. Spontaneous bruising and epistaxis reflect a prothrombin deficiency. The blood pressure is low. Sparse body hair, vascular spiders, palmar erythema, white nails and gonadal atrophy are common. Ascites and

edema of the legs is frequently associated. The liver may be enlarged (early stages), with a regular edge, or contracted and impalpable (late stages). The spleen may be palpable.

CHILD-PUGH CLASSIFICATION[10,12,13,14]:

The clinical tool used most widely to determine prognosis in patients with cirrhosis is the Child-Turcotte-Pugh (CTP) score and Child (or Child-Pugh) classification. This simple classification system, which was designed specifically toassess the risk of mortality following portocaval shunt surgery in cirrhotic patients with variceal bleeding, has gained favour as a rapid method for determining the prognosis of patients with various chronic liver diseases. The Child classification is as effective as quantitative liver function tests and disease-specific prognostic models for determining short-term prognosis in groups of patients awaiting liver transplantation. Despite its limitations, the Child classification has been adopted widely for risk stratifying patients with cirrhosis because of its simplicity and ease of use. Five-year survival rates for patients with cirrhosis decrease dramatically as the CTP score and Child's class become higher at the time of clinical presentation.

TABLE 1. CHILD PUGH CLASSIFICATION OF CIRRHOSIS

Score	1	2	3
Encephalopathy	None	Mild	Marked
Bilirubin (mol/L)	<34	<34-50	>50
Albumin (g/L)	>35	28-35	<28
Prothrombin time (seconds prolonged)	<4	4-6	>6
Ascites	None	Mild	Marked
Add the indvidual scores: <7=Childs'A 7-9=Childs'B >9=Childs'C			

The total score classifies patients into grade A (5-7) B (7-9) or C (>10). Poor prognosis is associated with a prolonged prothrombin time, marked ascites, gastrointestinal bleeding, advanced age, high daily alcohol consumption, high serum bilirubin and alkaline phosphatase, low albumin values, and poor nutrition.

The Child classification has some limitations, however; for example, it does not discriminate survival well among patients within each Child class. Furthermore some parameters that make up the CTP score, such as ascites and encephalopathy, are assessed by subjective interpretation.

Recently the Child-Pugh system has been replaced by the model for end-stage liver disease (MELD) score for assessing the need for liver transplantation. The MELD score is a prospectively derived scoring system designed to predict prognosis of patients with liver disease and portal hypertension. It is calculated using three noninvasive variables—the prothrombin time expressed as international normalized ratio (INR), serum bilirubin, and serum creatinine.

Patients with compensated cirrhosis become decompensated at the rate of 10% per year. Ascites is the usual first sign. Decompensated patients have around a 20% 5-year survival [10,12,13]. According to Madhotra et al (2002)[15] and Zaman et al(2001)[16]the prevalence of esophageal varices in cirrhosis increases with severity of liver disease, as assessed by Child Pugh Classification.

The following points are useful prognostically:

- Liver Size. A large liver carries a better prognosis than a small one because itis likely to contain more functioning cells.
- Hemorrhage from oesophageal varices. If liver function is good, hemorrhage may be tolerated; if poor, hepatic coma and death are probable.
- Persistent hypotension (systolic BP<100 mmHg) is serious.
- Ascites worsens the prognosis.
- If decompensation has followed hemorrhage, infection or alcoholism, theprognosis is better than if it is spontaneous, because the precipitating factor iscorrectable.
- Jaundice, especially if persistent, is a serious sign.Neurological complication. - The significance of encephalopathy depends onthe clinical circumstances. Developing in the course of progressive hepatocellular failure, it carries a bad prognosis. Chronic and those with an extensive portal systemic collateral circulation who respond well to medical treatment carry good prognosis.
- Biochemical tests. If the serum albumin is less than 25g/L the outlook is poor.Hyponatraemia (serum sodium<120mmol/L), if unrelated to diuretic therapy, is grave. Serum transaminase and globulin levels give no guide to prognosis.

• Alcoholic cirrhotics, if they abstain, respond better than those with 'cryptogenic' cirrhosis

• The response to therapy. If the patient has failed to improve within 1 month of starting hospital treatment, the outlook is poor.

• Hepatic histological changes. Sections are useful in evaluating the extent of necrosis and of inflammatory infiltration. A fatty liver responds well to treatment.

Table 2: Survival in Cirrhosis

Child Pugh's Grade	1 year survival %	5 years survival %	10 years survival %	Hepatic Deaths %
A	82	45	25	43
B	62	20	70	72
C	42	20	0	85

MELD score[13,17]:

In contrast to Child–Pugh score, the variables of MELD score have beenselected in a given population and the score has been validated thereafter in anindependent sample. Recently, studies have been reported confirming that MELD is a robust risk score in patients undergoing TIPS, with a statistics for 1 year survival of about 0.70. MELD score has been tested in the setting of acute liver failure and emergency re transplantation for early graft failure. The MELD has been widely validated for predicting survival in patients with cirrhosis, including patients who have undergone TIPS placement, and is more accurate for this purpose than the Child classification.

PORTAL HYPERTENSION [10,12,13]

The portal system includes all veins that carry blood from the abdominal part of the alimentary tract, the spleen, pancreas and gallbladder. The portal vein enters the liver at the porta hepatis in two main branches, one to each lobe; it is without valves in its larger channels. The portal vein is formed by the union of the superior

mesenteric vein and the splenic vein just posterior to the head of the pancreas at about the level of the second lumbar vertebra. Portal pressure is about 7mmHg normally.

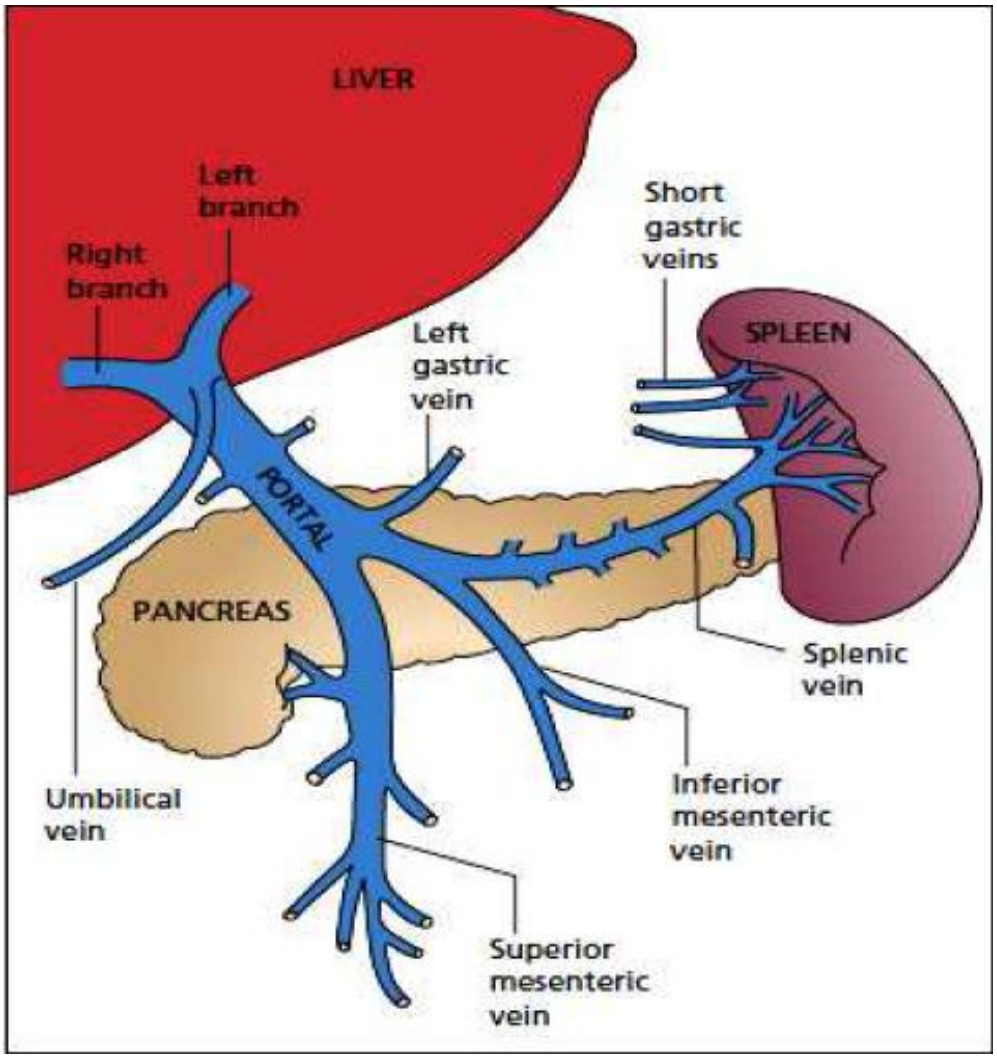


Figure 1. The anatomy of the portal venous system. The portal vein is posterior to the pancreas

COLLATERALS: [12]

When portal pressure reaches a critical value, porto-systemic collaterals may develop. In alcoholic cirrhosis, a corrected portal pressure of 10 to 12mm Hg appears to be necessary for the development of oesophageal varices[23]. These collaterals represent the opening of embryonic channels or redirection of flow within existing

veins, rather than the formation of new blood vessels.

1. Group I: where protective epithelium adjoins absorptive epithelium:

(a) At the cardia of the stomach, where the left gastric vein, posterior gastric and short gastric veins of the portal system anastomose with the intercostal, diaphragm-oesophageal and azygos minor veins of the caval system. Deviation of blood into these channels leads to varicosities in the sub mucous layer of the lower end of the oesophagus and fundus of the stomach.

(b) At the anus, the superior haemorrhoidal vein of the portal system anastomoses with the middle and inferior haemorrhoidal veins of the caval system. Deviation of blood into these channels may lead to rectal varices.

2. Group II: in the falciform ligament through the paraumbilical veins, relics of theumbilical circulation of the fetus.

3. Group III: where the abdominal organs are in contact with retroperitoneal tissues oradherent to the abdominal wall. These collaterals run from the liver to diaphragm andin the spleno-renal ligament and omentum. They include lumbar veins and veinsdeveloping in scars of previous operations or in small or large bowel stomas.

4. Group IV: portal venous blood is carried to the left renal vein. This may be through blood entering directly from the splenic vein or via diaphragmatic, pancreatic, left adrenal or gastric veins.

PATHOPHYSIOLOGY OF PORTAL HYPERTENSION

Portal hypertension is one of the prime complications of cirrhosis. Patientsdeveloping clinical features or complications of cirrhosis usually have portal venous pressures above 12 mmHg.

Normal Physiology

The movement of portal blood across the liver is dependent on the pressuregradient between the portal and hepatic veins[13]. Hepatic venous pressure in partreflects the state of central venous filling pressure. Portal pressure is determined by the product of portal venous inflow and the vascular resistance of this flow:

Portal pressure = portal flow x vascular resistance.

Normally, the difference between portal venous pressure and hepatic venouspressure is never greater than 4mm Hg. A compliant liver acts as a blood reservoir to maintain a normal hepatic pressure gradient[18]. When outflow pressure increases, an increasing number of sinusoids are recruited to accommodate these changes. Thus, elevations of hepatic venous pressures do not result in similar increases in portal pressure.The main site of portal vascular resistance in humans appears to reside at the level of the hepatic sinusoids[19].Portal venous inflow is the sum of the flows from the 3 main splanchnicTributaries[20]. The splenic vein joins the inferior mesenteric vein at the level of thepancreatic body and tail, where pancreatico duodenal vessels also enter. Superior mesenteric venous drainage from the small and proximal large intestine joins the splenic vein at a site superior to the pancreatic head, forming the portal vein trunk.

The coronary vein drains the venous circulation of the lesser gastric curvature into the proximal portal vein. The gastroduodenal vein collects drainage from the area of the pancreatic head.Total portal venous flow in a normal man ranges between 600 and 1200ml/min, as measured intra operatively and by Doppler flowmetry.

The volume of portal flow is regulated by the vascular resistance of thesplanchnic arteries[21]. Changes in portal inflow result from modifications in splanchnic arteriolar resistance, as seen with physiologic events such as a change in posture or in the postprandial state. The increase in portal blood flow after a meal can be prevented by pre-administration of somatostatin, an inhibitor of the release of several gastrointestinal hormones that may mediate the arteriolar vasodilatation that occurs after feeding. Portal venous oxygen content decreases after a meal because of increased intestinal arteriovenous extraction of oxygen.

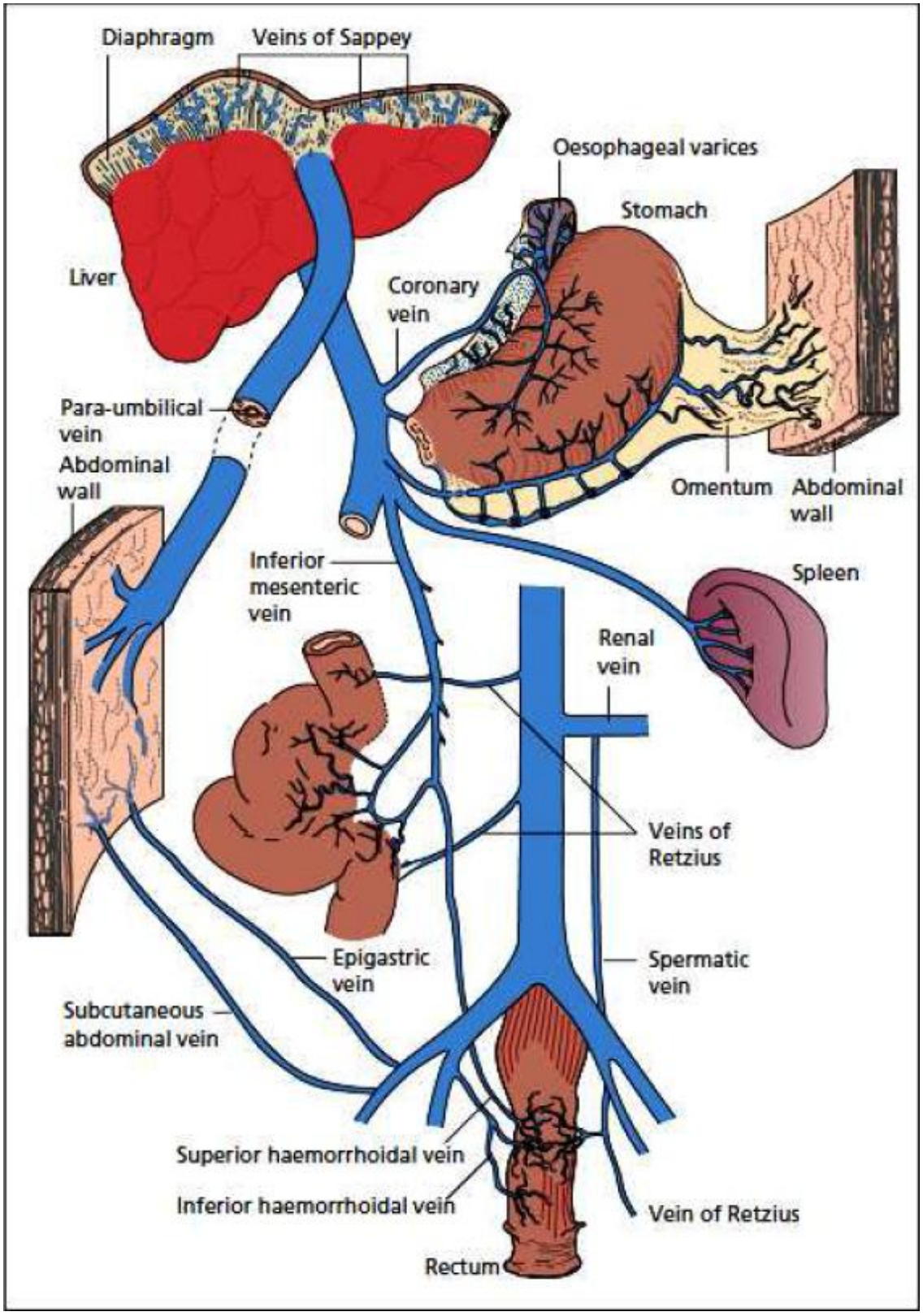


Figure 2: The sites of the portal-systemic collateral circulation in cirrhosis of the liver.

HEMODYNAMICS IN PORTAL HYPERTENSION

Vascular Resistance

Theoretically, a rise in portal pressure could stem from an increase in either portal flow or vascular resistance. Under normal conditions, a rise in portal flow can be accommodated by the compliant hepatic sinusoidal bed so that portal pressure increases only in extreme conditions. For example, although splenic flow increases markedly in the presence of massive splenomegaly, the critical threshold in the portal flow-pressure relationship is not reached and portal flow pressure relationship is not reached and portal hypertension does not develop unless increased vascular resistance is also present. This hemodynamic combination can be seen in conditions with splenomegaly, such as Felty's syndrome, sarcoidosis, or lymphomas. An exception is portal hypertension caused by a high portal flow from an arterio venous fistula, as with splenic artery splenic vein communications, where the flow-volume relationexceeds a critical threshold.

The genesis of portal hypertension involves an increase in portal vascular resistance and is the basis for its classification. Insight into the location of vascular resistance in human cirrhosis has been provided by combined hepatic vein and portal pressure measurements[22]. Most measurements in non-alcoholic cirrhosis show a higher portal venous pressure than hepatic venous wedge pressure, an estimate of sinusoidal pressure. This indicates the presence of a pre sinusoidal component, probably related to inflammatory activity or fibrotic changes in the portal triads. In alcoholic cirrhosis, the vascular resistance must reside at the level of the sinusoids because portal and hepatic venous wedge pressures are similar.

The pathogenesis of the increased sinusoidal resistance in alcoholic cirrhosis is controversial. The concept of a pathogenic role for the architectural rearrangement and development of fibrotic septa in cirrhosis has been replaced by an emphasis on sinusoidal events. Hepatocyte enlargement, resulting from an alcohol-induced accumulation of fat and protein, may compress the liver sinusoids and obstruct portal flow.

Studies of pre cirrhotic portal hypertension in baboons chronically fed alcohol have suggested that the degree of perivenular and pericellular fibrosis induced by alcohol correlates with in vivo measurements of portal pressure. This further implicates the hepatic sinusoids as the site of increased vascular resistance in alcoholic cirrhosis. Capillarization of these low-resistance channels, with loss of sinusoidal fenestrae, appearance of collagen in the space of Disse, and the presence of contractile myofibroblasts, may contribute to the development of increased sinusoidal resistance.

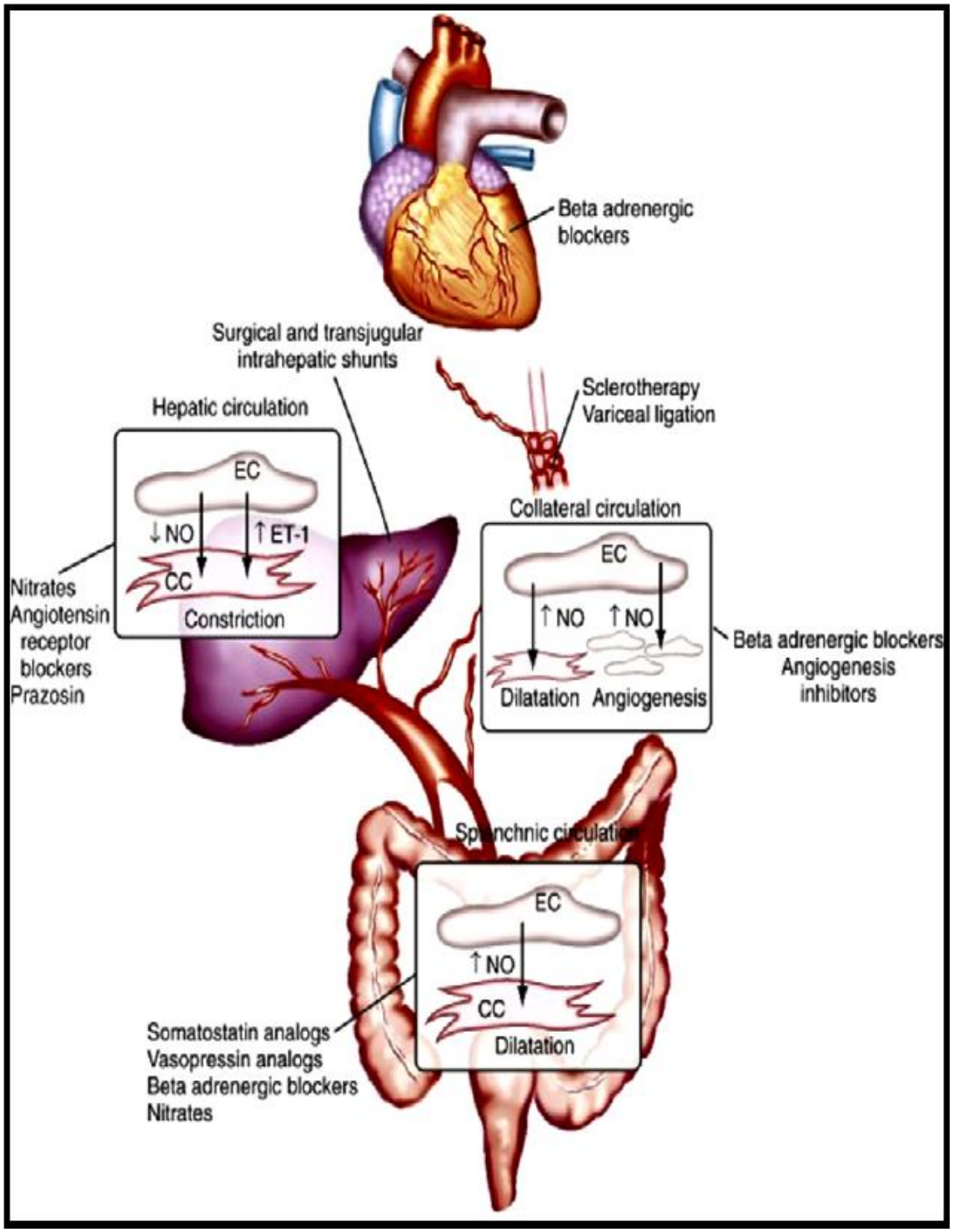


Figure 3: Vascular disturbances in portal hypertension and sites of action of portal pressure-reducing therapies. CC, contractile cell; EC, endothelial cell

A relation between hepatocyte size and intrahepatic pressure in alcoholic liver disease was found for only mild to moderate pressure elevations, although the accuracy of intrahepatic pressure measurements has not been confirmed by others. In non-alcoholic cirrhosis, a more complex relation exists between these parameters.

Portal blood flow and the systemic circulation

Two models have been proposed to explain the alternations of portal flow in response to portal hypertension: the "backward" and "forward" flow hypotheses. The first is based on a rise in portal venous pressure triggering a myogenic response that reduces splanchnic arterial inflow. As a net result, portal pressure values drift back toward normal. If the splanchnic circulation is considered as 2 organs in series (the gastrointestinal tree and the liver), the backward flow hypothesis predicts that inflow into the gastrointestinal tree would be reduced as a result of this rise in portal venous pressure. Even when portal hypertension is fully established, the backward component contributes to its maintenance.

The forward flow hypothesis, in which portal venous inflow is increased, is based on observations in several experimental models and patients. This paradoxical increase in portal venous inflow contributes to the maintenance of portal hypertension. As a hemodynamic syndrome, portal hypertension is unique in exhibiting both increased inflow and increased resistance.

The increase in portal inflow occurs as part of a more generalized hemodynamic disturbance, the `hyperdynamic" circulation. This is characterized by peripheral vasodilatation, a reduction in peripheral vascular resistance, and an increase in plasma volume. As a result, cardiac output and heart rate increase.

Decreases in splanchnic and muscular arterial resistance are the main factors contributing to the decrease in systemic vascular resistance. Variable effects are seen on the renal circulation, in which compensatory mechanisms such as renal sympathetic nerve activity, renin-angiotensin, and circulating catecholamines may induce renal vasoconstriction in spite of a decreased peripheral vascular resistance.

The hyperdynamic circulatory state is seen in many forms of portalhypertension. Humoral factors may be responsible for the development of peripheral vasodilatation. Glucagon levels are elevated in the presence of portal hypertension and portosystemic shunts. Other postulated humoral factors include prostacyclin, prostaglandins, bile salts and endotoxin mediated activation of nitric oxide.

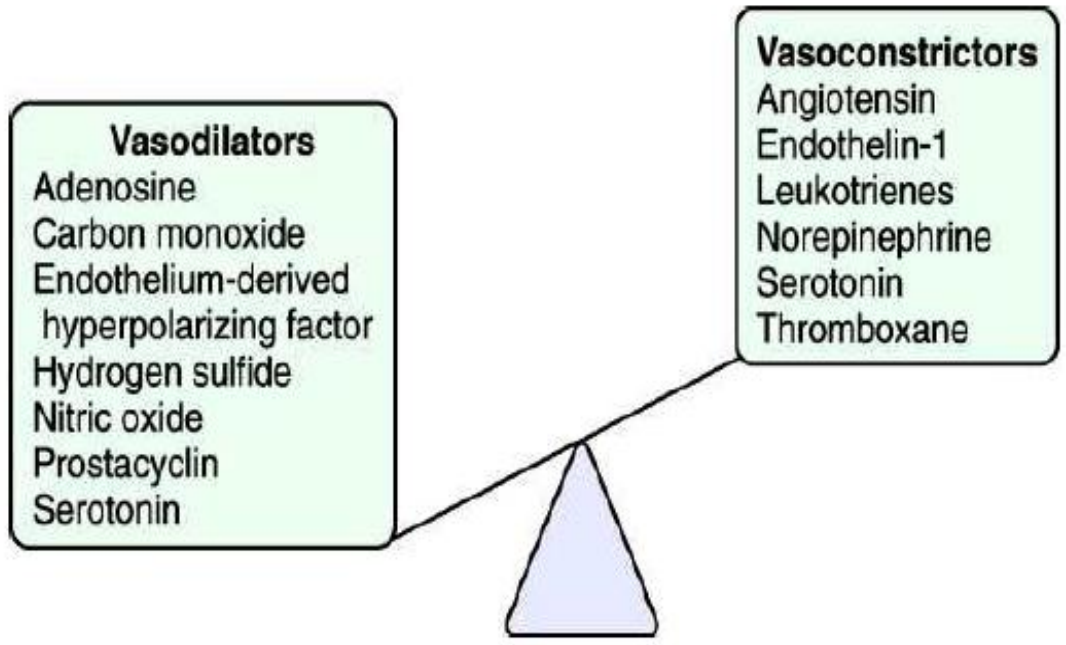


Figure 4: Representative vasodilator and vasoconstrictor molecules implicated in the vascular abnormalities in portal hypertension

PORTAL HYPERTENSION AS A HEMODYNAMIC SYNDROME

Splanchnic hemodynamics

- Increased portal vascular resistance
- Increased portal venous inflow
- Portosystemic shunting

Systemic hemodynamics

- Arterial vasodilatation
- Increased plasma volume
- Decreased systemic vascular resistance
- Increase in cardiac output
- Reduction in mean arterial pressure
- Rise in heart rate

Regional blood flows

- Increased muscle blood flow
- Decreased cerebral blood flow
- Variable renal blood flow

A sequence of events that leads to the hyperdynamic state has been proposed. Although the primary pathophysiologic event is arterial vasodilation, a hyperdynamic state would not develop unless sodium was retained by the kidney, a process mediated by the activation of compensatory mechanisms triggered by the same vasodilatation.

Plasma volume is then expanded, which triggers a further decrease in peripheral vascular resistance.

Alternations in the volume of blood flow may also induce changes in the vascular resistance of the collateral bed. A rise in flow increases vessel diameter and a 24 reduction of flow results in opposite changes, with a smaller vessel offering an increased resistance to flow. The resistance to flow of a fluid in a non-distensible vessel is related to the length of the vessel (1) and the fluid's viscosity (n) and is inversely related to the further power of the radius (r), so that minor changes in vessel diameter markedly affect resistance to flow (Poiseuille's law).

Resistance = 8nlπr4

Most pharmacologic agents used for the treatment of portal hypertensionreduce portal pressure by reducing portal blood flow. The relation between vessel radius and vessel flow that has been delineated indicates that a reduction in flow may cause a rise in vascular resistance. This is an important principle in the pharmacologic treatment of portal hypertension.

Rupture of oesophageal varices

The mechanisms for the rupture of oesophageal varices have not been fully elucidated. The "corrosion" hypothesis postulated that reflux of gastric acid injured the mucosa of the lower part of the oesophagus with subsequent erosion into the submucosal varies. However, measurements of lower sphincter pressure and pH in the lower oesophagus failed to show evidence of increased gastroesophageal reflux in patients with bleeding oesophageal varices. Attention has shifted to the "explosion" theory, in which oesophageal wall tension reaches a critical level and rupture occurs.

Wall tension in a system of artificial varices is related to the intraluminal pressure and the vessel's radius and is inversely related to its wall thickness. Laplace's law states that a vessel's radius plays a major role in wall tension, providing a physical basis for the clinical observation that large varices[24] and those at a higher pressure are more prone to bleed. Measurements of oesophageal wall thickness, the third element in this equation, cannot be made with current technology but may be of importance when they are available. A relation between variceal pressure and the risk of hemorrhage has been studied by measuring variceal pressure by means of an endoscopic capsule[25]. Patients who bled from varices had a considerably higher pressure than non bleeding patients with cirrhosis and oesophageal varices.

High portal pressures can arise from common daily activities. Elevation of portal pressure to values greater than 100mm Hg has been observed during the Valsalva maneuver. Administration of an anticholinergic can also increase variceal size. The genesis of variceal rupture may be related to daily events in which pressure rises abruptly to extremely high values[26].

Influences of Portal Hypertension on Other organs :

Hypersplenism may occur in the absence of splenomegaly. Alterations of the splenic microcirculation, with fibrotic changes in the splenic sinusoids, favour entrapment of red cells, white cells (especially polymorphonuclear leukocytes), and platelets. However, the bone marrow remains active, and infection or bleeding seldom results from leukopenia or thrombocytopenia, respectively. In the absence of other factors that affect the platelet count (alcohol, medications), thrombocytopenia, between 50,000 and 125,000 platelets/mm^3 is an indicator of portal hypertension in

cirrhosis.

Hypoxemia, with an arterial partial pressure of oxygen between 60 and 80 mm Hg, is a common finding in established portal hypertension. Administration of 100% oxygen does not correct the hypoxemia, suggesting that functional pulmonary arteriovenous shunting is the basic defect. Anatomic connections have been demonstrated on the pleural surface and termed lung "spiders". Vasodilatation of pulmonary capillaries, as part of the generalised process of systemic vasodilatation may increase the distance for oxygen diffusion between the blood and alveolus, resulting in functional shunt. The degree of hypoxemia can be severe.

Pulmonary hypertension develops in a few patients, regardless of the etiology of portal hypertension. The pathophysiology is unclear. Histologic studies do not suggest microscopic pulmonary embolism as a possibility. Rather, vasoactive substances arising from the splanchnic territory, which now by pass the liver, may induce permanent changes in the pulmonary vasculature. Serotonin, thought to be elevated in these patients, is of particular interest as it has been implicated in the pathogenesis of pulmonary hypertension associated with the carcinoid syndrome.

CLASSIFICATION OF PORTAL HYPERTENSION

A logical classification of portal hypertension is based on the site of increased resistance to portal flow. Five main groups can be delineated according to pre sinusoidal, sinusoidal, or post sinusoidal block. Pre sinusoidal and post sinusoidal portal hypertension can be further subdivided into intra-or extrahepatic causes.

Although the differential diagnosis is extensive, liver cirrhosis is the leading cause of portal hypertension in the West.

Pre sinusoidal Pre hepatic

Pre sinusoidal pre hepatic portal hypertension is most commonly due to portal vein thrombosis. A blood clot in the portal vein can have several causes; however, a definitive diagnosis cannot be made for many patients. Many of these idiopathic cases may represent an early manifestation of a myeloproliferative syndrome. When thecolony-forming units were quantitated after bone marrow culture, a diagnostic criterion for myeloproliferative syndrome, many patients with idiopathic portal hypertension met criteria for the diagnosis of this hematologic disorder.

Catheterization of the umbilical vein in newborns has been associated with the development of omphalitis with secondary portal vein thrombosis. Over the years, bridging collaterals develop toward the liver, resulting in a "cavernous" appearance of the portal vein. The prognosis is relatively good because these patients have normal liver function, variceal hemorrhage is better tolerated, and the incidence of bleeding decreases after the second decade.

Disorders of the coagulation system may present as portal vein thrombosis. These include congenital deficiencies of natural anticoagulants such as deficiency of antithrombin III, protein C, protein S, and plasminogen activator. An acquired lupus anticoagulant may also predispose patients to this thrombotic event.

Diseases of the adjacent organs may also cause portal vein thrombi. Invasion into the portal vein by carcinoma of the head of the pancreas or common bile duct

denotes inoperability; carcinomas of the pancreatic body and tail affect the splenic vein. Cirrhosis has been viewed as predisposing to portal vein thrombosis because of stasis.

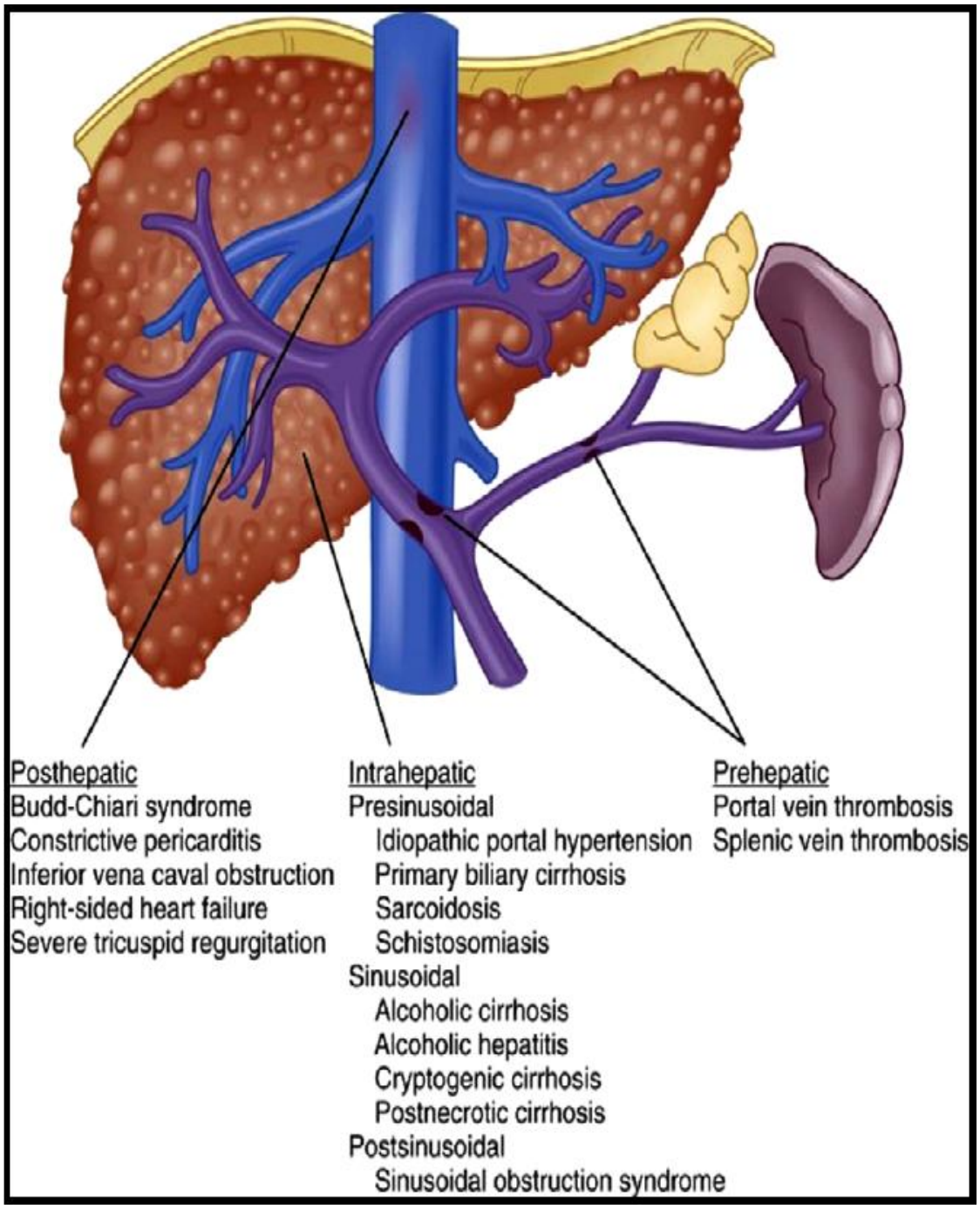


Figure 5: Classification of portal hypertension

CLASSIFICATION OF PORTAL HYPERTENSION

Pre sinusoidal portal hypertension

- **Extrahepatic**

- Portal vein thrombosis

- **Intrahepatic**

- Schistosomiasis (S.mansoni, S.japonica)
- Sarcoidosis
- Felty's syndrome
- Arsenic poisoning
- Idiopathic portal hypertension
- Congenital hepatic fibrosis
- Primary biliary cirrhosis

Sinusoidal portal hypertension

- Alcoholic cirrhosis
- Vitamin A intoxication
- Renal transplantation
- Nodular regenerative hyperplasia

Post sinusoidal portal hypertension

- **Intrahepatic**

- Veno-occulsive disease
- Senecio alkaloids
- Alcoholic hepatitis (venular sclerosis type)

➢ **Extrahepatic**

- Budd-Chiari syndrome
- Congenital web

Splenic vein thrombosis may give rise to gastric varices with hemorrhage. If the liver is normal, the gastric varices drain toward the liver through the coronary vein and esophageal varices may be absent. Chronic pancreatitis and many of the previously discerned disorders that cause portal vein thrombosis may also give rise to this segmental abnormality.

Pre sinusoidal intrahepatic

A wide range of disorders are included in this category, but portal venuleobstruction is the common link. It can occur as a result of vascular obliteration (non cirrhotic portal fibrosis) or as a result of inflammatory activity in the portal triad (early stage of primary biliary cirrhosis, lymphoma) that impinges on the portal venule system.

Schistosomiasis is the most common entity in this group. Eggs shed by theparasite into the splanchnic venous tributaries lodge in the portal vein radicles within the liver. A granulomatous, fibrotic reaction develops around the eggs of either Schistosoma mansoni or Schistosoma japonicum, obstructing portal venous flow. As a result, prominent hepatomegaly can be detected. Splenomegaly and portosystemic collaterals arise as a consequences of portal hypertension. With progression of the

disease, cirrhotic changes may develop, resulting in an additional component of sinusoidal resistance to portal flow.

Non cirrhotic portal fibrosis (idiopathic portal hypertension) is a common cause of portal hypertension in Asia. Obliteration of small portal venules is its characteristic feature and liver function is preserved. Non cirrhotic portal fibrosis can be reproduced in experimental animals by injection of inactivated Escherichia coli into the portal vein, this implies that enteric infection is a possible cause. Arsenic poisoning may also present with pre sinusoidal features.

Inflammatory infiltration of the portal triads coexists with splenomegaly in another group of disorders. Examples include Felty's syndrome, lymphoma, and sarcoidosis. Several chronic hepatic disorders have a pre sinusoidal component of portal hypertension; these include non alcoholic cirrhosis and primary biliary cirrhosis. Congenital hepatic fibrosis may appear with portal hypertension as its initial manifestation.

Sinusoidal

Sinusoidal portal hypertension is the characteristic feature of alcoholic liver disease. Hepatitis B-related cirrhosis has also been reported to involve a sinusoidal resistance site.

Peri sinusoidal fibrosis with portal hypertension can be seen with vitamin A intoxication and after renal transplantation. In the latter, azathioprine may be involved in its genesis. Endothelial damage can also be caused by other compounds with thiol groups.

Classified within this group is nodular regenerative hyperplasia. The nodules in this entity are delineated not by fibrous tissue but by collapsed liver parenchymal cells. Mainly reported in patients with rheumatoid arthritis, it has been described in a wide variety of disorders, including myeloproliferative disorders, lymphoma, macroglobulinemia, and myeloma. Occlusion of small portal venules may be the primary disorder that leads to collapse of the reticulin framework and the appearance of nodules not surrounded by fibrous tissue. Partial nodular transformation, with nodularity confined to the area of the hepatic hilum, may be a variant of this disorder.

Postsinusoidal

This can occur within or outside the liver. Most of these entities present with ascites as the main manifestation of portal hypertension.

Primary increase in Portal Venous inflow

Apart from the classification described earlier, increased portal venous inflow is a rare event that occurs with a direct communication of a splanchnic artery to the portal venous system. Examples include a traumatic arteriovenous fistula arising from the splenic artery and rupture of an aneurysm of the hepatic artery into the portal vein. Aneurysms of the splenic artery are seen in the presence of splenomegaly and portal hypertension. They arise as a consequence of increased splenic flow and are small, can be multiple, and seldom cause complications.

INVESTIGATION OF THE PORTAL HYPERTENSIVE STATE

Physical Examination

A full clinical evaluation of patients with portal hypertension should include elucidation of the cause, evaluation of hepatic function, and screening for complications. The physical examination may provide special clues to the differential diagnosis.

When patients present with variceal bleeding, cirrhosis cannot be assumed to be present and pre sinusoidal causes should be considered. However, when patients with portal hypertension also exhibit ascites, a pre sinusoidal etiology is unlikely unless severe hypoalbuminemia alters the relation between hydrostatic and oncotic pressure in the intestinal capillaries. Cirrhosis may eventually develop in schistosomiasis, and ascites may result from sinusoidal portal hypertension.

Liver size may offer clinical clues. A small liver in the presence of portalhypertension is suggestive of cirrhosis. The consistency of the liver edge can provide additional information, because a normal edge argues against a sinusoidal etiology. The detection of a hepatic bruit may suggest primary carcinoma presenting with variceal bleeding as its initial manifestation. A venous hum in the periumbilical area indicates high flow through a patent umbilical vein, excluding portal vein thrombosis as a cause.

The appearance of a common ailment such as hemorrhoids can seldom be

interpreted as an initial sign of portal hypertension. However, proctoscopic examination may reveal additional signs, such as the presence of rectal varies.

IMAGING THE PORTAL VENOUS SYSTEM[10,11,12,13]

A chest radiography may show an enlarged azygos vein appearing as a mass in the right hilar region or enlarged pulmonary arteries when pulmonary hypertension is associated with portal hypertension. Fundico antral varices may be misinterpreted as mass lesions on upper gastrointestinal radiographs.

Angiography of mesenteric vessels provides anatomic information and some functional data. Splenoportography offers the best anatomic detail but has seldom been used because of concern about splenic puncture. Small-gauge needles may be safe when optimal imaging is needed. Venous phases of arterial injections can be enhanced with subtraction techniques, giving better anatomic detail.

Ultrasound:

A large portal vein suggests portal hypertension. If collaterals are seen, this confirms portal hypertension.

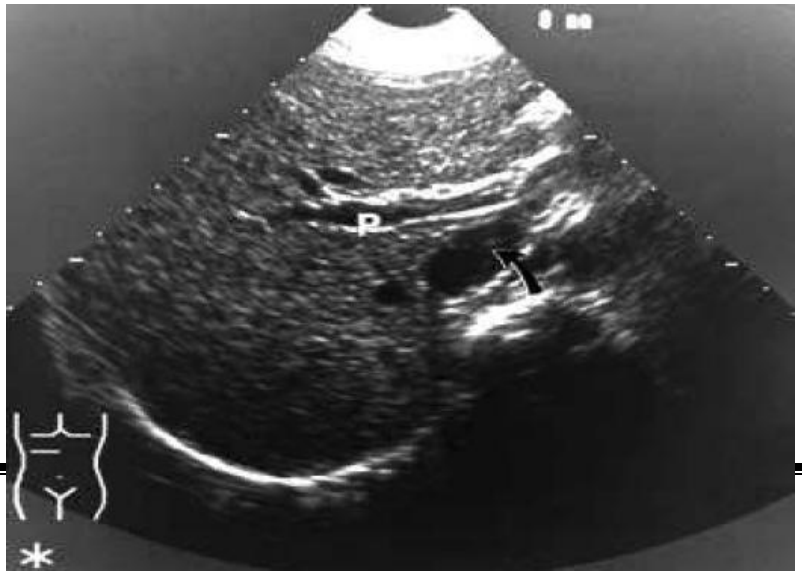


Figure 6: Transverse US shows a patent portal vein (P); the arrow indicates the inferior vena cava

Doppler ultrasound

Doppler US demonstrates the anatomy of the portal veins and hepatic artery. Doppler US shows spontaneous hepato-fugal flow in portal, splenic and superior mesenteric veins in patients with cirrhosis. Variceal bleeding is more likely if the flow is hepato-petal. Colour Doppler is a good way of demonstrating portal systemic shunts and the direction of flow in them. Duplex Doppler has-been used to measure portal blood flow. In cirrhosis, the portal vein velocity tends to fall and when less than 6 cm/s portal hypertension is likely.

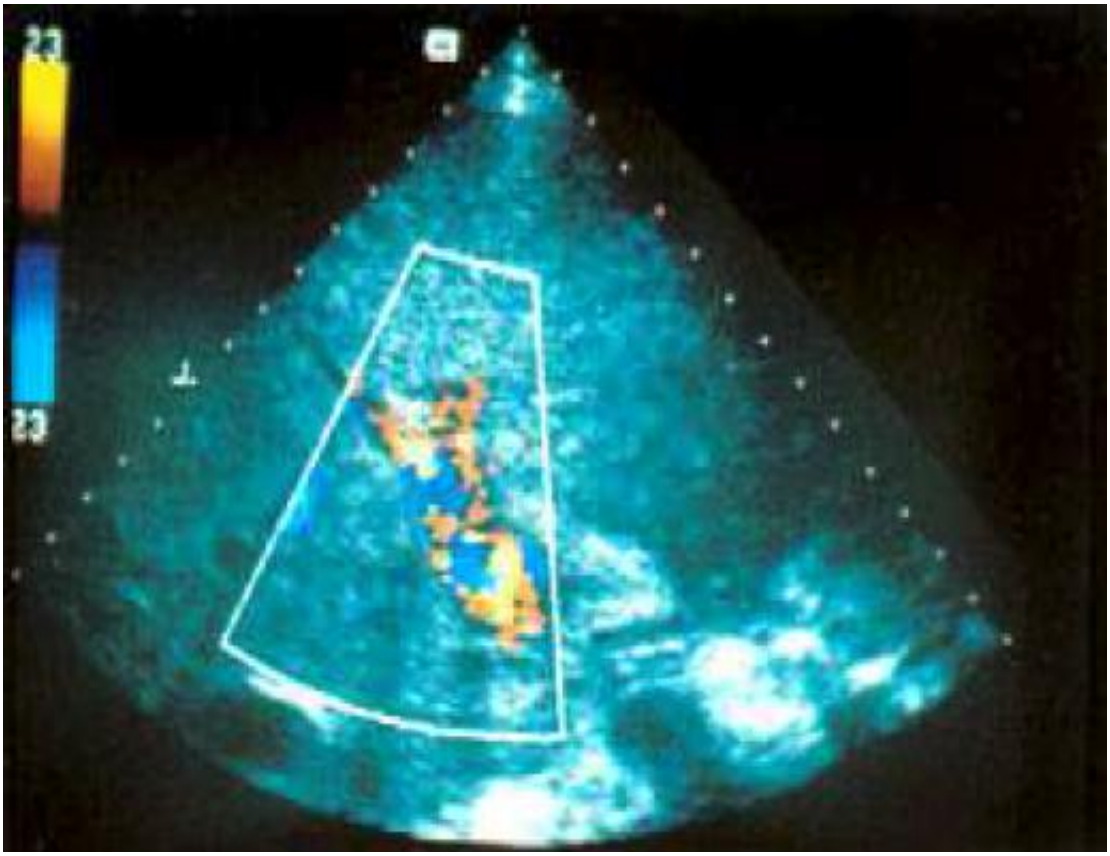


Figure 7: Colour Doppler US of the porta hepatis shows the hepatic artery in red and portal vein in blue

C.T scan

After contrast, portal vein patency can be established and esophageal varices may be shown as intraluminal protrusions enhancing after contrast. Gastric varices show as rounded structures, indistinguishable from the gastric wall. In cirrhosis, the venogram varies widely. It may be completely normal or may show filling of large numbers of collateral vessels with gross distortion of the intra-hepatic pattern ('tree in winter appearance).

MEASUREMENT OF PORTAL PRESSURE

Direct measurements of portal venous pressure can be obtained by directpuncture of portal tributaries or of venules within the liver. Splenic pulp pressure, measured at the time of splenoportography, may accurately reflect portal venous pressure but is associated with risk of hemorrhage from the puncture site.

Catheterization of the umbilical vein, has been re-evaluated with use of the Doppler technique. Percutaneous trans hepatic measurements of portal pressure can be obtained at the time of portography. Direct measurements in portal tributaries can also be made at the time of surgery.

All these techniques require an additional measurement of hepatic venous pressure to evaluate the pressure gradient across the liver. Also, organ puncture can occur in patients with liver disease and coagulopathy. The alternative is to approach the liver by way of the hepatic vein. During hepatic venous catheterization, the catheter is maximally advanced and the vein occluded so that a sinusoidal pattern can be seen during injection of dye. Value at this point reflect hepatic venous wedge pressure under normal conditions. Withdrawal of the catheter into the hepatic vein. allows estimation of hepatic venous free pressure. Use of the balloon catheter allows measurements of free and wedge pressure from one position in the hepatic vein.

When the etiology of portal hypertension is unclear, pressure measured by hepatic venous catheterization can provide useful clinical information. A low hepatic venous pressure gradient in the presence of oesophageal varices, strongly argues for a pre sinusoidal etiology. This is the hemodynamic pattern in early hepatic schistosomiasis. A high pressure gradient confirms the presence of parenchymal liver disease, but diagnosing its etiology requires additional testing. Percutaneous

transhepatic measurements are useful in the diagnosis of the Budd - Chiari syndrome.

Measurements of pressure are important when therapeutic measures are planned. During surgery to relieve portal hypertension, evidence of adequate decompression is provided by intraoperative pressure measurements. The success of transjugular intrahepatic portosystemic shunt (TIPSS), a nonsurgical technique in which a metallic stent is placed between the portal and hepatic veins, can be measured by the reduction of portal pressure. When considering pharmacologic therapy with beta - adrenergic blockers, reduction of the portal venous pressure gradient to critical levels decreases the occurrence of gastrointestinal hemorrhage.

MEASUREMENT OF BLOOD FLOW

Portal Venous Flow

Measurement of portal blood flow had been considered inaccessible in the nonsurgical setting, but the use of Doppler flowmetry has allowed estimation of portal flow. With this technique, portal mean velocity is measured with the Doppler signal in the middle of the vessel. Flow is obtained by multiplying an estimate of the crosssectional area of the portal vein (from the ultrasonographic image) by the calculated mean velocity. The technique can also be used for measurement of arterial inflow, which permits estimation of arteriolar resistance. Doppler flowmetry has also been used to assess the effects on portal hypertension of histologic events, such as feeding, and the responses to pharmacologic agents. A diminished response of portal vessels to respiration may signal a critical reduction in compliance.

Numerous technical problems may interfere with the accuracy of

Dopplermeasurements. These include body habitus, the extent of collateralization (Portal vein flow may be markedly decreased with high collateral flow), and respiratory variations. Intra and inter observer variability in measurements of flow and velocity is considerable. Doppler flowmetry is best suited for comparison within the same subject rather than between groups. Nonetheless, its non invasive nature is attractive.

ENDOSCOPIC SCREENING FOR OESOPHAGEAL VARICES

Endoscopic grading of varices-paqet

Grade I : Small varices without luminal prolapse.

Grade II : Moderate-sized varices showing luminal prolapse with minimal

obscuring of the gastro-oesophageal junction.

Grade III : Large varices showing luminal prolapse obscuring

the gastro oesophageal junction.

A major cause of death in patients with cirrhosis is gastrointestinal

hemorrhage, most often as a result of the portal hypertensive state[27]. The 1- year

bleeding rate of unselected patients with cirrhosis, without a history of hemorrhage, ranges from 6% to 76% and depends on endoscopic features as well as the degree of hepatic decompensation[28]. Mortality for the first variceal hemorrhage ranges from 10% to 65%[29,30] the majority of deaths occur within the first 6 weeks after the

bleeding episode[31]. After variceal bleeding has occurred, life expectancy is dramatically reduced, with a 1 - year survival of 22% to 60%. Patients who die within the first 2 years of their index hemorrhage tend to succumb to variceal bleeding and liver failure; those who survive beyond this period die of other complications.

The prevalence of oesophageal varices on a single endoscopic examination in unselected cirrhotic patients ranges widely. Data on the relation of the presence of varices and variceal size to the degree of liver injury, as measured by the Child- Pugh score, are conflicting. In some cross - sectional studies using the Cox regression analysis, a high Childs, score was predictive of large varices[32].

In others, no direct correlation was found. Varices may be present in patients with Child's A cirrhosis and absent in those classified with Child's C disease. On this basis, all patients with a diagnosis of cirrhosis should be evaluated by upper endoscopy. In one study of patients without varices on an initial examination, 31% and 70% had varices on subsequent examinations at 1 and 2 years, respectively[33].

The Japanese Research Society for Portal Hypertension has proposed general rules for recording endoscopic findings of oesophageal varices. In a retrospective analysis, these guidelines were used to establish endoscopic criteria to assess the risk of the first episode of hemorrhage[34]. Those criteria proposed as predictive of variceal bleeding included a serpiginous form, red colour markings, and a fundamental blue colour, while esophagitis was not predictive. Prospective studies have confirmed the discriminant function of size and red colour signs in predicting the first variceal hemorrhage[35,36]. Although grading systems for estimation of variceal size differ and have not been completely standardized, an endoscopic evaluation should include assessment of diameter percentage lumen occupancy, and a straight or serpiginous

form.

Large, serpiginous varices bleed commonly than small, straight vessels; still, varices of any size may rupture. Most studies show no relation of variceal size to intravariceal pressure as determined by needle puncture or the wedged hepatic - inferior vena cava pressure gradient. The size of varices may wax and wane on serial endoscopic studies. Spontaneous regression in size occurs with improvement of the underlying liver injury. If small varices are seen on initial examination, yearly evaluation should be performed. Every 2 years evaluation may be adequate for those without varices on the initial evaluation.

Red colour markings include cherry red spots, red wale markings, and hematocystic spots. These represent dilated intraepithelial and subepithelial venous channels on the surface, of and in communication with, the deeper submucosal variceal veins. Red spots correlate with variceal size and are found on 21%, 42%, and 80% of small, medium, and large varices, respectively. The presence of red colour signs is not related to Child score. High variceal pressures, however, may be important in their development and they may be markers for the presence of higher portal pressures. Mean intravariceal pressure determined by needle puncture is 40% higher in patients with red colour signs. The risk of bleeding is increased 2-fold in the presence of red colour signs. The independence of red colour signs and variceal size, however has been disputed[37.]

The importance of these endoscopic findings is highlighted by the increasing consideration of prophylactic therapy to prevent variceal hemorrhage. If the prediction of hemorrhage is accurate, prophylactic therapy could be reserved for patients who are at risk of bleeding.

VARICEAL BLEEDING

It is one of the most dangerous complications of portal hypertension. Variceal bleeding occurs from oesophageal varices that are usually located within 3-5 cm of the oesophagogastric junction or from gastric varices. The size of the varices, endoscopic variceal features such as red spots and red stripes, high portal pressure and liver failure are all general factors that predispose to bleeding. Drugs capable of causing mucosal erosion, such as salicylate and other non – steroidal anti - inflammatory drugs (NSAIDs), can also precipitate bleeding. Variceal bleeding is often severe, and recurrent bleeding occurs if preventive treatment is not given. Bleeding from varices at other sites is comparatively uncommon but most often occurs from varices in the rectum or intestinal stomas.

Predicting rupture[12]

Sixty five per cent of cirrhotic patients with varices will not bleed within 2 years of diagnosis, but 50% will die of the first hemorrhage. There is a strong correlation between variceal size assessed endoscopically, and the probability of bleeding. Intravariceal pressure is less important, although a portal pressure above 12 mmHg appears necessary for varices to form and subsequently bleed. 'Red spots', danger signs seen at endoscopy, are valuable indictors of imminent hemorrhage. Child's grade is used to assess hepato-cellular function. It is the most important predictor of the likelihood of bleeding. It correlates with variceal size, with the presence of endoscopic red signs and with the response to treatment. These three variables - size, presence of red signs and hepatocellular function-are the best predictors of bleeding. Patients with alcoholic cirrhosis may be at the most risk.

Doppler sonography predicts the likelihood of bleeding. This is based on velocity and diameter of the portal vein, spleen size and the presence of collaterals.

Prevention of bleeding

Liver function must be improved, for instance, by abstaining from alcohol. Aspirin and NSAIDs should be avoided. Propranolol is a nonselective β-blocker, which reduces portal pressure by splanchnic vasoconstriction and, to a lesser extent, by reducing cardiac output. The drug is given in a dose, which reduces the resting pulse rate by 25% 12h after intake. The portal pressure must be maintained at 12mm Hg or lower. Propranolol is recommended for those with large varices and with red endoscopic danger signs. Patients with an HVPG greater than 12mmHg should be treated whatever the size of the varices. Nadolol gives equivalent results. Isosorbide-5 mononitrate is equally effective in prophylaxis of the first bleed, but the probability of death is significantly greater, particularly in those more than 50 years old. The addition of nitrate to β-blocker should be reserved for those failing therapy with the β-blocker alone. Variceal sclerotherapy or ligation is not as satisfactory or cost effective as vaso-active active drugs.

Diagnosis of bleeding

The clinical features are those of gastro intestinal bleeding with the added picture of portal hypertension. Endoscopy is performed routinely to confirm the source of the bleeding.

Prognosis[12]

Between 30 and 50% will die within 6 weeks of the first bleed. The prognosis

is determined by the severity of the hepatocellular disease. The ominous triad of jaundice, ascites and encephalopathy is associated with 80% mortality. The 1-year survival in good-risk (Child grade A and B) patients is about 85% and in bad – risk (Child grade C) patients about 30%. Alcoholics have a worse prognosis, as hepatocellular disease is greater.

Management of acute variceal bleeding

The priority in acute bleeding from oesophageal varices is to restore the circulation with blood and plasma, not least because shock reduces liver blood flow and causes further deterioration of liver function. Even in patients with known varices, the source of bleeding should always be confirmed by endoscopy because about, 20% of such patients are found to be bleeding from some other lesion, especially acute gastric erosions.

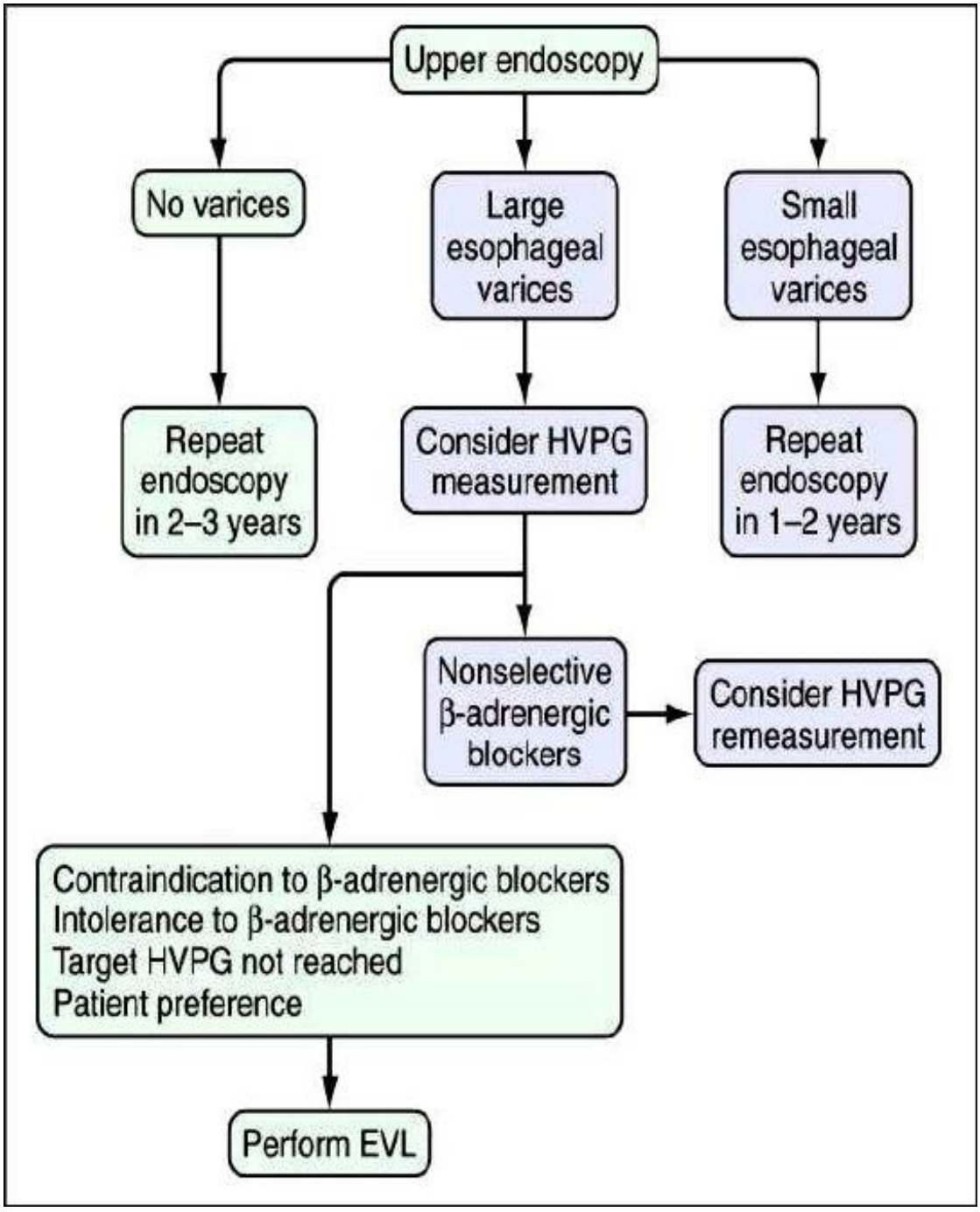


Figure 8: Algorithm for primary prophylaxis of esophageal variceal hemorrhage. EVL-Endoscopic variceal ligation

ASCITES

Ascites refers to the accumulation of free fluid in the peritoneal cavity and is a

complication of portal hypertension.

ASCITIC FLUID ANALYSIS

Abdominal paracentesis with ascitic fluid analysis is the most rapid and cost effective method of determining the cause of ascites. Under aseptic precautions, a standard 1.5 inches needle (22 gauge) is inserted below the percussed air-fluid interface and about (50-100ml) fluid is aspirated for analysis. The fluid is analysed for protein, content, sugar, cell count, cytology, gram's stain and culture.

SERUM ASCITES-ALBUMIN GRADIENT (SAAG)

Ascitic fluid protein concentration is almost entirely dependent on serum protein concentration (direct relationship) and portal pressure (inverse relationship).

It is physiologically based on oncotic hydrostatic balance. Portal hypertension results in an abnormally high hydrostatic pressure gradient between the portal bed and ascitic fluid. Albumin exerts more oncotic force per unit weight than other proteins. The difference between serum and ascitic fluid albumin concentration correlates directly with portal pressure[38]. The SAAG is superior to the exudate-transudate concept in the differential diagnosis of ascites[39].

Calculating the SAAG involves measuring the serum albumin concentration and ascitic fluid albumin concentration and subtracting the ascetic fluid from the serum value. The serum values should always be greater. SAAG is not a ratio. If the SAAG is > 1.1 g/dL, the person has portal hypertension with more than 95% accuracy. Conversely if the SAAG <1.1 g/dL, the patient does not have portal

hypertension with more than 95% accuracy. This test is accurate despite ascitic fluid infection, diuresis, therapeutic paracentesis, albumin infusion and etiology of liver disease.

COAGULATION ABNORMALITIES IN CIRRHOSIS

A variety of hemostatic disorders have been described in cirrhotic patients. In general, these can be categorized into abnormalities of platelet number or function, increased fibrinolysis, or deficient synthesis of clotting factors. Cirrhosis is associated with both quantitative and qualitative platelet abnormalities. Approximately 40% of cirrhotic patients have abnormal prolongation of the bleeding time to values of more than 10 minutes and platelet counts less than 100,000/mm^3[40] . The severity of the thrombocytopenia increases with the Child - Pugh classification. This decrease in the number of circulating platelets is related in part to platelet pooling in the spleen caused by portal hypertension and splenomegaly, in part to immunologic destruction of platelets[41], and based on recent studies, in part to diminished hepatic production of thrombopoietin.[42.]

Several studies have confirmed the presence of platelet – associated IgG in cirrhosis, and immunoglobulin levels increase in proportion to the severity of the liver disease[43]. This is a particular concern in hepatitis C, in which platelet - associated IgG is increased and thrombocytopenia is observed in 41% of patients (as compared with 19% of hepatitis B patients). Hepatitis C may also have direct effects because viral RNA can be detected in circulating platelets. Finally diminished platelet production may play a role in addition to increased platelet sequestration or destruction. Specifically, circulating levels of thrombopoietin, a peptide hormone produced

primarily in the liver that stimulates platelet production, are decreased in some patients with cirrhosis and thrombocytopenia.

Cirrhosis is also associated with functional abnormalities when circulating platelet are not activated in a normal manner, resulting in defective clot formation[44]. The decrease in platelet aggregation, as measured by the restitution test, may be related to decreases in glycoprotein Ib levels in the platelet membrane[45]or to defective signal transduction within the platelet. Patients with bleeding times longer than 7 minutes or a clinical history of bleeding have the lowest glycoprotein Ib levels.

Causes of abnormal hematological indices in cirrhosis[62]

1. Portal hypertension-induced splenic sequestration

2. Alterations in erythropoietin

3. Bone marrow suppression mediated by toxins (eg, alcohol, hepatitis B and C)

4. Increased blood loss (eg, hemorrhage, hemolysis)

Causes of thrombocytopenia in cirrhosis[62]

1. Portal hypertension-induced splenic sequestration

2. Alterations in thrombopoietin

3. Bone marrow suppression mediated by toxins (eg, alcohol, hepatitis B and C)

4. Consumptive coaguloapathy (eg, low-grade disseminated intravascular coagulation, acquired intravascular coagulation and fibrinolysis)

5. Increased blood loss (eg, hemorrhage)

Causes of leucopenia in cirrhosis[62]

1. Portal hypertension-induced splenic and splanchnic sequestration

2. Alterations in granulocyte-colony stimulating factor and granulocyte macrophagecolony stimulating factor.

3. Bone marrow suppression mediated by toxins (eg, alcohol, hepatitis B and C)

Diagnosis

Low platelet counts are commonly associated with physical manifestations of portal hypertension, including ascites and splenomegaly. In general, platelet counts above 70,000/ mm are well tolerated and do not cause prolongation of the bleeding time unless there are associated qualitative platelet abnormalities. Other causes of thrombocytopenia, including diminished production, interferon or other medications, or decreased thrombopoietin)[42], must be excluded by history and bone marrow examination when necessary. Splenic sequestration is most often a diagnosis of exclusion, but increased platelet trapping can be visualized directly using indium tropolone - 111 labeled platelet when uncertainty exists. Platelet associated IgG levels (antiplatelet antibodies) should be measured in most patients, especially those with hepatitis C and autoimmune hepatitis, to assess the possible contribution of immune – mediated platelet destruction. Prolongation of the bleeding can also reflect impaired platelet function. When necessary formal studies of platelet aggregation induced by restitution or other measurements can be performed.

Management

In thrombocytopenia related to portal hypertension and splenic sequestration, there has been limited clinical experience with splenic embolization, aiming to achieve a 40% to 60% reduction in splenic blood flow. Although there is some short - term morbidity with this procedure, it can prolong platelet survival time and decrease the spleen / liver uptake ratio of platelet uptake. In addition, splenic embolization decreases platelet - associated IgG levels, suggesting that the improvement in platelet counts is due not only to effects on splenic pooling but also to immunologic mechanisms.

Transjugular intrahepatic portosystemic shunts represent an attractive approach to treatment of splenic platelet sequestration by lowering portal pressures. However, clinical series are limited in number and do not yet allow definitive conclusions. In a retrospective analysis of 21 patients, there was a significant rise in platelet counts after shunt placement in patients with a post shunt portal pressure gradient less than 12 mm Hg. However, in a larger prospective series, this procedure has no beneficial effect on thrombocytopenia. Thus, transjugular intrahepatic portosystemic shunt cannot be advocated as a treatment for thrombocytopenia.

In view of association between platelet count, spleen size, presence of ascites, child pugh's score etc in patients with cirrhosis with portal hypertension, we tried to correlate the non invasive parameters with endoscopic finding in portal hypertension in an effort to non invasively predict chances of bleed from varices in patients with cirrhosis of the liver.

SPLENOMEGALY

According to study by Chalasani et al. (1999)[56] splenomegaly and low platelet

count were independent predictors of large esophageal varices. On the basis of these variables, cirrhotics were stratified into high risk groups for the presence of large esophageal varices. Patients with platelet count of ≥ 88,000/cu mm and no splenomegaly by physical examination had a risk of large esophageal varices of 7.2%. Those with splenomegaly or platelet count < 88,000/cu mm had a risk of large esophageal varices. Their data showed that clinical predictors could be used to stratify cirrhotic patients for the risk of rupture of large esophageal varices and such stratification could be used to improve the cost effectiveness of screening endoscopy.

Torres et al (1996)[63] investigated the association and correlation betweenultrasonographic parameters of portal hypertension and the presence and level of portal hypertension (determinate by the serum-to-ascites albumin concentration gradient). They demonstrated that ultrasonographic splenomegaly studied by longitudinal diameter of the spleen discriminate patients with portal hypertension with a high positive predictive value (94.4%), although it didn't happen with transverse diameter of the spleen.[63]

NON INVASIVE -PARAMETERS FOR PREDICTION OF ESOPHAGEAL VARICES

Studies have attempted to identify characteristics that non-invasively predictthe presence of any esophageal varices or of large esophagealvarices[50,51,52,53,54,55,56,57,58,59,60,61]These studies have shown that biochemical, clinical,and ultrasonographic parameters alone or together have good predictive power for non-invasively assessing the presence of esophageal varices. Overall, the most common result of these studies was that parameters directly or indirectly linked toportal hypertension, such as splenomegaly and decreased platelet count, werepredictors of the presence of esophageal varices.

In a study by Thomopolos et al (2003)[46] seventeen variables consideredrelevant to the presence of esophageal varices were tested and they came to theconclusion that Thrombocytopenia, splenomegaly and ascites are independentpredictors of large esophageal varices in cirrhotic patients.

Sharma SK et al[49] in a prospective study included newly diagnosed patients with cirrhosis and no history of gastrointestinal bleeding were scheduled to undergo UGIE.

Of the 101 patients (median age 45; range 15-74 years; 87 male; Child-Pugh class: A 18, B 31, C 52), 46 had LEV. On univariate analysis, five variables were significantly associated with the presence of LEV. These included pallor ($P = 0.026$), palpable spleen ($P = 0.009$), platelet count ($P < 0.002$), total leukocyte count ($P < 0.0004$) and liver span on ultrasound ($P = 0.031$). On multivariate analysis, two of these parameters, namely low platelet count and presence of palpable spleen, were found to be independent predictors of the presence of LEV. They concluded that presence of palpable spleen and low platelet count are independent predictors of presence of LEV in patients with cirrhosis. Use of these parameters may help identify

patients with a low probability of LEV who may not need UGIE. This may help reduce costs and discomfort for these patients and the burden on endoscopy units.[49]

Zaman A et al[47] studied ninety-eight patients without a history of variceal hemorrhage underwent esophagogastroduodenoscopy as part of a liver ransplant evaluation. The causes of cirrhosis among the 67 men and 31 women (mean age, 48 yr) included 28% Hepatitis C/alcoholism, 25% Hepatitis C, 13% alcoholism, 9% primary sclerosing cholangitis/primary biliary cirrhosis, 9% cryptogenic, 6% Hepatitis B, 1% Hepatitis B and C, and 9% other. Patients were Child-Pugh class A 34%, B 51%, and C 15%. Endoscopic findings included esophageal varices in 68% of patients (30% were large), gastric varices in 15%, and portal hypertensive gastropathy in 58%. Platelet count <88,000 was the only parameter identified by univariate/multivariate analysis ($p < 0.05$) as associated with the presence of large esophageal varices (odds 55 ratio 5.5; 95% confidence interval 1.8-20.6) or gastric varices (odds ratio 5; 95%confidence interval 1.4-23). Platelet count <88,000 is associated with the presence of esophago-gastric varices. A large prospective study is needed to verify and validate these findings and may allow identification of a group of patients who would most benefit from endoscopic screening for varices.

RELEVANCE OF PLATELET COUNT/SPLENIC DIAMETER RATIO

Gianni et al (2003)[54] proposed platelet count/ splenic diameter ratio as a non invasive marker for predicting esophageal varices in patients with liver cirrhosis. Parameters directly or indirectly linked to portal hypertension, such as splenomegaly and decreased platelet count, were predictors of the presence of esophageal varices. However, in patients with chronic liver disease the presence of decreased platelet count may depend on several factors other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses. On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension. With this in mind, the study used the platelet count/spleen diameter ratio as a parameter linking thrombocytopenia to spleen size in order to introduce a variable that takes into consideration the decrease in platelet count which most likely depends on hypersplenism caused by portal hypertension.

In the study by Gianni et al. Maximum spleen bipolar diameter was estimated by means of ultrasound scan and was expressed in millimetres (mm). Platelet count/spleen diameter ratio of all patients was calculated. They found that Spleen diameter was higher while platelet count/spleen diameter ratio was lower in patients with esophageal varices. Receiver operating characteristic curve (ROC curves) were 56 used to assess the platelet count/spleen diameter ratio cut off with the best sensitivity and specificity for a diagnosis of esophageal varices (cut off=909, sensitivity=100% (95% CI 100–100); specificity=93% (95% CI 82–98)). The prevalence adjusted positive and negative predictive values for a platelet count/spleen diameter ratio 909 were 96% and 100%, respectively. Moreover, accuracy of this platelet count/spleen diameter ratio cut off as evaluated by the c index was 0.981 (95% CI 0.943– 0.996). Both spleen diameter and platelet count cut offs with the best

sensitivity and specificity for a diagnosis of esophageal varices that were identified by means of ROC curves had prevalence adjusted positive and negative predictive values and accuracies that were lower than those of the platelet count/spleen diameter ratio.

Gianni et al (2003)[54] report that the use of this ratio is of interest and is not redundant, and this hypothesis is supported by a number of both clinical and statistical reasons. Firstly, from a clinical point of view, platelet count may decrease for several reasons in patients with chronic liver disease. Thus the use of platelet count alone as a non-invasive predictor of esophageal varices can be misleading and cannot be solely attributed to portal hypertension. Indeed, the use of the platelet count/spleen diameter ratio bypasses this possible drawback since it "normalizes" platelet count to splenic sequestration, most likely representing the aliquot of thrombocytopenia caused by portal hypertension. Secondly, from a statistical point of view, the platelet count/spleen diameter ratio was the only parameter independently associated with the presence of esophageal varices that was selected by a multivariate analysis which also included the single parameters. The study showed that the use of the platelet count/spleen diameter ratio would have avoided performing unnecessary endoscopies in all patients with a cut off >909 without running the risk of not diagnosing esophageal varices. As far as cost benefit analysis is concerned, applying the "platelet count/spleen diameter ratio strategy" would lower the cost of esophageal varices screening in patients with cirrhosis.

According to Giannini et al (2005)[64] after initial endoscopy, the 106 cirrhotic patients without oesophageal varices who participated in their previous study were followed-up with annual or biannual surveillance endoscopy. Patients were censored at the time of diagnosis of oesophageal varices or at their last visit, and at that time

platelet count and spleen diameter were recorded. Sixty-eight patients made up the study cohort after excluding patients who were lost to follow-up or died before undergoing control endoscopy. During the follow-up, 27 patients (40%) developed oesophageal varices. Patients with higher baseline platelet count/spleen diameter ratios ($p < 0.0001$) as well as a ratio above 909 were less likely to develop oesophageal varices ($p < 0.0005$). At follow-up, a platelet count/spleen diameter ratio ≤909 had 100% negative predictive value and 84% efficiency in identifying the presence of oesophageal varices. The use of the platelet count/spleen diameter ratio proved to be an effective means for ruling out the presence of oesophageal varices even in the longitudinal follow-up of patients.

WW Baig et al[65] in their study of 150 patients of cirrhosis evaluated laboratory and ultrasonographic variables prospectively. Only stable patients were included in the study. Patients with active gastrointestinal bleeding at the time of admission were excluded. All patients underwent screening upper gastrointestinal endoscopy. The platelet count, spleen diameter and platelet count to spleen diameter ratio in patients with EVs were significantly different from patients without EVs. The platelet count to spleen diameter ratio had the highest accuracy among the three parameters. By applying receiver operating characteristic curves, a platelet count to spleen diameter ratio cut-off value of 1014 was obtained, which gave positive and negative predictive values of 95.4% and 95.1%, respectively. The accuracy of this cut-off value as evaluated by applying receiver operating characteristic curves was 0.942 (95% CI 0.890 to 0.995).

Barrera et al[66] in their prospective study of adult cirrhotic patients without previous variceal bleeding were included. Platelet count/spleen diameter ratio was

biochemical variables with HREV on upper GI endoscopy were tested using univariate and multivariate analysis. 67 patients were included. The prevalence of HREV was 50%. Age and PC/SD ratio were parameters independently associated with HREV in multivariate analysis. The PC/SD ratio cut off value of 830.8 predicted HREV with 76.9% sensitivity, 74.2% specificity and 77.8% negative predictive value. They concluded that PC/SD ratio was significantly associated with HREV but with suboptimal sensitivity and specificity. Therefore results of this study do not support routine use of PC/SD ratio for screening of HREV.

Elliot Schwarzenberger et al[67] conducted a retrospective analysis of 137patients with cirrhosis over the age of 18 that underwent screening endoscopy for varices between January 2003 and October 2005. The data collected were age, sex, etiology of cirrhosis, spleen diameter, prothrombin time/ international normalized ratio, total bilirubin, platelet count, albumin, Child-Pugh score, and endoscopic findings. There were 137 patients with 87 (63.5%) men and a mean age of 56 years. Seventy-six (55%) patients had esophageal varices. The mean age, sex, and etiology of cirrhosis were similar between those with and without varices. Using a platelet count/spleen diameter ratio with a cut-off value of 909, a negative predictive value of only 73% and a positive predictive value of 74% was obtained. They concluded that the platelet count/spleen diameter ratio with a cut-off value of 909 may not be sufficiently accurate in predicting the presence of esophageal varices. Upper endoscopy remains the method of choice to screen for the presence of varices.[67]

Abu El Makarem MA et al[68] prospectively studied laboratory and ultrasonographic and imaging variables in 175 egyptian patients with liver cirrhosis.

The platelet count/ bipolar spleen diameter ratio in patients with EVs was significantly lower than in patients without EVs. In an analysis of the receiver operating characteristic curves (ROCs), they calculated an optimal cut off value of 939.7 for this ratio, which gave 100% sensitivity and negative predictive values,86.3% specificity, a 95.6% positive predictive value, and an area under the ROC curve of 0.94 ± 0.02, reflecting its overall diagnostic accuracy.

The platelet count/ bipolar spleen diameter ratio has excellent accuracy in the non invasive assessment of EVs in patients with compensated or decompensated liver cirrhosis. It is easy to calculate and can lower the financial and sanitary burdens of endoscopy units, especially in developing countries like India.

METHODOLOGY

The present study was conducted in the department of General Medicine at KLES Dr Prabhakar Kore Hospital and Medical Research Centre Belagavi from January 2015 to December 2015.

STUDY DESIGN

The study design was a One year Observational study

STUDY PERIOD

The present study was carried out from January 2015 to December 2015

SOURCE OF DATA

All patients admitted with cirrhosis of liver with various aetiology in department of General Medicine.

SAMPLE SIZE

A total of 70 patient with cirrhosis of liver were included in the study

SAMPLINIG PROCEDURE

Based on this formula a sample size of 70 patients was considered

Sample size : 70

Sample size calculation:

- $n = 4za^2pq/d^2$
- n - sample size
- 91% Sensitivity
- 3% Error

- 54% Prevelance
- where 4za - 1.96(constant) , p - sensitivity(91)- as from previous studies,q(100-p)
- d - absolute error

INCLUSION CRITERIA

- Patients with cirrhosis of liver without any past history of upper gastrointestinal bleed will be included in the study.
- Diagnosis of cirrhosis based on a combination of history, clinical findings, impaired liver function tests, deranged clotting profile and abdominal ultrasound.

EXCLUSION CRITERIA

1.Patients with present or previous history of variceal bleed.

2.Patients on previous/current treatment with Beta blockers, Diuretics (or) anti platelet drugs.

3.Patients who have undergone sclerosis (or) band ligation of esophageal varices, TIPSS (or) surgery for portal hypertension.

4.Patients with history of fever in the past and who are on drugs knowing to cause thrombocytopenia will be excluded.

5.Patients with asplenia / splenectomy and partial splenectomy.

ETHICAL CLEARENCE

Prior to the beginning, the study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College Belagavi.

INFORMRED CONSENT

The patients who fulfilled the selection criteria were informed about the nature of study and a written informed consent was obtained (annexure-1)

DATA COLLECTION

Patients were interviewed and demographic data, history of present illness, other co-morbid conditions, personal history were obtained. Further these patients underwent clinical examination followed by systemic examination. These findings were noted on a predesigned and pretested proforma (annexure-2)

INVESTIGATIONS CARRIED OUT

1. Complete Hemogram :

a) Platelet count

2. Liver function tests.

5. Ultrasound Abdomen / CT Abdomen

6. Upper Gastrointestinal Endoscopy (Taken as gold standard)

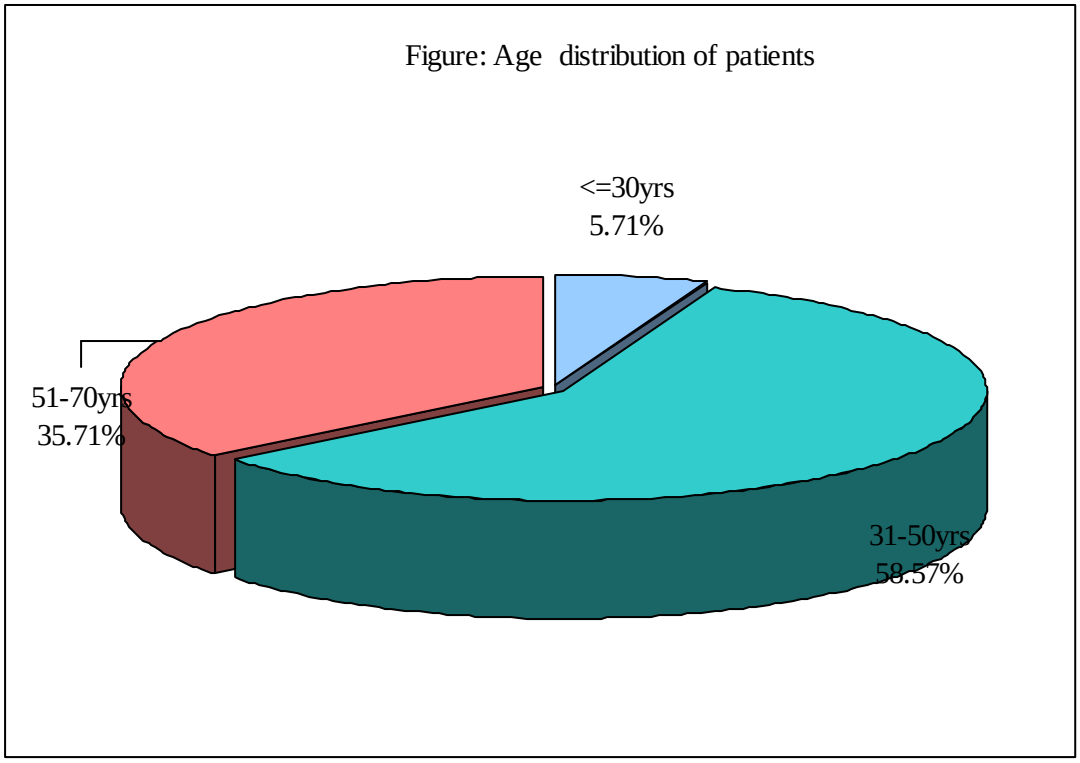
STATISTICAL METHODS

The data obtained was entered into the Microsoft excel spreadsheet (annexure-3). The categorial data was expressed in terms of rates, ratios and percentages and comparison was done using chi-square test. The continuous data was expressed as mean +- standard deviation and comparison was done using independent 't' test. A Probability value (p- value) of less than or equal to 0.05 was considered as statistically significant.

Table 1 : Age distribution :

Gender	No of patients	% of patients
<=30yrs	4	5.71
31-50yrs	41	58.57
51-70yrs	25	35.71
Total	70	100.00
Mean age	47.09	
SD age	10.41	

Figure: Age distribution of patients

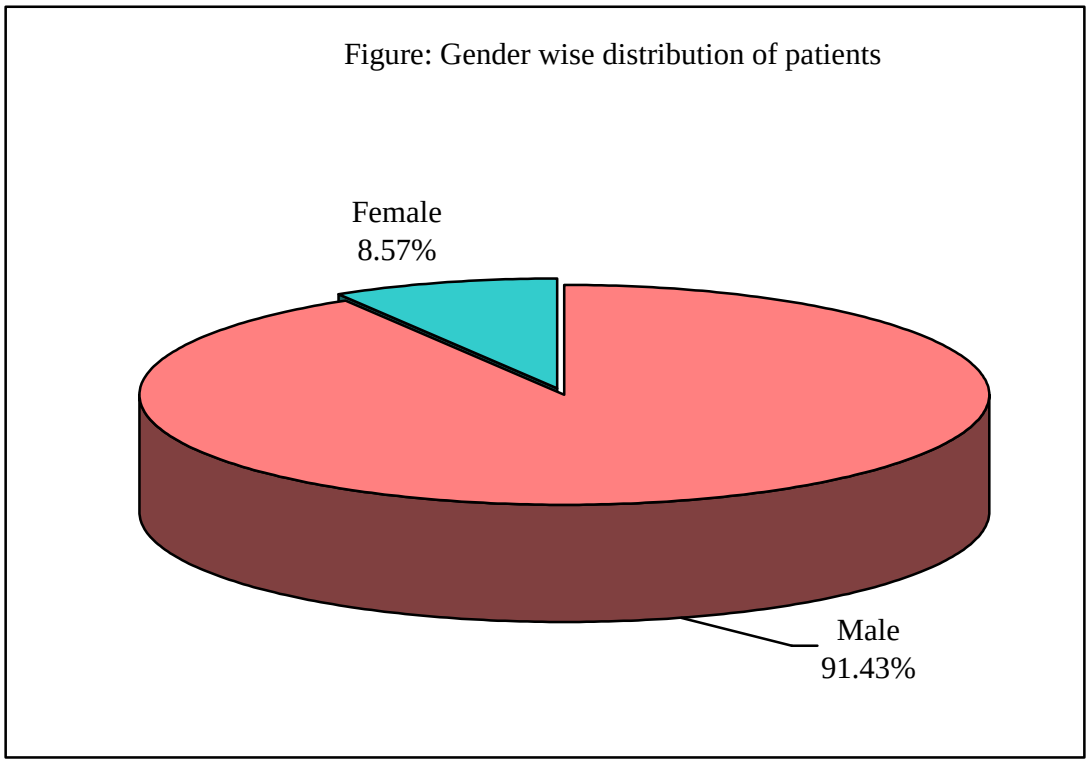


In our study population, Patient's age range from 26 to 70 years. Maximum number of patients were in age group of 31-50 years (58.57%), followed by 51-70 years (35.74%).

Table 2: Sex distribution

Gender	No of patients	% of patients
Male	64	91.43
Female	6	8.57
Total	70	100.00

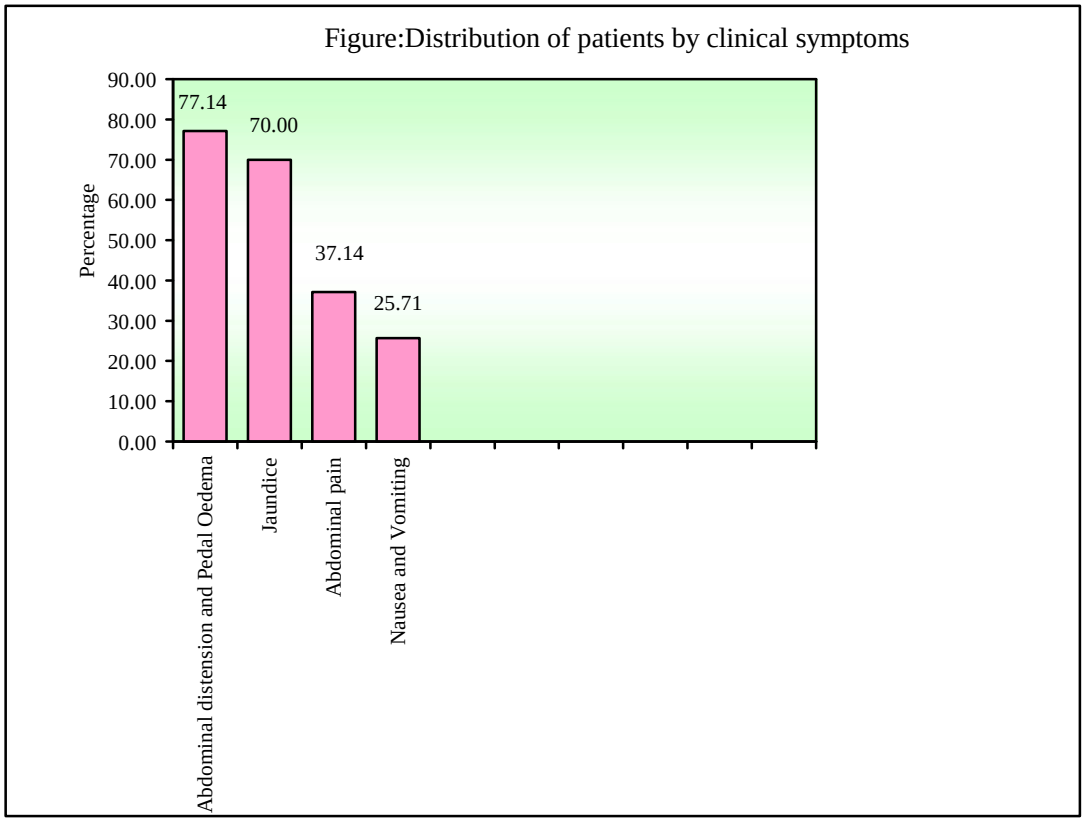
Figure: Gender wise distribution of patients



Out of 70 patients, 64 (91.43%) were male and 6 (8.57%) were females. Male preponderance was seen.

Table 3 : Clinical Presentation :

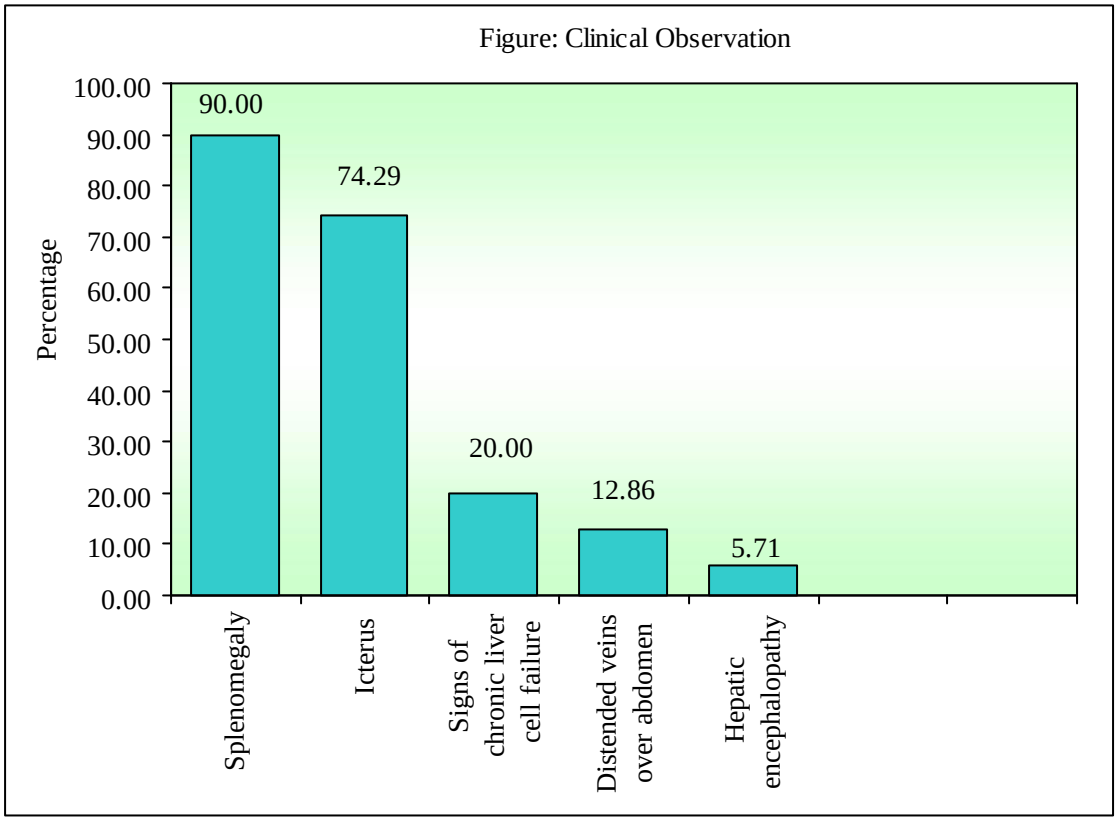
Clinical symptoms	No of patients	% of patients
Abdominal distension and pedal oedema	54	77.14
Jaundice	49	70.00
Abdominal pain	26	37.14
Nausea and Vomiting	18	25.71



In our study, Abdominal distension with pedal oedema (77.14%) was common presenting symptom followed by Jaundice (70.00%) , Abdominal pain (37.14%) and Nausea and vomiting (25.71%).

Table 4 : Clinical Observation :

Clinical signs	No of patients	% of patients
Splenomegaly	63	90.00
Icterus	52	74.29
Signs of chronic liver cell failure	14	20.00
Distended veins over abdomen	9	12.86
Hepatic encephalopathy	4	5.71

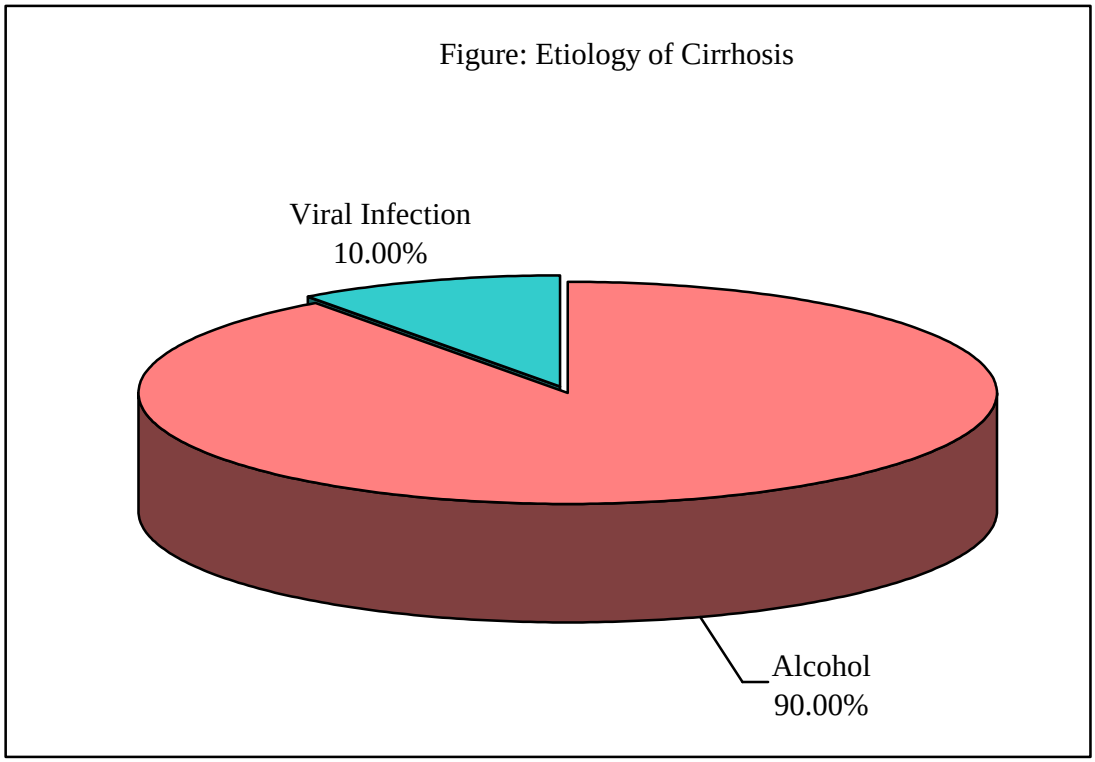


We observed, 63 (90.00%) patients having splenomegaly on either clinical or radiological examination, 52 (74.29%) with icterus, 14 (20.00%) with signs of chronic liver cell failure, 9 (12.86%) with distended veins over abdomen and 4 (5.71%) with hepatic encephalopathy.

Table 5: Etiology of Cirrhosis:

Etiology	No of patients	% of patients
Alcohol	63	90.00
Viral Infection	7	10.00
Total	70	100.00

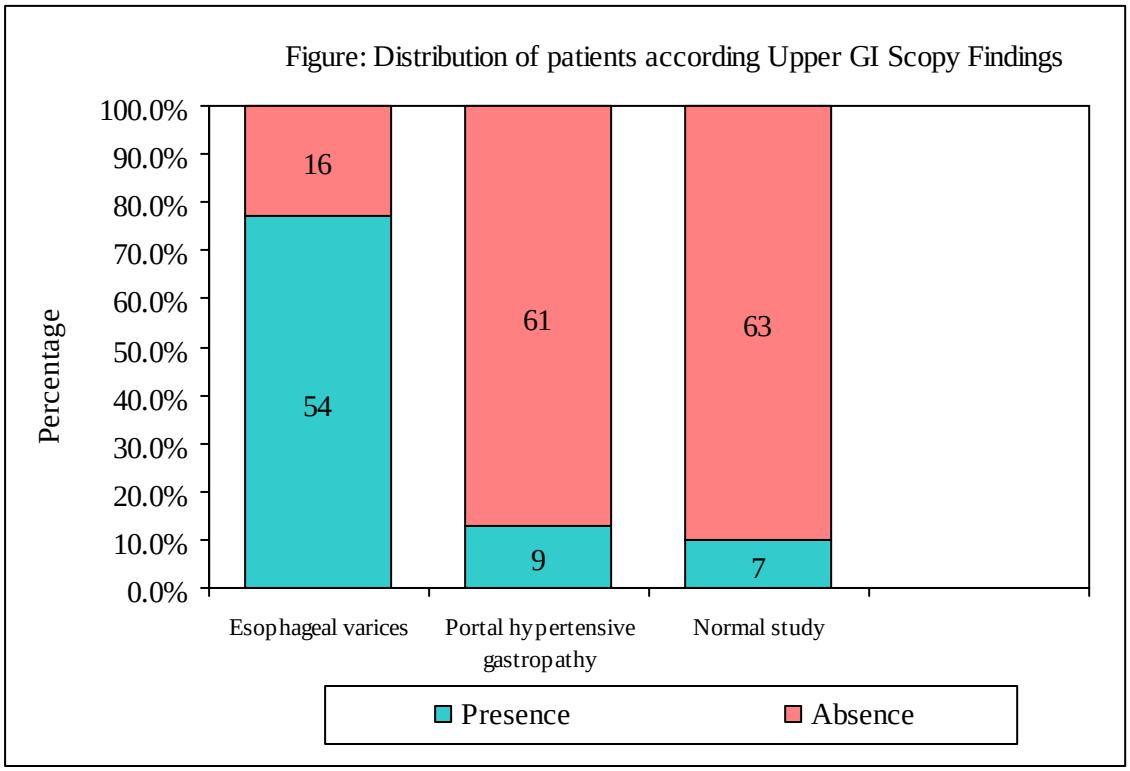
Figure: Etiology of Cirrhosis



In our study, Majority of patients had alcohol induced liver disease (90.00%) and remaining were due to hepatotrophic virus infection.(10.00 %).

Table 6 : Upper GI Scopy Findings :

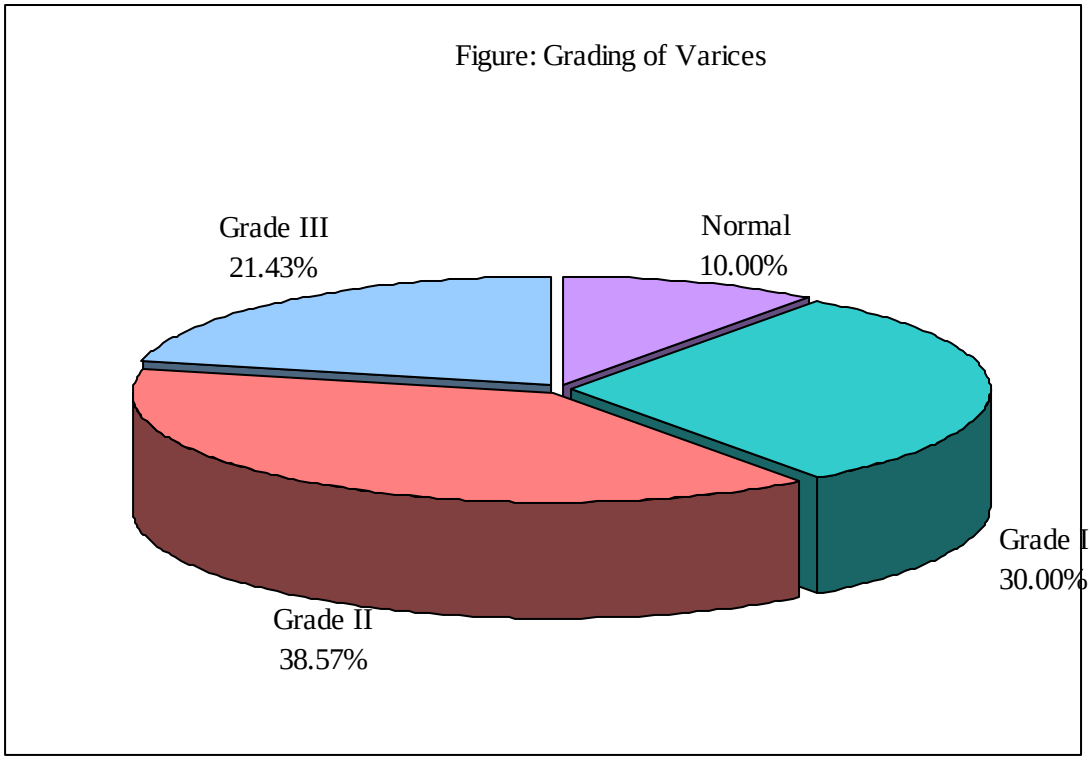
Endoscopy Findings	Presence	%	Absence	%	Total
Esophageal Varices	54	77.14	16	22.86	70
Portal Hypertensive Gastropathy	9	12.85	61	87.14	70
Normal	7	10.00	63	90.00	70



In our study , Upper GI scopy revealed 54 (77.14%) patients with varying degree of esophageal varices, Portal hypertensive gastropathy in 9 (12.85%) patients and 7 (10.00%) were normal.

Table 7 : Grading of varices :

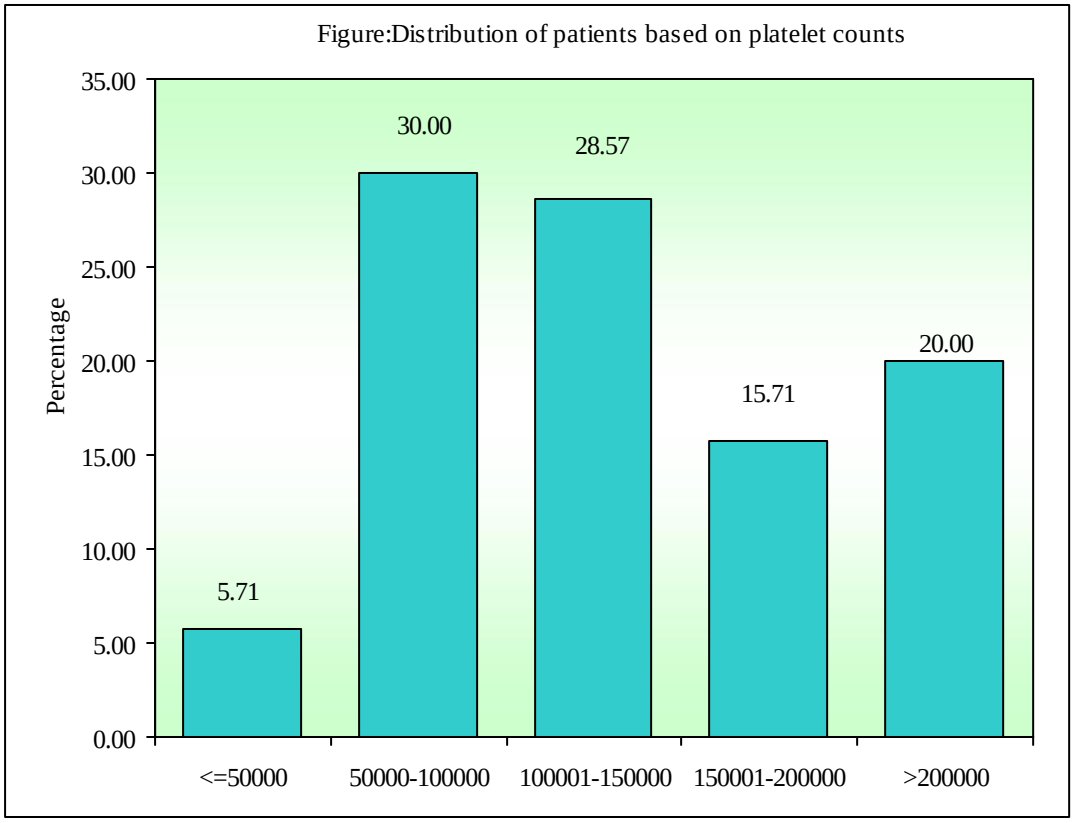
Grades	No of patients	% of patients
Normal	7	10.00
Grade I	21	30.00
Grade II	27	38.57
Grade III	15	21.43
Total	70	100.00



In our 70 patients, 27 (38.57%) patients had grade 2 esophageal varices, 21 (30.00%) had grade 1 varices, 15 (21.43%) had grade 3 varices and 9 patients with grade 1 and 2 varices also had portal hypertensive gastropathy.

Table 8 : Distribution of patients based on platelet counts wise :

Platelet counts	No of patients	% of patients
<=50000	4	5.71
50000-100000	21	30.00
100001-150000	20	28.57
150001-200000	11	15.71
>200000	14	20.00
Total	70	100.00

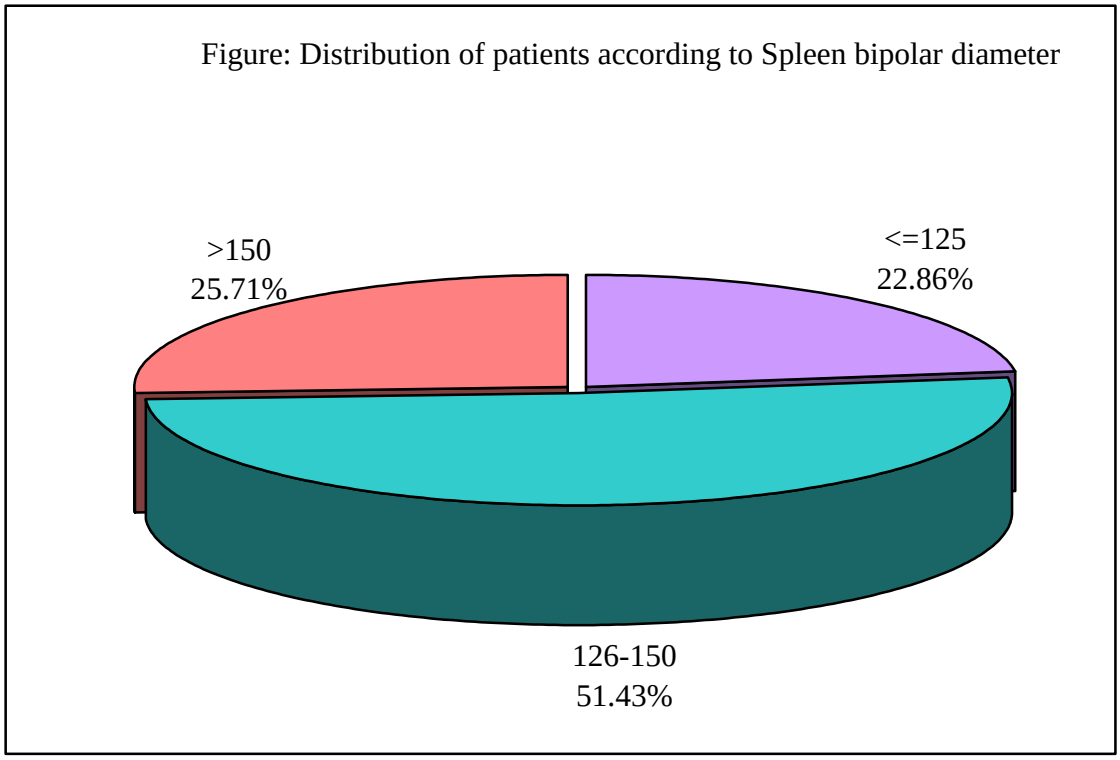


In our study, 35.71% patients belonged to platelet ranging below 100000. 44.28 % patients belonged to platelet range from 100000 – 200000 and 20.00% patients had platelet range above 200000.

Table 9: Distribution on spleen bipolar diameter:

Spleen bipolar diameter	No of patients	% of patients
<=125 mm	16	22.86
126-150 mm	36	51.43
>150 mm	18	25.71
Total	70	100.00

Figure: Distribution of patients according to Spleen bipolar diameter

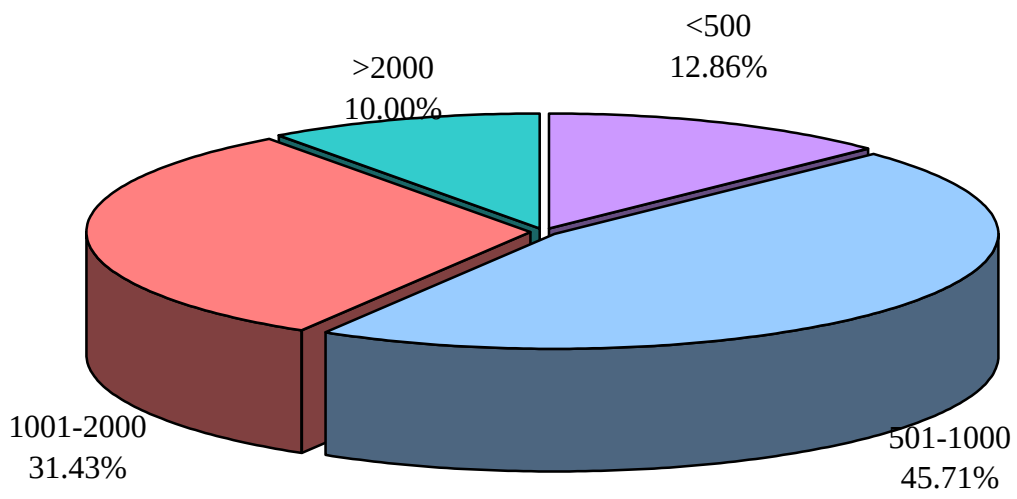


In our 70 patients, we observed 36 (51.43%) patients having spleen diameter ranging from 126-150 mm, 18 (25.71%) patients with diameter more than 150mm and 16 (22.86%) patients having range below or equal to 125mm.

Table 10 : Distribution of patients with PLATELET COUNT/SPLEEN DIAMETER RATIO :

Platelet count /spleen diameter ratio	No of patients	% of patients
<500	9	12.86
501-1000	32	45.71
1001-2000	22	31.43
>2000	7	10.00
Total	70	100.00

Figure: Distribution of patients according to Platelet count/spleen diameter ratio

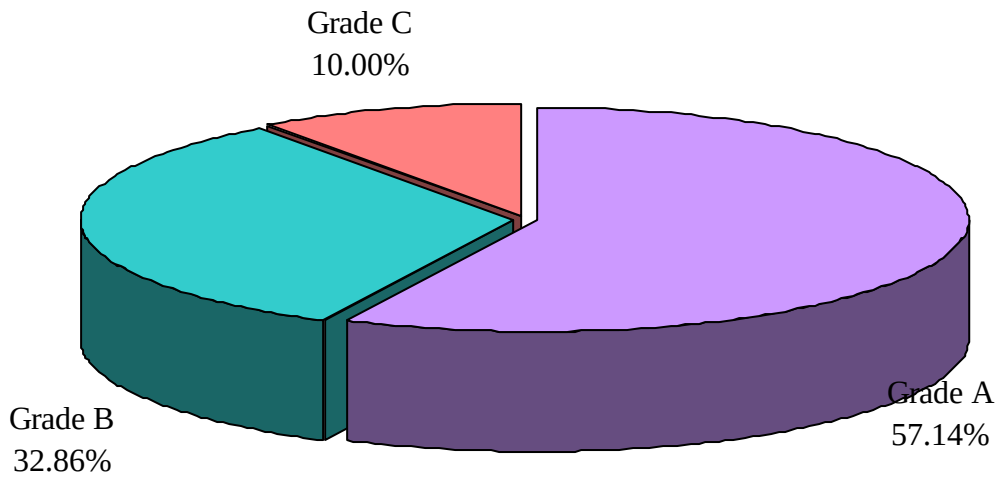


We observed that in 41 (58.57%) patients , ratio of platelet count/spleen diameter was below 1000 and in remaining 29 (41.43%) patients, ratio was more than 1000 as shown in above table.

Table 11: Distribution of patients according to Child Pugh Classification:

Grades of Child Pugh	No of patients	% of patients
Grade A (5 – 6)	40	57.14
Grade B (7 – 9)	23	32.86
Grade C (>10)	7	10.00
Total	70	100.00

Figure: Distribution of patients according to Child Pugh Grade



In the present study, we observed 40 (57.14%) patients were in grade A Child Pugh class, 23 (32.86%) patients in grade B Child Pugh class and only 7 (10.00%) in grade C Child Pugh class.

Table 12: Comparison of Different Parameters (Lab / USG) with Varices :

Variables	Summary	Present varices	Absent varices	Total	t-value	p-value
Platelet Count	**Mean**	**124351.85**	**212187.50**	144428.57		
	SD	58866.06	114401.18	82987.44	-4.1282	**0.0001***
Spleen Bipolar Diameter	**Mean**	**142.52**	**130.63**	**139.80**		
	SD	13.20	12.85	13.97	3.1840	**0.0022***
PLT/Spleen Diameter Ratio	Mean	**884.35**	**1647.88**	1058.87		
	SD	439.58	911.85	658.38	-4.6413	**0.0001***
S. bilirubin	Mean	6.43	4.08	5.90		
	SD	7.32	6.33	7.13	1.1596	0.2502
SGOT	Mean	86.69	135.00	97.73		
	SD	58.09	154.05	90.38	-1.9140	0.0598
SGPT	Mean	45.17	282.44	99.40		
	SD	22.11	839.67	404.62	-2.1112	**0.0384***
T.Protein	Mean	6.53	6.64	6.55		
	SD	1.08	0.92	1.04	-0.3617	0.7187
S. Albumin	Mean	2.25	2.88	2.39		
	SD	0.65	0.69	0.71	-3.3743	**0.0012***
INR	Mean	1.73	1.51	1.68		
	SD	0.53	0.55	0.54	1.5088	0.1360

*$p<0.05$

In all our 70 patients, when we compared with different parameters (lab/USG) with or without varices, we found significant correlation with platelet count, spleen bipolar diameter, PC/SD ratio, SGPT and serum albumin, which is shown in above table.

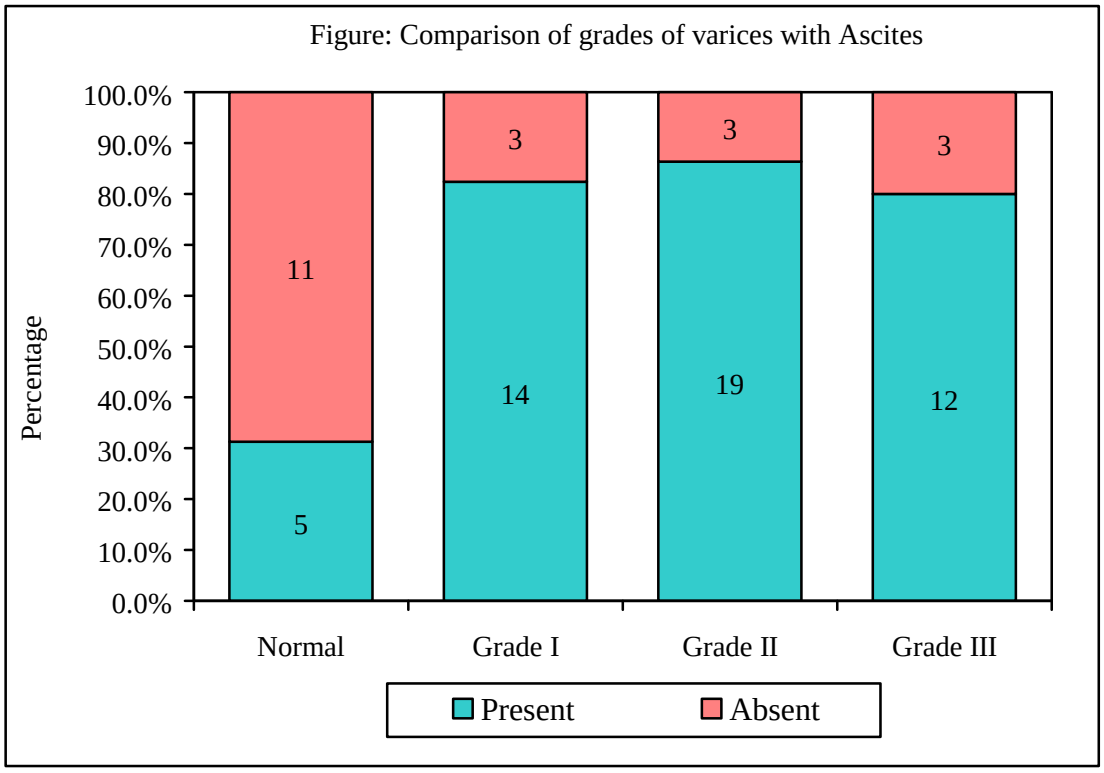
Table 13: Correlation of platelet count, spleen bipolar diameter and platelet count/spleen diameter ratio with grades of varices:

Variables	Normal	%	Grade I	%	Grade II	%	Grade III	%	Total
Platelet counts									
<=50000	1	25.00	2	50.00	1	25.00	0	0.00	4
50000-100000	1	4.76	4	19.05	11	52.38	5	23.81	21
100001-150000	4	20.00	8	40.00	6	30.00	2	10.00	20
150001-200000	2	18.18	1	9.09	3	27.27	5	45.45	11
>200000	8	57.14	2	14.29	1	7.14	3	21.43	14
Spleen bipolar diameter									
<=125	8	50.00	2	12.50	4	25.00	2	12.50	16
126-150	7	19.44	12	33.33	9	25.00	8	22.22	36
>150	1	5.56	3	16.67	9	50.00	5	27.78	18
PLT/spleen diameter ratio									
<500	1	11.11	3	33.33	3	33.33	2	22.22	9
501-1000	4	12.50	11	34.38	12	37.50	5	15.63	32
1001-2000	5	22.73	3	13.64	7	31.82	7	31.82	22
>2000	6	85.71	0	0.00	0	0.00	1	14.29	7
Total	16	22.86	17	24.29	22	31.43	15	21.43	70

In our study, Correlation of platelet count, spleen diameter and PC/SD ratio with grades of varices, we found that patients with platelet count ranging from 50000-100000 had more esophageal varices. Similarly patients with spleen diameter ranging from 126-150 had more varices and patients having PC/SD ratio less than 1000 had more esophageal varices.

Table 14 : Correlation of Ascites with grades of varices :

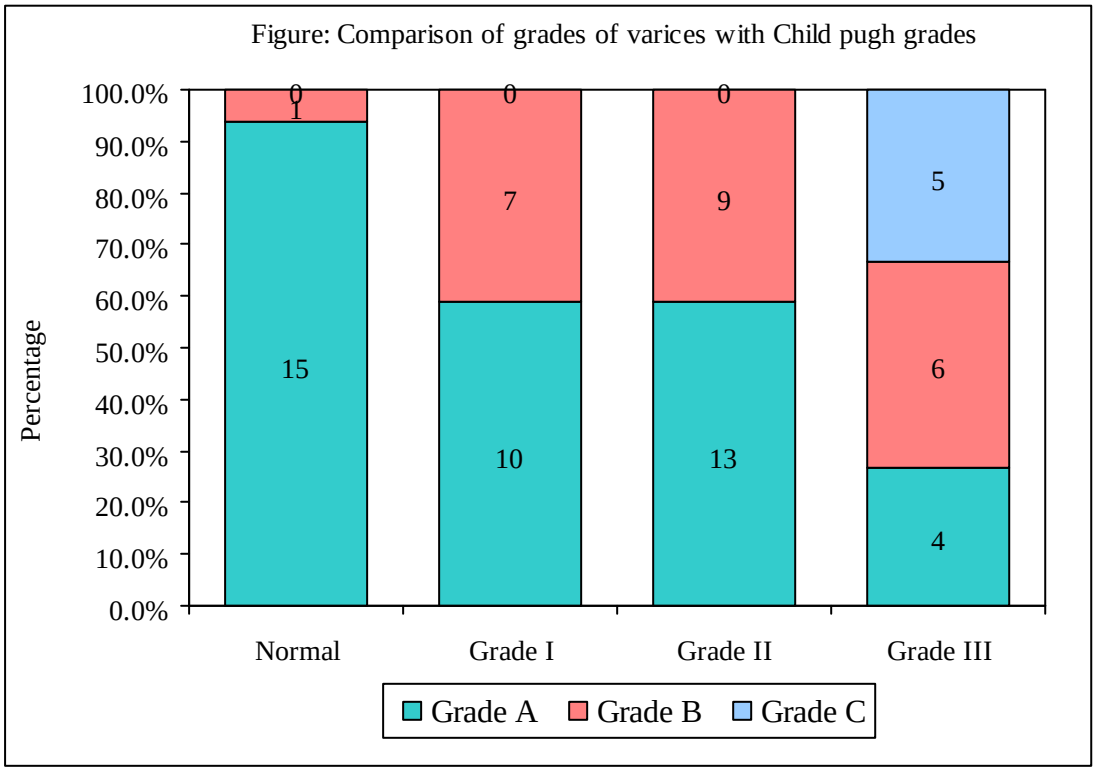
Ascites	Normal	%	Grade I	%	Grade II	%	Grade III	%	Total
Present	5	10.00	14	28.00	19	38.00	12	24.00	50
Absent	11	55.00	3	15.00	3	15.00	3	15.00	20
Total	16	22.86	17	24.29	22	31.43	15	21.43	70



Majority of patients with ascites had varying degree of esophageal varices (45 patients) as compared to those without ascites.

Table 15 : Correlation of Child Pugh Class with Grades of Varices :

Child Pugh Grades	Normal	%	Grade I	%	Grade II	%	Grade III	%	Total
Grade A	15	35.71	10	23.81	13	30.95	4	9.52	42
Grade B	1	4.35	7	30.43	9	39.13	6	26.09	23
Grade C	0	0.00	0	0.00	0	0.00	5	100.00	5
Total	16	22.86	17	24.29	22	31.43	15	21.43	70



In our study, correlation of Child Pugh class and grades of varices were studied. We found that 42 patients belong Child Pugh class A with varying degree of varices. Similarly 23 patients belong to Child Pugh class B and only 5 patients belong to Child Pugh class C.

Table 16 : Comparison between Platelet count/Spleen diameter ratio with Presence of varices :

Varices:	PC/SD Ratio	PC/SD Ratio	Total
	<909	>909	
Absent	5	11	16
Present	36	18	54
Total	41	29	70

Sensitivity	77 %
Specificity	79 %
Positive Predictive value	88 %
Negative Predictive value	62 %

In our study, we categorized our patients into two group based on a cutoff value of 909 for platelet count/spleen diameter ratio. And same was applied for evidence of esophageal varices. And based on these findings, we calculated Sensitivity and Specificity. We found that Sensitivity of 77% and Specificity of 79% which is shown in above table.

DISCUSSION

In the present study of 70 patients with cirrhosis of liver of various aetiologies were studied for Correlation of Platelet count, Spleen bipolar diameter and platelet count/spleen diameter ratio for diagnosis of esophageal varices.

In our study the patient age ranged from 26-70 years, the maximum number of patients that is 41 (58.57%) were in the age group of 31-50 years, followed by 25 (35.71%) ranging from 51-70 years. This is almost similar to study done by Cherian et al[70], and Sarangapani et al.[69]

Taking gender into consideration we observed in our study that males 64 (91.43%) were more compared to females 6 (8.57%), with male to female ratio of 12:1.This similar was studied by Sarangapani et al[69].

In our study population the majority of the patients presented with abdominal distention and pedal oedema, constituting about 54 (77.14%) patients. Other common symptoms noted were jaundice49 (70%) and abdominal pain26 (37.14%) patients. To the best of our knowledge when we tried to search for various studies to compare clinical presentation the information is lacking.

On comparing clinical observation, we found splenomegaly in 63 (90%) patients on either clinical or ultrasound examination followed by clinical signs like Ascites in 50(71.43%) , Icterus in 52(74.29%) , signs of chronic liver cell failure in 14(20%) and hepatic encephalopathy in 4 (5.71%) patients. In our study the correlation between ascites and presence of varices was observed. Similar observation was noted in the study by Schwarzenberger et al[67] and in study by Barrera et al[66].

However, study by Cherian et al[70] and Sarangapani et al[69] did not find significant difference between ascites and presence of varices.

We made an attempt to find out the aetiologies of cirrhosis of liver, we found 63 (90%)patients had cause of alcoholism, 7 (10%) were due to hepatotrophic virus infection of which 4(5.71%) were HbsAg related and 3(4.28%)HCV related. This is almost similar to study by Cherian et al[70] and Baig et al[65].

However, this is in sharp contrast to study by Schwarzenberger et al[67] and Sarangapani et al[69] who observed hepatotropic viruses as main cause of cirrhosis of liver in this study as compared to alcohol as cause.

Among 70 patients of cirrhosis studied 54 (77.14%) had esophageal varices on Upper GI endoscopy. Varices were graded in 3 grades according to severity. In majority of patients had grade 1(30%) and 2 (38.57%) esophageal varices. Similar observation were studied by Cherian et al[70], Sarngapani et al [69], Baig et al[65], Abu El Makeram[68], Taferal[69] et al and Barrera et al[66]. Our study showed similar proportion of varices as many of studies mentioned earlier.

In our study considering platelet count, we observed that 25(35.71%) patients had platelet ranging below 100000, 31(44.28%) patients belonged to range from 100000 – 200000 and 14(20%) had platelet count above 200000.Studies by other authors has shown platelet cutoffs from 68000-160000 have sensitivities and specificities ranging from 71-90% and from 36-73% respectively.

When we attempted to correlate platelet count with esophageal varices, it was observed that there was significant correlation between platelet count and evidence of esophageal varices. P value being statistically significant. ($p<0.0001$). (ie. Those who

had low platelet count has significant evidence of esophageal varices).Studies by Giannini et al[54], Sarangapani et al[69], Cherian et al[70], Barrera et al[66], Schwarzenberger[67], Baig et al[65], Abu El Makeram[68], Tafarel et al[74], and Sharma et al[49] had similar observation.

This is in sharp contrast to study byAbbasi et al[71]in which there was inverse correlation between platelet count with varices($r=0.321$, $p<0.001$).

In present study, we took spleen bipolar diameter into consideration, we observed that36(51.43%) patients having spleen diameter ranging from 126-150mm and 18(25.71%) had diameter more than 150mm.

Similarly, when we made an attempt to correlate spleen diameter with varices, we fount significant correlation between splenic bipolar diameter and esophageal varices. P value being statistically significant.($p<0.0022$)

Similar observations were drawn by Giannini et al[54], Sarangapani et al[69], Cherian et al[70], Barrera et al[66], Schwarzenberger et al[67], Baig et al[65], Abu El Makeram, Tafarel et al[74] in this study.Platelet count/spleen diameter ratio has been shown by several studies to correlate well with the presence of varices. Several studies have been performed to validate this new parameter.

When attempt was made to correlate between platelet count/spleen diameter ratio with varices, we observed that 41(58.57%) patients had ratio below 1000 and 29(41.43%) had ratio more than 1000.Many authors had observed the similar results.

Child Pugh classification was taken into consideration, we observed 40(57.14%) patients were in grade A Child Pugh class, 23(32.86%) in class B and only 7(10%) in Child Pugh class C.

When same was compared with the presence of varices, we observed significant correlationof presence of varices with Child Pugh classification. (There is significant varix in Class A and Class B as compared to Class C)Similar observation was drawn by Cherian et al[70] and Abu El Makeram et al[68].

In our study, we also correlated platelet count,spleen diameter and PC/SD ratio with grades of varices, we found that patients with platelet count ranging from 50000-100000 had more varying grades of varices. Similarly, patients with spleen bipolar diameter ranging from 126-150 had more varices and patients having PC/SD ratio less than 1000 had more varying grades of esophageal varices. Similar study was done by Schwarzenberger et al[67] and Mattos et al[75].

When an attempt was made to correlate ascites with grades of varices, we found that majority of patients with ascites had varying degree of esophageal varices as compared to those without ascites. Similar finding was noted in the study by Schwarzenberger et al[67] and in study by Barrera et al[66]. This was statistically significant in our study.

Lastly, Considering the PC/SD ratio cut off 909 as suggested by Gianniniet al[54] (which yielded 100% sensitivity and 93% specificity).In our study, we categorized our patients into two groups based on this cutoff value of 909 for platelet count/spleen diameter ratio. And same was applied for evidence of esophageal varices.And based on this findings, we calculated sensitivity and specificity which yielded a sensitivity of 77% and specificity of79%.

Other studies which are carried out with thesame ratio of 909 were compared and following observation were made.Baig et al[65] showed cut off of 909 with sensitivity 80% and specificity of 89%.Gianniniet et al[55] showed cut off of 909 with

sensitivity 100% and specificity 93%.Sarangapani et al[69] showed cut off of 909 with sensitivity 88.5% and specificity 83%.

Chawla S et al[72] reviewed meta analysis examining the test characteristics of the PC/SD ratio for predicting esophageal varices and the analysis revealed sensitivity of 89% and specificity of 74%. And drawn conclusion that this results may not be reliable, because of heterogeneity of patients. As far as their etiologies are concerned with alcohol for cirrhosis may have false positive results. This is because thrombocytopenia may be due to bone marrow suppression by alcohol. And B12 deficiency could be because of malnutrition or dietary deficiency. In addition, alcohol is associated with lower thrombopoietin levels and increased antibody-mediated platelet destruction. Hence, cirrhosis due to alcohol may have more false positive results.

When compared with other noninvasive predictor tools, the PC/SD ratio is elegant, simple, and inexpensive. With some minor modifications, it may become a helpful tool to limit the number of endoscopies in primary prophylaxis to be performed in patients with portal hypertension.

To the best of our knowledge, there are no randomized-controlled trials in the published literature to find out efficacy of the PC/SD ratio and its relevance inthese patients.

SUMMARY

In the present study of 70 patients titled '**CORRELATION OF PLATELET COUNT/SPLENIC DIAMETER RATIO FOR THE DIAGNOSIS OF ESOPHAGEAL VARICES IN PATIENTS OF CIRRHOSIS OF LIVER**' during the period from January 2015 to December 2015 in the department of General Medicine, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi. The findings of the study has been summarized as follows:

- There were more cases of cirrhosis with esophageal varices in age group of 31-50years.
- In our study there were 91% males and 9% females.
- Most Common Clinical presentation was Abdominal distension ,pedal oedema and jaundice.
- Majority of patients had Splenomegaly and Ascites on clinical observation.
- Out of 70 patients maximum number of patients were alcoholic liver disease.
- We studied non invasive parameters like platelet count, splenic diameter and platelet count/spleen diameter ratio for evidence of esophageal varices
- In our study, 54 patients had evidence of esophageal varices with varying degree grades with majority had grade 1 and 2 varices, remaining were normal.
- Out of 70 patients, majority had low platelet count , high splenic diameter more than 125mm and platelet count/splenic diameter ratio less than 1000 in our study.
- There were more patients with low PC/SD ratio having varying degree of esophageal varices in our study.

- Severity of liver disease by Child Pugh Classification, there were significant number of patients with esophageal varices more in Class A and Class B.
- The sensitivity of PC/SD Ratio of ≤909 in predicting presence of esophageal varices 68% and specificity was 92%.

CONCLUSION

In the present study of 70 patients with cirrhosis of liver we observed significant correlation with non invasive parameters like platelet count, splenic diameter and platelet count /spleen diameter ratio for diagnosis of esophageal varices.

Based on the findings of the present study the prominent features are:

- In patients with aetiology of cirrhosis was more attributable to alcoholism as compared to HBV and HCV.
- There is strong evidence of esophageal varices with thrombocytopenia, splenomegaly and low platelet count/spleen diameter ratio.
- Comparison with other lab parameters like SGPT, serum albumin has statistical significance.
- We did not find significant correlation with gender and clinical presentation.
- There is also strong correlation between platelet count, splenic diameter and platelet count/spleen diameter ratio with various grades of esophageal varices.
- With this study, use of the platelet count/spleen diameter ratio may be proposed as a safe and reproducible as it is easily available in any hospital setup including peripheral centers.
- Thesenon invasive and cost effective parameters can overcome the lack of availability of endoscopy units and expertise in peripheral centers.
- Owing to small sample size (70 patients), a large sample size may be required to overcome these limitations.

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ANNEXURE I – CONSENT FORM

"CORRELATION OF PLATELET COUNT/SPLENIC DIAMETER RATIO FOR THE DIAGNOSIS OF ESOPHAGEAL VARICES IN PATIENTS OF CIRRHOSIS OF LIVER"

Objective and purpose of the study:

- To Identify the correlation of platelet count, spleen size and their ratio with presence of oesophageal varices in patients of cirrhosis of liver without any previous evidence of GI bleeding.
- To Assess the ability of these parameters as non invasive tool to diagnose the presence of oesophageal varices.
- The principal investigator of the study is **DR.** _____ under the guidance of **Dr.** _____

Need of the Study :

- The use of Platelet count and Platelet count/ Splenic diameter ratio in appropriate subgroups of cirrhotic patients for screening and follow up of esophageal varices can substantially reduce the cost of health care and discomfort for patients as well as reduce burden on Endoscopy units.

Procedure:

- If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations including both invasive and non-invasive procedures.

Risk and Benefits:

- The risk and possible discomfort you might get is while taking blood from my arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

- Patient is subjected for upper GI endoscopy which is a safe procedure however it carries very small risk of complications like Bleeding, Infection , Tearing or erosions of gastrointestinal tract and perforation.

- Patient is subjected for Abdominal ultrasonography which carries no risk of procedure and complication.

- Benefit of the study is to avoid subsequent endoscopies for esophageal varices evaluation by calculating platelet count/ splenic diameter ratio and it is cost effective and non invasive tool for diagnosis of EV in patients of cirrhosis of liver.

Alternatives:

- Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change my mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsorer may stop your participation in this study any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

Cost of Participating in the Research:

- All investigations will be done free of cost.

Privacy and Confidentiality:

- All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy/ Compensation:

- In case of any injury related to the study,treatment will be made available at KLES Dr Prabhakar Kore Hospital and MRC,Belgaum.There is no compensation or payment for such medical treatment by law.

Voluntary Participation/ Withdrawal :

- Your participation in this study is entirely voluntary and you may withdraw from the study at anytime.

Financial incentives for participation :

- You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results :

- The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.
- If you have any questions about your rights as a participant you may call :

Dr. _____

Investigator,
PG in Gen.Medicine,
JNMC, Belgaum
Phone No. _____
Extn. –

Dr. _____

Professor and Unit Head,
Department Of Gen.Medicine
JNMC, Belgaum
Phone No. _____
_____

In case of queries regarding your right as participant you may contact:

Dr._____
MD,
Chairman,
J.N.M.C Ethical Committee for Human Research,
Professor and Head, Department of Pathology, JNMC belgaum
Phone number: _____. Extn: _____

CONSENT STATEMENT

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered. I will be given a copy of this consent form.

Signature /Left Thumb print of the Participant or legally authorized representative.

Participant's Name : …….

Signature/ Left Thumb
Impression of the participant's : …….
Name of the legally
authorized representative : …….

Signature/ Left Thumb
Impression. : …….

Witness's Name : …….

Signature/ Left Thumb
Impression. :…….

Investigators name and Signature : …….

Date and Place : …….

ANNEXURE II – PROFORMA

PROFORMA

"CORRELATION OF PLATELET COUNT/SPLENIC DIAMETER RATIO FOR THE DIAGNOSIS OF ESOPHAGEAL VARICES IN PATIENTS OF CIRRHOSIS OF LIVER"

IP No: **Date:**

Name: **Marital Status:**

Age : **sex:**

Educational status: **Occupation status:**

BRIEF HISTORY :

HISTORY OF PRESENT ILLNESS:

1) **Jaundice** : Duration- Pruritis-Associated yellowish discoloration of urine-

2) **Pedal Oedema :**

Duration- Mode of onset- Progressive/Non progressive-

3) **Abdominal distension :**

Duration - Progressive or non progressive

4) **Abdominal pain:**

SiteCharacterDurationFrequency

RadiationAggravating and relieving factors

5) **Vomiting/nausea :**

DurationProjectile or nonprojectile Bilious or non bilious

Associated with hematemesis Aggravating or relieving factors

6) **Malena or hematochezia :**

7) **Fatigue :**

8) **Weight loss/anorexia :**

9)Oliguria : Duration- Quantity Frequency per day -

10) Fever: Onset-Duration-
Severity- Character-
intermittent/remittent/continuous

11) Symptoms of Hepatic Encephalopathy

Altered sleep rhythm-Behavioural disturbance (as noticed by pt attenders)-

PAST HISTORY:

History of drug intake (diuretics, b-blockers) -

History of blood transfusion-

Previously diagnosed of Liver parenchymal disease-

History of jaundice-

History of tuberculosis-

History of hematemesis or malena-

History of interventions-

History of exposure to STD-

FAMILY HISTORY:

Type2 DM- HTN - IHD-

PERSONAL HISTORY:

Diet –veg / mixed

Appetite –good /poor

Sleep –sound /disturbed

Marital status –married /unmarried

Bowel and Bladder –regular / altered

Habits-

Smoker yes / no - No of cigarettes/day -

Alcoholic yes / no - Amount - Duration -

Tobacco chewer yes / no –

OBSTETRIC & MENSTRUAL HISTORY:

No of children - LMP - Cycles- regular/irregular-

PHYSICAL EXAMINATION:

1. Built: well built / moderate / poorly built

Ht- cms. Wt.- kg. BMI-

2. Pallor-

3. Icterus-

4. Clubbing- Grade-

5. Cyanosis-

6. Koilonychia-

7. Lymphadenopathy-

8. Pedal edema

9. **Signs of liver cell failure:**

i. Alopecia-

ii. Fetor hepaticus-

iii. Parotid swelling-

iv. Gynaecomastia/testicular atrophy -

v. Spider naevi -

vi. Palmar erythema -

vii. Duputreyn's contracture -

viii. Asterixis -

ix. Scanty axillary or pubic hair. -

10. JVP -

11. Signs of bleeding: skin/nose/gums -

VITALS: Pulse : Blood Pressure:
Temperature - Respiratory rate (/ min) -

SYSTEMIC EXAMINATION: PER ABDOMEN
INSPECTION

- Shape –normal/scaphoid/distended
- Umbilicus- normal/everted/scarring
- Skin- striae /pigmentation/puncture mark
- Visible swellings- Site - Size-Shape - Movement with respiration-

  Distended veins- Direction of flow-
- Caput medusa -
- Peristalsis -
- Scars or sinuses -
- Genitalia and hernia orifices

- **PALPATION**
  Tenderness - Guarding-

  Rigidity-
  Liver : Normal/Enlarged

  Liver span – Tenderness- Consistency- Margins-
  Surface -

  Pulsations-

- Spleen : Enlarged-mild/moderate/severe Margins
  Surface- Tender/non tenderConsistency-

- **PERCUSSION :**

Shifting dullness-present/absent Fluid thrill- present/absent

- **AUSCULTATION** : Bowel sounds- Bruits- Venous hum - Hepatic or splenic rub
- **PER RECTAL EXAMINATION**:
- **HERNIAL SITES :**

CVS: Inspection Palpation Percussion Auscultation

RS: Inspection Palpation Percussion Auscultation

CNS : a. Mental status examination -

b. Cranial Nerves -

c. Motor system -

d. Sensory system -

e. Cerebellar examination -

f. Meningeal signs –

g. Asterixis/Flaps -

CHILD PUGH SCORE:

PlateletCount /Spleen Diameter Ratio:–

Oesophageal Varices (on UGI Endoscopy) : –

DIAGNOSIS:

CONCLUSION :

Signature of Guide Signature of Student

ANNEXURE-3- MASTER CHART

KEY TO MASTER CHART

HE –HEPATIC ENCEPHALOPATHY

HB- HEMOGLOBIN

PLT- PLATELET COUNT

S. BILIRUBIN- SERUM BILIRUBIN

D. BILIRUBIN- DIERCT BILIRUBIN

SGOT- SERUM GLUTAMATE OXALOACETATE TRANSAMINASE

SGPT- SERUM GLUTAMATE PYRUVATE TRANSAMINASE

ALK. PH. – ALKALINE PHOSPHATASE

INR - INTERNATIONAL NORMALIZED RATIO

PC/SD- PLATELET COUNT/SPLEEN DIAMETER