"ROLE OF COLOUR DOPPLER ULTRASONOGRAPHY IN THE EVALUATION OF PORTAL VENOUS HYPERTENSION"

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Dissertation submitted to the

B.L.D.E. (DEEMED TO BE UNIVERSITY) VIJAYAPURA, KARNATAKA

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

In

RADIO-DIAGNOSIS

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2018

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ACKNOWLEDGEMENT

This piece of work has been accomplished with the grace of almighty God. It gives me immense pleasure to express my heartfelt gratitude to all. I dedicate this page to each and everyone who has helped me to explore the expanses of knowledge.

I express my profound gratitude and sincere thanks to ***Dr. Bhushan Lakhkar*** $_{M.D.,}$ *Professor & Head, Department of Radiology, B.L.D.E.DEEMED TO BE UNIVERSITY's Shri B. M. Patil Medical College, Vijayapura, and my guide* ***Dr. Ramesh C Pattanshetti*** $_{M.D.,}$ *for their constant and unfailing support, professional insight, valuable suggestions, motivation and exemplary guidance to carry out and complete this dissertation. I am deeply grateful to them for providing me necessary facilities and excellent supervision to complete this work.*

I offer my sincere thanks to ***Dr. M. S. Biradar****, Vice Chancellor,* ***Dr. S. P. Guggarigoudar****, Principal and* ***Dr. Vijaykumar*** *Medical Superintendent B.L.D.E.U's Shri B. M. Patil Medical College, Vijayapura, for their support and inspiration.*

I am deeply indebted and grateful to my professor ***Dr. B R Dhamangaonkar and Dr. M. M Patil,*** *Department of B.L.D.E.DEEMED TO BE UNIVERSITY's Shri B. M. Patil Medical College, Vijayapura, who with their valuable suggestions and constant guidance supported me throughout the preparation of this dissertation work.*

My thanks to ***Dr. Satish Patil, Dr S. V Patil****, Associate professors,* ***Dr. Bhushita Lakhkar & Dr. Vishal S. Nimbal****, Assistant professors****, Dr. Chandalingappa Kuri****, Dr. Ravi Kumar & Dr. Suresh Kanamadi*** *, Senior Residents****,*** *Department of Radio-diagnosis, B.L.D.E.DEEMED TO BE UNIVERSITY's Shri B. M. Patil Medical College, Vijayapura, for their valuable suggestions and encouragement which have definitely helped me improve my research work.*

*I acknowledge my gratitude to**, Dr. Adiraju Karthik,, Dr. Iranna M.H, and Dr. Namit Garg,** Postgraduate colleagues, Department of Radiology, B.L.D.E.DEEMED TO BE UNIVERSITY's Shri B. M. Patil Medical College, Vijayapura, for their support, advice and help in data collection. I also thank all my seniors Dr. Holebasu Ballur, Dr. Parth Vaishnav, Dr. Rohini Pattanshetti and Dr. Avinash Garg, my juniors Dr. Suhas.C.N, Dr. Sri Kalyan, Dr. Shanthala, Dr. Siddaling, Dr. Arjun Kamath, Dr. Mohit Lohey, Dr. Shabharish and Dr. Prakriti for their co-operation during the preparation of this dissertation.*

I am thankful to all the Technical and non-teaching staff of the Department of Radiodiagnosis including Mrs. Sapna, Mrs. Saraswati, Mr. Patil, Mr. Anil and BSc MIT students, Shri B.M. Patil Medical College, Vijayapura for their help and co-operation.

*I thank **Mr. Mohd. Shannawaz**, Statistician for his masterly guidance and statistical analysis. I sincerely acknowledge the support and kindness shown towards me by Shivakumar and all other staff of Central Library, Shri B. M. Patil Medical College, Vijayapura, at all times.*

*My heartfelt thanks to my beloved parents **Mr. Jayadev .D.S and Mrs. Poorna Jayadev,** other family members **Mrs. Pooja Jayadev, Dr. Punya Jayadev and Dr. Manjunath .M** for their encouragement, support and sacrifices.*

*Special thanks to my all **friends** for their timely help and support.*

*I thank **Preeti Net Zone**, for their meticulous computerized layout of this dissertation.*

Last but not the least, my sincere thanks to all the patients of this study for their cooperation without which this study would not have been possible.

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ABSTRACT

BACKGROUND:

Portal hypertension is the hemodynamic abnormality frequently associated with serious liver disease, although it is also recognized less commonly in a variety of extrahepatic diseases, which often results in most lethal complications including ascites, variceal bleeding, renal failure and bacterial peritonitis. So accurate diagnosis of portal hypertension helps in timely implementation of surgical and medical management and thus prevents complications. Colour Doppler Ultrasonography helps in evaluation of portal hypertension by differentiation of presinusoidal, sinusoidal and post sinusoidal causes of portal hypertension and assessing sequelae like portal vein thrombosis and esophageal varices and thus helps in deciding the management plans. Spleen stiffness measurements by acoustic radiation force impulse (ARFI) imaging have been recently proposed as a new, non-invasive parameter for portal hypertension.

AIMS AND OBJECTIVES:

1. To evaluate spectrum of colour Doppler sonographic findings in portal hypertension.
2. To study flowmetric changes in portal hypertension.
3. To look for presence of various portosystemic collaterals.
4. To study associated findings like liver parenchymal disease, splenomegaly and ascites.
5. To evaluate the diagnostic value of spleen stiffness measurements by acoustic radiation force impulse (ARFI) imaging in assessing the severity of portal hypertension.

MATERIALS AND METHODS:

65 clinically suspected / diagnosed cases of portal hypertension who were referred to the Department of Radiodiagnosis, BLDEU's Shri B.M. Patil Medical College Hospital and Research Center, in a period from November 2016 to April 2018 underwent colour Doppler Ultrasonography of abdomen and spleen stiffness measurements by ARFI imaging. Severe portal hypertension was defined as Damping Index>0.6.

RESULTS:

Among 65 patients in the study group, males were most commonly affected with cirrhosis being the most common etiology. Dilated portal vein >13 mm was seen in 62%cases, loss of respiratory phasicity (<20%) in 79% of cases, decreased PV flow velocity (<15cm/s) in 69.2 % cases, portosystemic collaterals in 69.2 % cases, thrombosis of portal vein in 10 cases Splenomegaly and Ascites in 84.6% and 87.7% of the cases respectively, Damping Index >0.6 in 69% of cases suggesting severe portal hypertension. The Spleen stiffness as measured by ARFI shear wave velocity ranged between 2.54 – 4.1 m/s with mean SS of 3.14 ± 0.28 m/s. The Spleen stiffness cut-off value of 3.11 m/sec was considered as the better indicator to rule out the presence of severe portal hypertension with a highest sensitivity of 93.3% and specificity of 80% ($p<0.05$).

CONCLUSION:

Colour Doppler Ultrasonography is an accurate non-invasive investigation for evaluation of portal hypertension. Damping Index and Spleen stiffness measurement by acoustic radiation force impulse (ARFI) imaging has showed a strong association with the severity of portal hypertension which needs to be confirmed in further studies with large patient population.

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INTRODUCTION:

Portal hypertension is the hemodynamic abnormality frequently associated with serious liver disease, although it is also recognized less commonly in a variety of extrahepatic diseases. Many of the most lethal complications of liver disease are directly related to the presence of portal hypertension; including ascites, variceal bleeding, renal failure and bacterial peritonitis. So accurate diagnosis of portal hypertension helps in timely implementation of surgical and medical management and thus prevents complications[1].

Portal hypertension is defined as an increase in portal pressure above the normal range of 6-10 mm Hg or an increased hepatic venous pressure gradient (HVPG) of more than 5 mm Hg[2]. Portal hypertension is classified as intrahepatic, extrahepatic or hyperdynamic. Extrahepatic is classified into prehepatic or posthepatic. Intrahepatic is further classified into presinusoidal, sinusoidal or post sinusoidal[3].

Ultrasonography with colour Doppler helps in evaluation of portal hypertension. It permits differentiation of presinusoidal, sinusoidal and post sinusoidal causes of portal hypertension[3]. It also allows to assess sequelae like portal vein thrombosis and esophageal varices and helps in deciding the management plans.

Doppler ultrasonography is non-invasive, cost-effective and has no risk of ionizing radiation. It can be performed rapidly, is widely available and easy for follow up, and thus the initial imaging of choice[4].

The spleen undergoes parenchymal remodelling in patients with Portal hypertension. Spleen stiffness measurements have been recently proposed as a new, noninvasive parameter for portal hypertension[5]. Spleen Stiffness measurement (SSM) by acoustic radiation force impulse (ARFI) imaging has showed acceptable diagnostic performance in predicting the presence, severity, and consequences of portal hypertension and in the alleviation of healthcare costs associated with variceal hemorrhage. SSM is increased in portal hypertension of unknown cause and pre-hepatic portal hypertension (PH), suggesting that it could be used as a surrogate for PH, irrespective of its cause in whom HVPG is not reliable[5,6].

The measurement of Spleen Stiffness could help in rapid risk stratification and identification of patients requiring further testing such as screening endoscopy or prophylactic treatment for decompensation[6].

Hence the purpose of this study is to assess the role of Colour Doppler Ultrasonography with an introductory application of Elastography of Spleen in evaluation of Portal Hypertension.

AIMS AND OBJECTIVES OF THE STUDY:

1. To evaluate spectrum of colour Doppler sonographic findings in portal hypertension.

2. To study flowmetric changes in portal hypertension.

3. To look for presence of various portosystemic collaterals.

4. To study associated findings like liver parenchymal disease, splenomegaly and ascites.

5. To evaluate the diagnostic value of spleen stiffness measurements by acoustic radiation force impulse (ARFI) imaging in assessing the severity of portal hypertension.

MATERIAL AND METHODS

SOURCE OF DATA:

The patients referred to the Department of Radiodiagnosis at BLDEU's Shri B.M. Patil Medical College Hospital and Research Center, Vijayapura for transabdominal ultrasound with clinical suspicion of portal hypertension between November2016 to April 2018.

STUDY DESIGN: Cross-sectional study

INCLUSION CRITERIA:

- All cases with clinical suspicion of portal hypertension.
- All cases of chronic liver disease.

EXCLUSION CRITERIA:

- Patients who underwent hepatobiliary surgery or recent surgery for any other reasons.
- Unstable cases.
- Traumatic cases.

METHODS OF COLLECTION OF DATA:

The patients referred to the Department of Radiodiagnosis, BLDEU's Shri B.M. Patil Medical College Hospital and Research Center with the clinically suspected / diagnosed cases of portal hypertension, in a period from November 2016 to April 2018 will be subjected for the study.

65 cases are intended to be taken up within the study period.

All patients included in the study will undergo ultrasonography of abdomen with two probes one with low frequency (5 to 8 MHz) and one with high frequency (3 to 12 MHz).

The machines which will be used in the study are SIEMENS ACUSON s3000 and PHILIPS HD11-XE.

SAMPLE SIZE:

A sample size of 65 subjects will allow the study to determine the incidence of portal hypertension with a confidence interval of +/- 5% with finite population correction.

$$n = \frac{Z^2 p(1- p)}{d^2}$$

Z = statistic at 5% level of significance,

d is margin of error,

p is expected prevalence rate

STATISTICAL ANALYSIS:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. Chi-square (χ^2) test was used for association between two variables by following formula:

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript “c” are the degrees of freedom. “O” is observed value and E is expected value.

C= (number of rows-1)* (number of columns-1)

ROC analysis for Sensitivity- specificity was done to check relative efficiency.

sensitivity or true positive rate (TPR)

eqv. with hit rate, recall

$$TPR = TP/P = TP/(TP + FN)$$

specificity (SPC) or true negative rate

$$SPC = TN/N = TN/(FP + TN)$$

precision or positive predictive value (PPV)

$$PPV = TP/(TP + FP)$$

negative predictive value (NPV)

$$NPV = TN/(TN + FN)$$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

ANATOMY OF PORTAL SYSTEM

The portal system includes all the veins draining the blood from the abdominal part of the digestive tube (with the exception of the lower part of the rectum) and from the spleen, pancreas, and gall-bladder. From these viscera the blood is conveyed to the liver by the portal vein. In the liver, the portal vein ramifies like an artery to form capillary-like vessels called as sinusoids, from which the hepatic veins convey the blood into the inferior vena cava[7,8].

The portal vein is about 8 cm in length, and is formed at the level of the second lumbar vertebra by the union of the superior mesenteric and splenic veins, which takes place in front of the inferior vena cava, behind the neck of the pancreas and obliquely to the right. It passes upward behind the superior part of the duodenum and then ascends in the right border of the lesser omentum to the right extremity of the portahepatis, where it divides into a right and a left branch[7,9].The right branch of the portal vein receives the cystic vein and enters into the right lobe of the liver. The left branch traverses porta hepatis from right end to left and gives branches to the caudate and quadrate lobes, and receives paraumbilical veins before entering the left lobe of the liver.

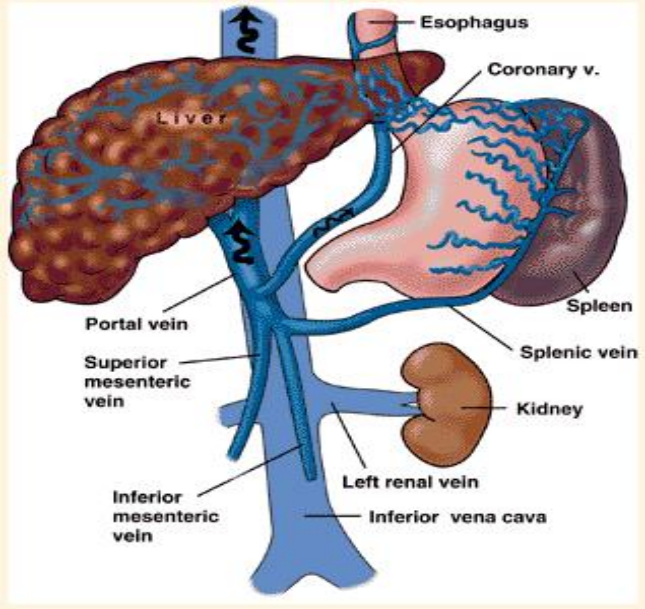


FIG 1: Anatomy of the portal venous system

The tributaries of the portal vein are:Splenic vein, Superior mesenteric vein,Coronary vein, Pyloric vein,Cystic vein and Paraumbilical veins[7].

The splenic veins (5 – 15 channels) originate at the splenic hilum and join near the tail of the pancreas with the short gastric vessels to form the main splenic vein. This proceeds in a transverse direction in the body and head of the pancreas, lying below and in front of the artery. It receives numerous tributaries from the head of the pancreas, and the left gastroepiploic vein enters it near the spleen[9].

The inferior mesenteric vein, bringing blood from the left part of the colon and rectum, usually enters its medial third. Occasionally, however, it enters the junction of the superior mesenteric and splenic veins.

The superior mesenteric vein is formed by tributaries from the small intestine, colon and head of the pancreas, and irregularly from the stomach via the right gastroepiploic vein.

The Coronary vein derives tributaries from both surfaces of the stomach and some esophageal veins. It then turns backward and passes from left to right behind the omental bursa and ends in the portal vein.

The Pyloric Vein is of small size, and runs from left to right along the pyloric portion of the lesser curvature of the stomach, between the two layers of the lesser omentum, to end in the portal vein.

The Cystic Vein drains the blood from the gall-bladder, and, accompanying the cystic duct, usually ends in the right branch of the portal vein.

Parumbilical Veins—In the course of the ligamentum teres of the liver and of the middle umbilical ligament, small veins (parumbilical) are found which establish an anastomosis between the veins of the anterior abdominal wall and the portal, hypogastric, and iliac veins[7].

PATHOPHYSIOLOGY

The liver receives approximately 25% of the cardiac output through a dual vascular supply. The portal venous circulation provides 75–80% of the blood supply through a low pressure system [8,9]. The hepatic artery delivers the rest of the blood supply. Blood from the portal vein and hepatic artery enter the hepatic lobule at the portal triad and mix together in the hepatic sinusoids. Because sinusoidal endothelial cells (SEC)

have large fenestrae and lack a basement membrane, the sinusoids are considered a ‘‘leaky’’ capillary bed. After passing through the hepatic cords, sinusoidal blood drains into the hepatic central vein and then out of the liver through the hepatic veins, eventually reaching the caudal vena cava for return to the right atrium[9].

Flow in the portal vein is generally stream –lined rather than turbulent. Generally in adult subjects, Portal blood flow is approximately 1000-1200 ml/min[9]. This portal blood flow contributes 75% of the hepatic blood supply. The fasting arterioportal oxygen difference is only 1.9 volumes per cent (range 0.4 – 3.3 volumes per cent) and the portal vein contributes 40 mL/min or 72% of the total oxygen supply to the liver. During digestion, the arterioportal venous oxygen difference increases due to increased intestinal utilization. The normal portal venous pressure is about 5 to 10 mmHg[9].

According to Ohm’s law: P(pressure)= Q(blood flow) x R(resistance), portal vein pressure (PVP) is equal to the product of portal blood flow (PBF) and the resistance to that flow (intrahepatic venous resistance[IHVR]): PVP=PBFxIHVR[10,11].

In the normal liver, PVP remains stable inspite of changes in PBF. A large reserve in the sinusoid and intrahepatic vasculature adaptive responses allow for a compliant vascular bed that increases its volume significantly to withstand additional PBF without much changes in pressure. Increased PBF activates SEC’s in releasing nitric oxide (NO), which causes dilatation of intrahepatic vessels thereby accommodating more blood volume[10,11]. Several factors affecting minor fluctuations in the PVP include, lower PVP due to anesthesia, inspiration, fasting, and exercise. Transient increase occurs

postprandially, during expiration, increaseed intraabdominal pressure (such as during or defecation), after expansion of blood volume and the injection of angiographic agents[9].

From a mechanistic view, portal pressure (pP) is directly proportional to the blood flow (Q) and/or resistance (R) (Fig 2)[12].

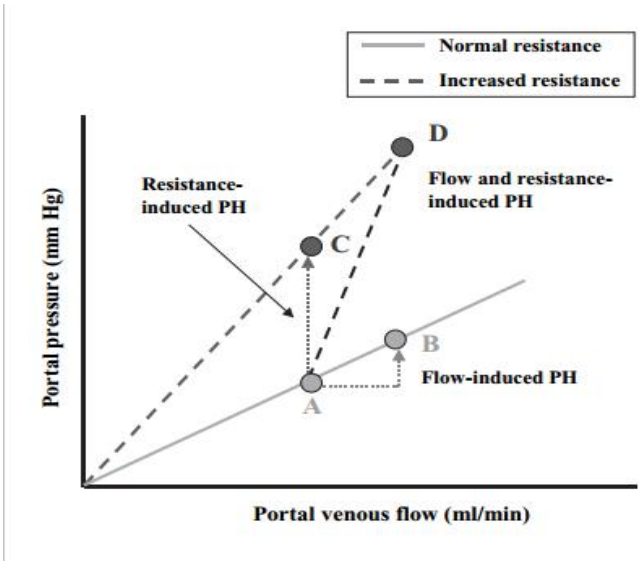


FIG. 2 : Hepatic resistance and portal venous flow determine portal pressure (pP). Circle A represents normal portal venous flow with normal portal pressure, the increase of pP is only induced by an increase in flow (B) or resistance (C); circle D, in contrast, represents an elevation in both. PH=Portal hypertension.

Portal pressure > 12mm Hg with concomitantly increased wedged hepatic vein pressure (WHVP) gradient between the pressure in the portal vein and inferior jejunal vein > 2-6mm Hg diagnose portal hypertension (PH)[13]. Portal pressure is measured by angiography as hepatic vein pressure gradient (HVPG) which is a difference between wedged hepatic venous pressure – WHVP (pressure in the venous sinuses) and free hepatic venous pressure FHVP. Determined difference > 5-12mm Hg is considered as

portal hypertension. Clinically it is diagnosed by catheterization of portal veins which is one of basic methods to detect portal hypertension[14].

CLASSIFICATION OF PORTAL HYPERTENSION:

Portal Hypertension (PH) is classified based on anatomical location and etiology as prehepatic, intrahepatic or posthepatic (Table 1)[10,13].

PREHEPATIC (Portal Vein)	INTRAHEPATIC (Liver)	POSTHEPATIC (Heart, CVC, Hepatic Veins)
Congenital portal vein atresia **Intraluminal obstruction** • Thrombus • Neoplasia • Stenosis **Extraluminal obstruction** • Neoplasia • Lymph node • Granuloma • Abscess	**Presinusoidal** • Primary hypoplasia portal vein (noncirrhotic portal hypertension) • Chronic cholangitis • Hepatic arteriovenous fistula • Schistosomiasis • Nodular hyperplasia • Ductal plate abnormalities (Caroli's disease) **Sinusoidal** • Cirrhosis/chronic hepatitis • Chronic cholangiohepatitis • Ductal plate abnormalities (Congenital hepatic • fibrosis) • Lobular dissecting hepatitis **Postsinusoidal** • Veno-occlusive disease (Sinusoidal obstruction syndrome)	**Right heart failure** • Congestive • Pericardial tamponade • Constrictive pericarditis • Intracardiac neoplasia **Congenital cor triatriatum** **CVC/hepatic vein obstruction (Budd-Chiari syndrome)** **Intraluminal** • Thrombosis • Vena cava syndrome • Neoplasia **Extraluminal** • Neoplasia • Kinking of IVC

Table 1. Classification of portal hypertension

A] Prehepatic PH occurs due to increase in resistance of the extrahepatic portal vein which is associated with following conditions:

1. Portal vein occlusion: Portal vein occlusion is quite common in the Indian population accounting for 20-30% of variceal bleeding. Umbilical infection with or without catheterization of the umbilical vein may be responsible in neonates[14]. The infection spreads along the umbilical vein to the left portal vein and hence to the main portal vein. Acute appendicitis and peritonitis are causative in older children. Portal vein thrombosis also known to occur in patients with Crohn's disease, ulcerative colitis and secondary to biliary sepsis. Other causes of portal vein block are secondary to trauma, post–splenectomy, hypercoagulable states, invasion and compressing by hepatic or pancreatic malignancies. Congenital blockage may exist anywhere along the line of the right and left vitelline veins which give rise to the portal vein (eg, congenital atresia or fibrosis). Portal vein thrombosis is known to occur with pregnancy and with oral contraceptive intake. Thrombosis in cirrhosis is a rare occurrence[14].

2. Splenic vein block: splenic vein block causes sinistral or left sided portal hypertension. Splenic vein thrombus is known to occur in pancreatic disease suchas pancreatitis, carcinoma. Furthermore, the etiological factors causing portal vein thrombosis also apply in splenic vein obstruction. If the obstruction is distal to the entry of the left gastric vein then the splenic vein decompresses through the short gastric veins into the gastric fundus and lower esophagus thereby reaching the left gastric vein and portal vein. This causes prominent gastric fundal varices with very few or no esophageal varices[14].

3. Hepatic arteriovenous fistulas results in prehepatic PH due to flow of arterial blood into the portal venous system, which are usually congenital, but may also develop secondary to trauma, surgery or vascular erosion by neoplasm. These factors results in portal hypertension due to hyperdynamic flow[14].

4. Splenomegaly : Some patients with splenomegaly due to any cause such asleukemia, lymphomas, Banti's syndrome develop portal hypertension. This is mainly due to increased venous blood flow into the portal vein form the enlarged spleen.

B] Intrahepatic PH is further divided into presinusoidal, sinusoidal and postsinusoidal PH[9].

1. Presinusoidal causes :Presinusoidal causes of obstruction to portal blood can occur due to (i)portal tract lesion (ii) toxic causes and (iii) hepato –portalsclerosis.

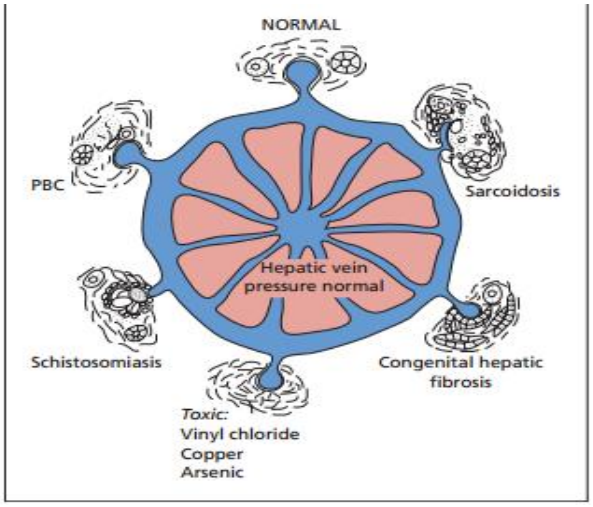


FIG.3[14] : Etiology of presinusoidal intrahepatic portal hypertension.

PBC- primary biliary cirrhosis.

(i) Portal tract lesions are caused by[14] :

a. Schistosomiasis which causes a fibrotic reaction by deposistion of its ova in portal vein radicals.
b. Congenital hepatic fibrosis with polycystic disease.
c. Myeloproliferative disease such as myelosclerosis, myeloid leukemia which cause infiltration of the portal zones.
d. Primary biliary sclerosis.

(ii) Toxic causes are due to injurious substances taken up by endothelial cell in Disse's space causing a fibrotic reaction.

(iii)Non cirrhotic portal fibrosis (NCPF) is a syndrome of obscure etiology, characterized by obliterative portal venopathy leading to splenomegaly, hypersplenism and portal hypertension without occlusion of portal and splenic veins and with no obvious pathology in the liver. The lesion in NCPF is generally vascular, present in portal vein, it's branches or in the presinusoidal area of liver. NCPF is also known by other names like idiopathic portal hypertension (Fig.4)[14], hepatoportal sclerosis, obliterative portal venopathy of the liver and non cirrhotic intrahepatic portal hypertension. NCPF has been reported from all over the world, with maximum cases reported from India. World wide it accounts for 3-5% of all patients with portal hypertension, but in India it accounts for 15- 20% of case of portal hypertension[1]. Most studies from India have reported a male predominance of 2:1 to 4:1[16]. NCPF is mainly a disease of young Indian men from low socioeconomic background. The mean age onset of NCF patient varies from 25 to 35 years[16].

The etiology of NCPF is poorly understood. A number of hypothesis have been proposed. Clustering of the disease mainly in low socioeconomic class suggests that malnutrition, exposure to toxins and chemical or recurrent intestinal infections could possibly be responsible[16].

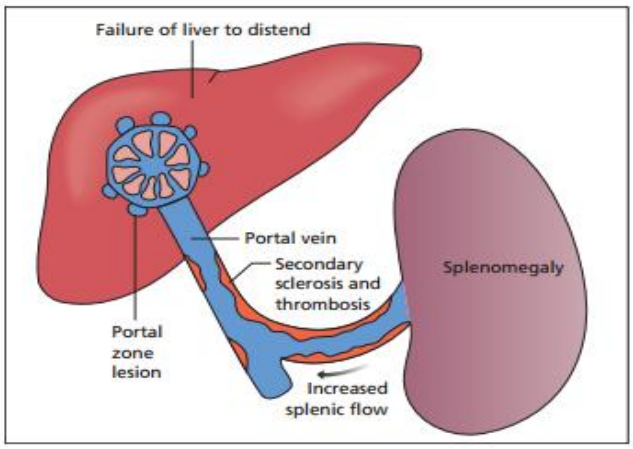


Fig.4 Factors concerned in idiopathic primary portal hypertension.

iv) Caroli`s disease- presents with abdominal pain and recurrent attacks of cholangitis with fever and jaundice. The periportal fibrosis type may present with pain or signs of portal hypertension, including haematemesis from oesophageal varices[3].

2. Sinusoidal causes : The most common cause of obstruction to the portal blood flow is cirrhosis. All forms of cirrhosis lead to portal hypertension and the primary event is obstruction to portal blood flow. Portal flow is diverted into collaterals and some is directly shunted into hepatic venous radicles in the fibrous septa of the sinusoids. Regenerating nodules largely derive their blood supply from the hepatic artery as more and more of the portal flow is shunted away. The progression of liver fibrosis and regenerative nodule formation in the cirrhotic liver leads to a distortion of the sinusoidal

structure and narrowing of the vascular lumen, which in turn leads to increased resistance to the portal blood flow and portal hypertension. These mechanical factors developed from the disruption of the liver vascular architecture have been considered as the main cause of the increase in the intrahepatic resistance in cirrhotic liver. However, besides these mechanical factors, intrahepatic vasoconstriction also plays an important role in the development of portal hypertension[3].

A previous study, which presented the decrease in portal pressure by vasodilators, suggested that intrahepatic vasoconstriction might contribute 10–30% of the increase in portal resistance, while other recent studies suggest that the role of intrahepatic vasoconstriction in the portal resistance might be even greater in the cirrhotic liver[14,17]. Enhanced contractility of hepatic stellate cells (HSCs) plays an important role in the development of intrahepatic vasoconstriction. They are involved in the regulation of the sinusoidal blood flow in the normal liver and HSC contractility is regulated by a balance between vasoconstrictors and vasodilators in normal condition. In cirrhotic liver, the decrease in the vasodilators, such as NO, and the increase in the vasoconstrictors, including ET-1, angiotensin II (AT-II), and α-adrenergic stimulus, promote intrahepatic vasoconstriction. Intrahepatic vasoconstriction in turn increases portal pressure and impairs adaptability of the intrahepatic vessels to respond to changes in portal blood flow thus accentuating the effect of increase in portal blood flow on portal pressure[17](FIG.5)[9].

Causes of Cirrhosis :

- Chronic alcohol use
- Chronic viral hepatitis:Hepatitis B,Hepatitis C
- Inherited metabolic liver disease

- Hemochromatosis
- Wilsons disease
- α-1 Antitrypsin deficiency
- Cystic fibrosis

- Autoimmune hepatitis
- Nonalcoholic steatohepatitis
- Cardiac cirrhosis
- Cryptogenic cirrhosis
- Chronic cholestatic syndromes

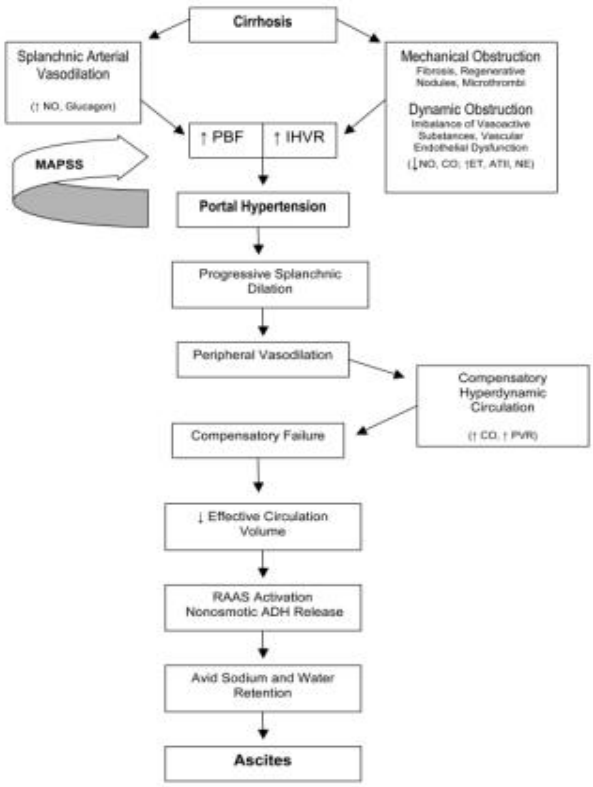


FIG.5: Pathophysiology of intrahepatic sinusoidal portal hypertension and ascites formation in cirrhosis.

C] Post – hepatic causes :

1. Inferior vena cava obstruction : This may be due to thrombus, tumours, membranous webs, or due to extrinsic compression.

2. Hepatic vein obstruction : Budd–Chiari syndrome can cause hepatic vein thrombosis. Veno-occlusive diseases can cause non-thrombotic obstruction of small hepatic veins. Post hepatic obstructions generally cause congestive hepatomegaly with vena cava collaterals.
3. Cardiac disease : Elevated pressures on the right side of the heart can be reflected back via the inferior vena cava to the hepatic veins and on to the hepatic sinusoids and the portal vein.

HAEMODYNAMICS:

Portal hypertension is caused by either an increase in hepatic vascular resistance or portal venous inflow[18]. There are two fields of view concerning the dynamics of blood flow in portal hypertension.

a)According to Ohm's law, if the resistance increased and the blood flow was constant, it would lead to an increase in pressure. This theory is the basis for the' backward flow theory of portal hypertension'. This theory states that the increase in pressure is due to increased vascular resistance. In addition, increased IHVR (intrahepatic venous resistance) is caused by dynamic changes in sinusoidal tone resulting in mechanical obstruction (Fig 6)[10-12]. The SECs normally produce vasoactive substances that regulate sinusoidal resistance. These include vasodilatory substances such as NO, carbon monoxide, and prostaglandin E2, and vasoconstrictors such as endothelin-1, angiotensin II, leukotrienes, and norepinephrine. In the diseased liver, overproduction of inflammatory mediators and the resultant oxidative stress cause SEC (sinusoidal endothelial cell) dysfunction, which leads to overproduction and enhanced sensitivity to

vasoconstrictors and underproduction of vasodilators. The net result is impaired sinusoidal relaxation[12]. The intrahepatic NO deficiency in portal hypertension is primarily caused by decreased endothelial nitric oxide synthase (NOS) activation[10,13,19]. Activation of hepatic stellate cells, lipid-storing cells surrounding the sinusoids, also lead to increased IHVR. Injury causes stellate cells to differentiate into contractile, fibrogenic myofibroblasts, which are involved in production of large amounts of extracellular matrix and secretion of inflammatory cytokines and vasoconstrictive substances like endothelin-1. These vasoconstrictors work in an autocrine fashion in stimulating contraction of stellate cell, that results in the reduction of the sinusoidal space diameter and increased IHVR[10,19].

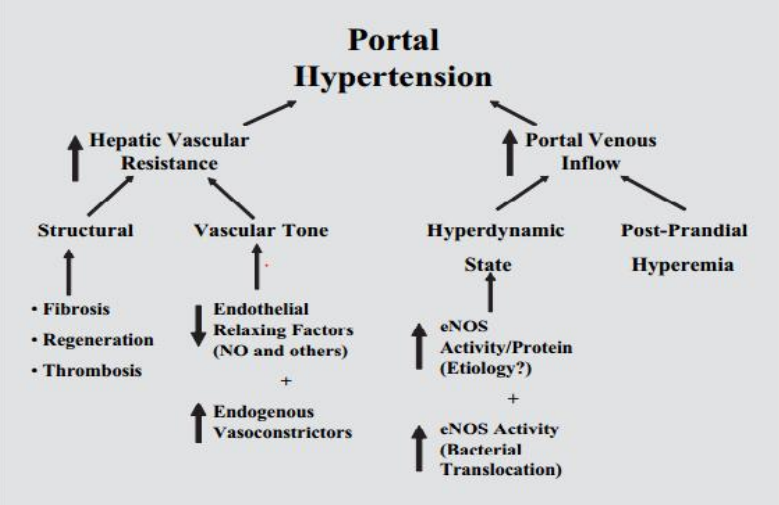


Fig. 6 overview of mechanisms contributing to portal hypertension.

b)The blood flow entering the portal venous system is greatly increased by an increment made up of blood that bypasses the liver in portosystemic shunts even though the hepatic flow may be reduced. There is marked increase in the splanchnic blood flow and most of this flow is shunted around the liver. This hyperkinetic circulation has a role

in elevation and maintenances of the portal pressure. It is characterized by decreased arteriolar resistance, peripheral vasodilatation in many vascular beds, such as, the splanchic, renal and skeletal muscle circulation. Vasodilatation is accompanied by increased cardiac output. This hyperdynamic circulatory state has been termed as the 'forward flow theory of portal hypertension. Unlike the vasoconstriction seen in the intrahepatic vasculature during PH, the splanchnic vasculature undergoes progressive vasodilatation because of an excess of vasodilatory substances, particularly NO[10,19]. The mechanisms responsible for the overproduction of NO include increased vascular shear stress and intestinal absorption of lipopolysaccharide. Other substances that contribute to peripheral vasodilatation include hydrogen sulfide, carbon monoxide, prostaglandins, and endocannabinoids. The combined action of the all these vasodilatory compounds mediates progressive and sustained vasodilatation of the splanchnic circulation leading to higher PBF, which maintains and aggravates the development of PH (Fig 6)[9].

Therefore, structural changes (fibrosis, thrombosis) together with increased vascular tone mediated by intrinsic and extrinsic vasoconstrictors and vasodilators are accompanied by a hyperdynamic state due to arterial underfilling and secondary fluid retention. Further consequences of portal hypertension include an increase in blood flow which will lead to a hyperdynamic state with fluid retention, leading to secondary involvement of other organs, such as cirrhotic cardiomyopathy, hepatopulmonary syndrome and hepatorenal syndrome. Finally, portal hypertension will end up in the formation of collateral vessels (varices)[12].

Porto-systemic collateral vessels develop in response to an increase in portal pressure. These collateral vessels form through the opening of pre-existing vessels or

angiogenesis[18] and are known to cause serious complications, including variceal bleeding and hepatic encephalopathy. A change in portal pressure is thought to be detected first by the intestinal microcircular vascular bed, followed by arteries of the splanchnic circulation. Subsequently, these vascular beds generate various angiogenic factors, such as VEGF and placental growth factor (PlGF), which promote the formation of porto-systemic collaterals[20].

The clinical syndrome of portal hypertension is constitited by collateral circulation formation which leads to directly communication between the portal blood vessels and systemic circulation, bypassing the liver[21,22]. Clinically significant portal hypertension refers to an increase in HVPG ≥ 10 mm of Hg; which marks the threshold for the development of complications of portal hypertension[23]. Portosystemic collaterals formation is a complex process of decompression of the portal system through opening, dilatation and hypertrophy of pre-existing vascular channels [24].

Whenever the portal circulation encounters an increase in resistance, wherever the block may be, a system of collateral circulation is established to return the blood to the systemic vein. Normally entire portal blood flow (100%) is recovered by the hepatic veins. The normal blood flow in the portal vein is about 1200 ml/min and the flow in hepatic artery is 400 ml/min. The normal hepatic vein flow is 1600 ml/min. In cases of obstruction to the blood flow at an intrahepatic level such as in cirrhosis, the hepatic veins only receive around 13% of the blood flow, the rest being shunted through the collateral circulation[24].

Anatomic sites of Portosystemic confluence:

Varices constitute the dilated end-organ veins that are vulnerable to bleed whereas shunts form the dilated collateral channels bridging between the portal and systemic vascular beds. Numerous and widespread portosystemic collateral channels can develop in portal hypertension with varied appearance. Intrathoracic manifestations of portosystemic collateral vessels characteristically develop by way of the coronary vein into esophageal or paraesophageal (22%-38%) varices and cardiophrenic varices (18%)[21]. Other common sites of portosystemic shunting involve paraumbilical, gastroesophageal, splenorenal, and inferior mesenteric collateral vessels. Other less common pathways for decompression of portal vein include pleuro-pericardialperitoneal, splenoazygos, pancreaticoduodenal and mesocaval collaterals (Figure 7).

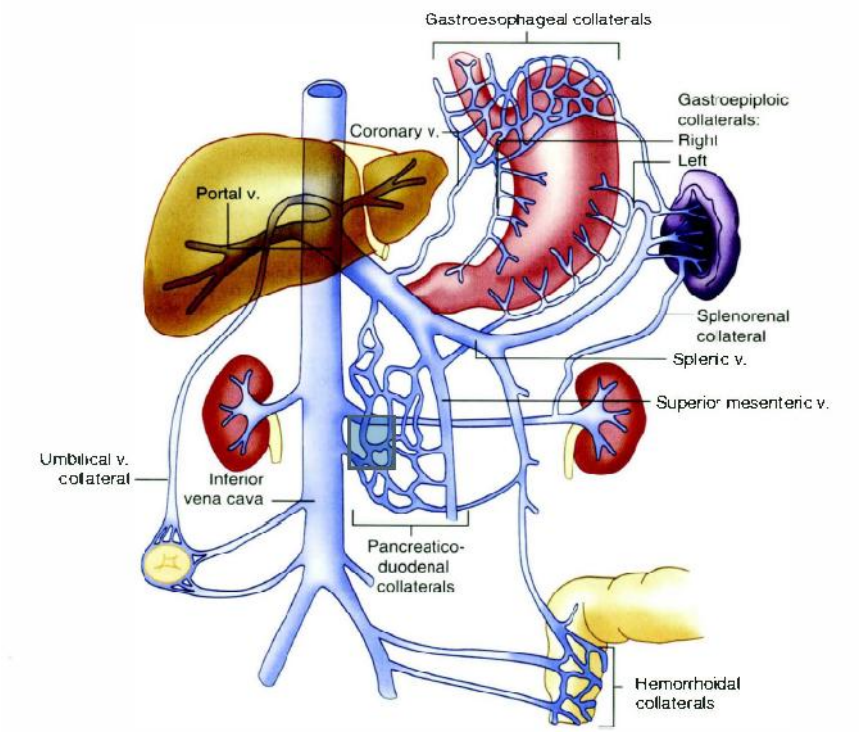


FIG. 7: Major portosystemic collaterals.

a) Esophageal, Paraesophageal, Coronary and Cardiophrenic Varices:

Coronary (or left gastric) veins that lies in the lesser omentum are the most frequently encountered varices, which are usually present in 80% of cross-sectional and 86% of angiographic studies in patients with portal hypertension[25]. A coronary vein larger than 5-6 mm in diameter on colour Doppler sonography or CT scan is considered abnormal and is suggestive of portal hypertension[25]. Esophageal or paraesophageal varices usually accompany the coronary venous collaterals. Anterior and posterior branches of the left gastric vein supplies the esophageal and paraesophageal varices respectively[25]. Esophageal varices (EV) are the most common and clinically important collateral vessels which are made up of dilated subepithelial and submucosal veins in the lower esophagus wall. Later these drain into the azygos or the hemiazygos system. The reported rate of variceal hemorrhage in patients with esophageal varices is estimated at 10%-30% per year, with the mortality from variceal hemorrhage high at 20%-35%[26]. Paraesophageal varices consists of venous collaterals which surround the esophagus through a network of multiple veins and connect the coronary vein with the azygos, hemiazygos veins and the vertebral plexus. As they are located external to the walls of the esophagus, they are not visualized with endoscopy. Their clinical significance is not entirely clear, however, Lin *et al* described that paraesophageal varices seen on chest CT carries a poor prognosis for patients with esophageal variceal hemorrhage undergoing sclerotherapy. Cardiophrenic angle varices are dilated pericardiacophrenic veins, which are seen in cirrhotic patients due to membranous obstruction of the inferior vena cava (IVC) with a prevalence of 18%. On radiography, they present as undulating masses along the cardiac borders, mimicking a tumor[26].

b) **Gastric Varices And Gastrorenal Shunts:**

Gastric varices together with esophageal varices, are the most common portosystemic pathways seen in portal hypertension with the reported prevalence ranging between 2% to 70%. Both these varices coexist frequently, as illustrated in the widely used Sarin endoscopic grading classification for gastric varices (Table 2)[21] (Fig.8)[27]. Gastric varices are usually supplied by the short gastric and posterior gastric veins, unlike Esophageal varices, which are more commonly supplied by the left gastric or the coronary vein. Dilated short gastric veins appear as a tortuous vessels in the medial aspect of the spleen near the hilum, making it difficult in distinguishing between the gastric fundus and individual vessels. Gastric varices are known to mimic tumors or thickening of rugae at endoscopy or barium study. Gastric varices usually drain into the esophageal or paraesophageal veins, but occasionally it can also drain into the left renal vein through a gastrorenal shunt. A gastrorenal shunt appears as a large left sided retroperitoneal venous channel, associated with left renal vein dilatation. These shunts may arise from pre-existing tiny portosystemic channels or from the adrenal and periadrenal venous system. In patients with gastrorenal shunts, large gastric varices may be seen in the absence of esophageal varices[21,27].

Category	**Description**
Gastroesophageal varix Type I	Continuation from esophageal varices extending along the lesser curve
Gastroesophageal varix Type II	Similar to type I but are more tortuous

Isolated gastric varix Type I	Varices are complex and tortuous occurings in the absence of esophageal varices and are located in the gastric fundus.
Isolated gastric varix Type II	located at the gastric body, antrum or pylorus and occur in the absence of esophageal varices.

Table 2: Sarin endoscopic grading classification for gastric varices

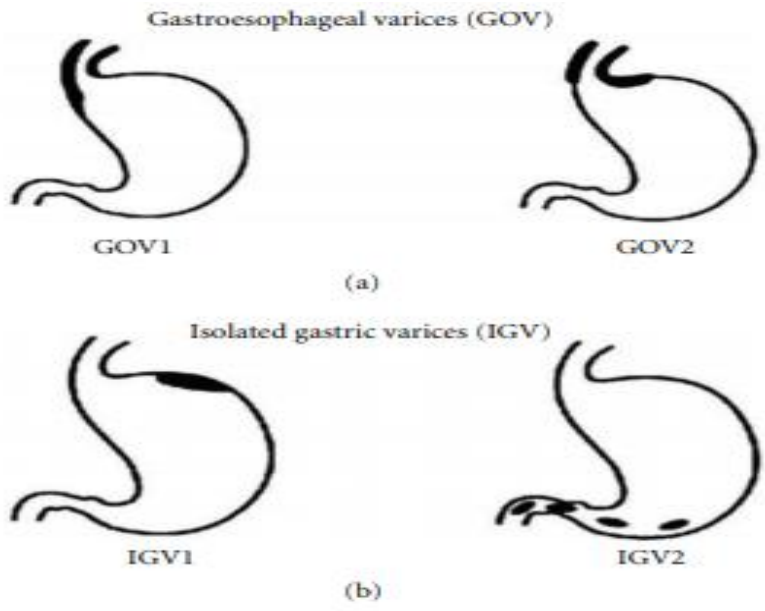


FIG. 8 : Sarin classification of gastric varices

c) **Perisplenic Varices, Splenorenal and Splenocaval/ Splenoazygos Shunts:**

Splenic varices which traverses through the splenocolic ligament are seen as dilated veins in the anteroinferior aspect of the spleen. there can be communication between perisplenic collaterals and the gastric veins. It should be noted that the dilated splenic veins commonly seen at the hilum of the enlarged spleen should not be called as perisplenic varices. A spontaneous splenorenal shunt is usually seen as large, tortuous

veins, in the region of the splenic and left renal hilum draining into an dilated left renal vein (Figure 9a)[25]. These shunts are so tortuous that it is difficult to locate the exact origin of the connection along the splenic vein. In the rare case of a splenocaval shunt, large veins can be seen extending from the lower aspect of the spleen to the pelvis and draining into the inferior vena cava through the left internal iliac vein or gonadal vein. Splenoazygos shunts comprise portal decompression through splenic vein to hemiazygos vein or posterior abdominal wall veins, which are best demonstrated on CT[21].

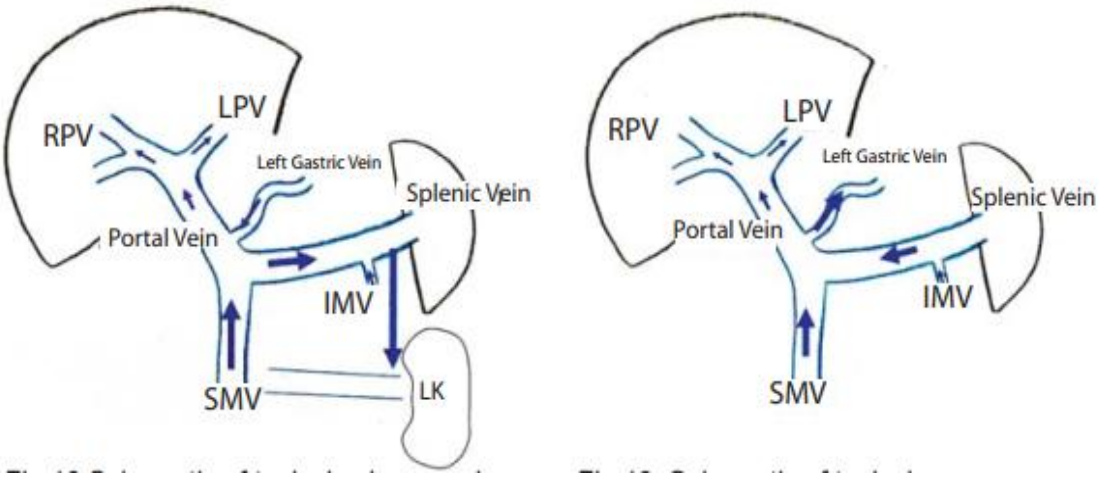


FIG.9 : schematic of a) splenorenal and b) gastroesophageal collateral flow pattern

D) **Paraumbilical and Abdominal Wall Collaterals:**

The paraumbilical vein arising from the left portal vein courses between the medial and lateral segments of the left hepatic lobe, along the anterior edge of the falciform ligament. The number and course of the paraumbilical collaterals is variable. On cross-sectional imaging, paraumbilical varices are seen as tubular structures greater than 2-3 mm in

diameter, anastomosing with the superior epigastric or internal thoracic veins. From there, drainage is typically either into the superior vena cava or anastomose with inferior epigastric vein to drain into the inferior vena cava via the external iliac vein. Occasionally, the paraumbilical vein drains into the abdominal veins, creating a "Medusa's head" appearance. The paraumbilical system is considered as a frequent abdominal portosystemic shunt, with reported prevalence of 30%-35%[21] (Fig.10)[25].

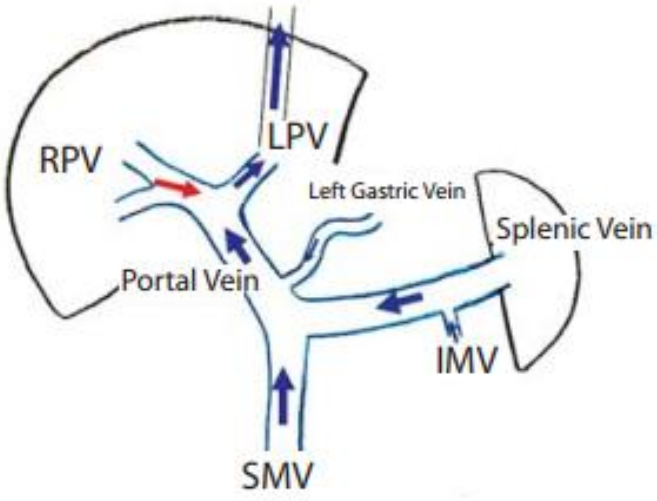


FIG. 10 : schematic of Paraumbilical collateral

E) **Omental And Mesenteric Collaterals:**

Omental collateral vessels are less commonly included in list of frequent portosystemic pathways because they are not well visualized with angiography or other modalities. Mesenteric collateral vessels are commonly seen as dilated and tortuous branches of the superior mesenteric vein within the mesenteric fat. These collateral vessels finally drain into the systemic venous system through the retroperitoneal or pelvic veins[21].

F) Rectal collaterals:

Rectal varices present as a dilation of the submucosal veins and constitute a pathway for portal venous flow between the superior rectal veins, a branch of the inferior mesenteric system and the middle inferior rectal veins from the iliac system[28]. Direct correlation exists between the progression of cirrhosis reflected by the Child Pugh or MELD scores and the degree of hyperdynamic circulation[29]. Hosking et al studied 100 patients with cirrhosis and reported that the overall prevalence of rectal varices was 44%, this prevalence increased with the degree of portal hypertension. In this study, hemorrhoids occurred independently of the presence of rectal varices and 30% of patients had rectal varices and coexistent hemorrhoids. However, a large study conducted in Japan by Watanabe et al[30] reported that 95% of patients with rectal varices had a history of esophageal varices and 87% of these patients had previously undergone endoscopic variceal obliteration for esophageal varices. The mechanism of rectal varices after treatment of esophageal or gastric varices is thought to be the result of obliteration of supplying vessels such as the left gastric, posterior gastric and short gastric veins leading to development of collateral vessels of the inferior mesenteric venous system and thus the formation of rectal varices. In this nationally representative study in Japan, the most frequent afferent vessel to the rectal varices was the inferior mesenteric vein, followed by the superior rectal vein and the efferent vessels included the internal iliac vein and the inferior rectal vein[30].

G) **Other Collateral Vessels:** There may be communication with the intrahepatic portal veins and hepatic venous branches or direct collateral formation with the left gastric vein, usually in the left lobe. A loose collateral plexus over the liver surface sometimes is broadly distributed over the parietal peritoneum, with branches piercing the diaphragm to join pericardial, pleural, and pulmonary veins (pleuropericardial-peritoneal collaterals)[26]. In the past, the term vein of Sappey was used indicating these small diaphragmatic collaterals, but it is now regarded as synonymous with the paraumbilical vein[21].

CONSEQUENCES OF PORTAL HYPERTENSION[27]:

a) Ascites: It occurs as a consequence of imbalances in Starling's law so that the forces keeping fluid in the vascular space are less than the forces moving fluid out of the vascular space[11,31]. In PH, increased PVP drives fluid into the interstitial space. When the capacity of the regional lymphatics is overwhelmed, ascites develops. The development of ascites is perpetuated by the splanchnic vasodilatation that accompanies PH. This vasodilatation results in pooling of blood in the abdomen, which leads to a decrease in effective systemic blood volume (FIG 11)[9]. Concurrent hypoalbuminemia secondary to hepatic synthetic failure lowers vascular colloid osmotic pressure that furthers aggravates ascites formation[31].

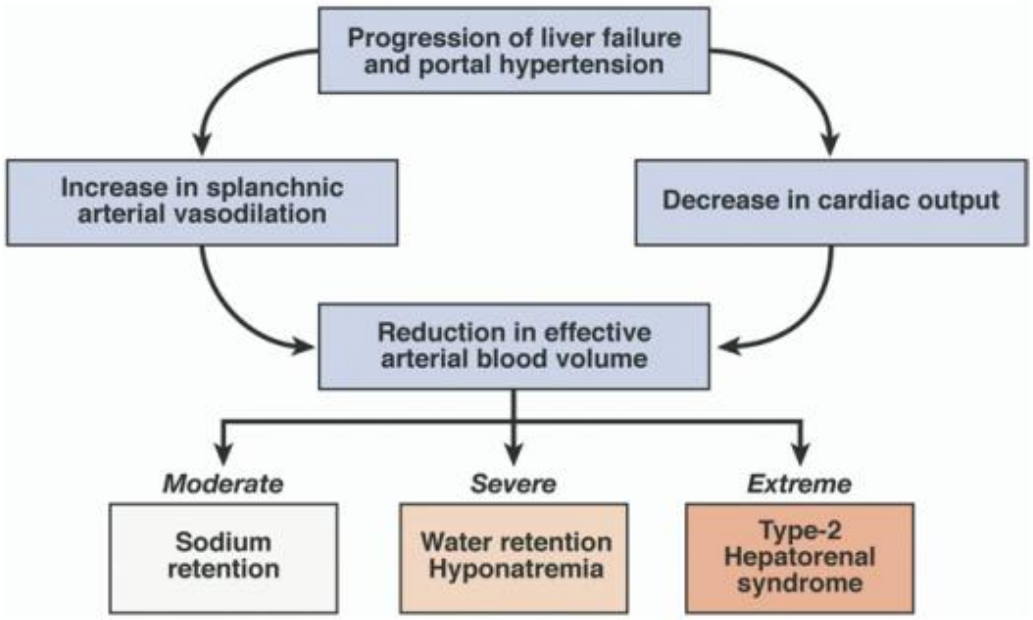


FIG.11 : Pathophysiology of ascites and hepatorenal syndrome.

b) Hepatic Encephalopathy: is a syndrome of neurocognitive impairment that clinically is manifested as a range of signs from subtle behavioral deficits to stupor and coma. The pathogenesis is multifactorial, and associated with toxins derived from the gastrointestinal tract that bypass hepatic metabolism.

c) Hyponatremia: The same forces that promote ascites formation can lead to development of dilutional (hypervolemic) hyponatremia. In human patients with cirrhosis, the development of hyponatremia is a marker of late stage disease and a negative prognostic indicator.

d) Hepatorenal Syndrome: a form of reversible renal failure, occurs as a consequence of profound renal vasoconstriction secondary to the release of angiotensin, norepinephrine, and ADH in response to splanchnic vasodilatation.

In humans, the syndrome is always accompanied by a state of refractory ascites and end-stage liver failure (FIG 11)[9].

e) Hepatopulmonary Syndrome, Portopulmonary Syndrome, and Hepatic Hydrothorax: Hepatopulmonary syndrome occurs because of microvascular pulmonary arterial dilatation leading to ventilation-perfusion mismatch. Portopulmonary hypertension is likely mediated by humoral substances that enter the systemic circulation through MAPSS. Initially, these substances cause vasoconstriction, but subsequent thrombosis leads to vessel obliteration. Hepatic hydrothorax is the presence of pleural effusion in patients with hepatobiliary disease[27].

f) Spontaneous Bacterial Peritonitis: is infection of ascetic fluid without a detectable nidus.

g) Hypersplenism: Splenomegaly is a common in humans with PH and can lead to hypersplenism.

h) Portal Hypertensive Gastropathy: In humans, gastric mucosal lesions associated with portal hypertensive gastropathy are present in 51–98% of patients with PH.

CLINICAL FEATURES OF PORTAL HYPERTENSION[32]:

History and general examination :

Patients usually presents with abdominal distention, haematemesis, jaundice, malena or symptoms of hepatic encephalopathy like lethargy, irritability and change in sleep pattern. History of alcoholism or jaundice should be asked. History of blood transfusion and lifestyles that predispose to hepatitis B or C should be asked. History of neonatal infection or umbilical sepsis should be considered if extrahepatic portal

hypertension due to thrombosis of portal vein is suspected. The signs of cirrhosis such as icterus, ascites, spidernaevi, palmar erythema should be looked for[27].

The most important, dreaded and dramatic presentation of PH is GI bleeding and is the commonest reason for patients to visit a hospital. Bleeding is spontaneous, profuse, and painless. Most of the time bleeding is from esophageal varices. In about 2-10% cases the bleeding may be from gastric varices. In cirrhotics about 30% patients with varices will bleed. Generally bleeding stops spontaneously in 50% patients. There are about 70% chances of rebleed within a year. About 20-30% patients are likely to die in each episode of bleeding. Risk of death is higher in cirrhotics especially with poor liver function, like in Child's Group C where the risk of death is about 70%[27].

In intrahepatic obstruction the epigastric veins may be dilated via the paraumbilical vein. In extrahepatic obstruction the veins of the left flank may be dilated. Prominent veins radiating outwards form the umbilicus are termed caput medusa. A venous hum may be heard on auscultation in the epigastrium. An enlarged spleen is the most important clinical sign of portal hypertension and is present in all cases of PHT. The splenic enlargement is maximal in cases of noncirrhotic portal fibrosis (NCPF)[27].

Ascites indicates hepatic decompensation. This occurs due to a combination of factors such as increased capillary filtration pressure, increased lymphatic flow and decrease in plasma oncotic pressure. Ascites in cirrhosis always points to liver cell failure in addition to portal hypertension.

Anorectal varices are dilated veins that originate more than 4 cm above the anal verge, clearly distinct from hemorrhoids, and not contiguous with the anal columns and/or

pectinate line. Anorectal varices are seen with sigmoidoscopy. They are visualized as blue tinted submucosal elevations located near the anus[33].

LABORATORY INVESTIGATIONS:

Laboratory investigation are not specific for portal hypertension and they can merely show defects in liver function. Anemia, hyperbilirubinemia, hypoproteinemia and impaired coagulation are the features associated with liver disorders which may be present in concurrence with portal hypertension[34]. A combination of markers of liver synthetic function (albumin, bilirubin and prothrombin time) that, together with two clinical variables (presence and severity of ascites and encephalopathy), constitute the Child-Pugh score[35].

Various indices have also been proposed for the evaluation of portal hypertension and/or the presence of EV[36].

The ratio of platelet count to spleen diameter (Plt/Spl) was reported to be strongly associated with the presence of esophageal collaterals, as shown in a multivariate analysis. A Plt/Spl cut-off value of 909 had 100% negative predictive value for diagnosis of EV[36].

A study combining albumin, aspartate aminotransferase (AST) and the international normalized ratio (INR) had an area under the receiver operating characteristic curve (AUROC) of 0.952 for prediction of clinically significant portal hypertension (CSPH) in a patients with compensated cirrhosis[37].

In a study by Sebastiani *et al*[38], "a combination of the Lok index (an index derived by AST and alanine aminotransferase (ALT) levels, platelet counts and prothrombin time (PT)INR; using a cutoff of 1.5) and the Forns' index (an index derived by age, platelet

counts, gammaglutamyl transferase (GGT) and cholesterol; using a cutoff of 8.8 had an AUROC of 0.80 (95%CI: 0.760.84) and a high negative predictive value (> 90%) for excluding clinically relevant EV".

These tests do not allow for clinical decisions on their own; although, they may be sufficient in use as a first level test[39], but their use would not exempt a clinician from undertaking further analysis with more accurate tests[40].

REVIEW OF LITERATURE

HISTORICAL ASPECTS :

In 1543, Vesalius drew an anatomical picture of the portal venous system (Figure 12) to which not much has been added [41]. In the 1650s, only 25 years after Harvey's discovery of the blood circulation, 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. Vesalius had already touched on the core of the pathophysiology by describing a case of bleeding haemorrhoids and suggested that this was due to a dilatation of the portal branches. During nineteenth century it became increasingly clear that the clinical picture of splenomegaly, ascites and gastrointestinal haemorrhage generally was due to obstruction to the flow in the portal system.The term portal hypertension was introduced by Gilbert in 1902[41]. The earliest pressure measurement of the portal circulation were carried out by Thompson and colleagues in 1937[42].Warren and Brannon successfully catheterized the hepatic veins in 1944[43.] Whipple classified portal hypertension into its intra and extra–hepatic types. Blackmore and Whipple instituted surgical therapy for portal hypertension in 1945[44].

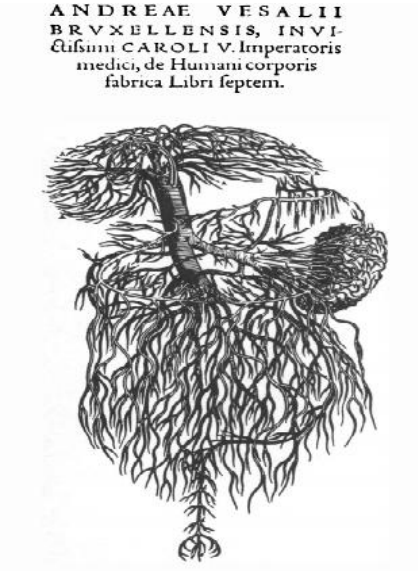


FIG 12 : Vesalius`s pictorial of the portal venous system

In 1942, Karl Theodore Dussik first used ultrasonic beams transmitting through the head to diagnose brain tumors, thereby becoming the pioneer of diagnostic ultrasound.

Douglass Howry with the help of Joseph Holmes in 1951 developed a B-mode linear compound ultrasound scanner.

In 1955, Shigeo Satomura and his team implemented Doppler shift techniques, which was first postulated by Christian Doppler in 1842[45], in monitoring the pulsations of a heart and peripheral blood vessels.

Frank Barber, Don Baker and John Reid in 1974, developed the first duplex pulsed Doppler scanner[46].

In 1981, Dokmeci and coworkers evaluated portosystemic collaterals by way of ultrasonography (USG). The standard of diagnosis for collaterals in PHT at the time was splenoportography, abdominal angiography, or percutaneous transhepatic portography which were quite invasive. The frequency of collateral detection using USG was 85% for coronary, 100% for paraumbilical, and 10% for short gastric veins (SGV). The authors concluded that real time sonography needs to be the first-choice procedure in demonstration of collateral veins and diagnosis of portal hypertension[47].

In 1983, Quantum Medical Systems introduced the concept of real time color Doppler imaging at the American Institute of Ultrasound in Medicine meeting.

Later in 1985, Chihiro Kasai, Koroku Namekawa and Ryozo Omoto realized that real time color flow imaging could be a practical possibility. Power Doppler imaging was

added to the Doppler imaging arsenal in 1993 through the work of Jonathan M. Rubin and Ronald S. Adler[48].

Patriquin et al in 1987 assessed PHT using qualitative Doppler Sonography and discovered that portal collateral pathways could be easily delineated using techniques that assessed portal blood flow volume, selective flow-velocity measurements, direction, and change in abdominal anatomy. They found that there was a significant association between upper gastrointestinal bleeding and size of left gastric vein (LGV) and esophagogastroscopy was important in such patients, where sclera-therapeutic procedures could be offered[47].

DIAGNOSTIC IMAGING IN PORTAL HYPERTENSION :

a) X - RAY of the Abdomen and Chest:

In 1975, P.J Moult et al conducted splenic venograms on 304 cases for suspected portal hypertension, Oesophageal collaterals had been filled on 145 occasions. In seven of these patients a plain chest radiograph shows a lower posterior mediastinal mass, which corresponds to dilated portosystemic collaterals on the splenic venogram. These seven patients form the subject of this report. Other patients with large oesophageal or paraoesophageal collaterals have been excluded when no mass is seen on the plain radiograph, either because the veins overlie the vertebral column in the anterior projection, or because they cannot be distinguished from the shadow of the descending aorta or the mediastinal pleural reflection[49].

In 1992, Ayuso et al[50] reviewed 10 patients with long-standing portal hypertension and calcification in portal vein, the splenoportal and mesenteric venous systems or

collateral vessels which were examined with abdominal plain film and CT. Calcium was seen on CT scans in nine cases and on abdominal plain films in only five.

A review of 21 cases of portal vein calcification reported by Kawasaki et al[51] in 1993, "revealed that the average age was 53.7 ± 10.2 years and the male-to-female ratio was 17:4, reflecting the higher morbidity in adult men. All the reported cases of portal vein calcification were associated with portal hypertension, and there was histological evidence of cirrhosis in the majority of cases. Most patients had esophageal varices and a clinical history of hematemesis".

In 2015, *Yen TS* et al[52] conducted retrospective study including more than 3000 cases from 2005 to 2014 and a total of 12 patients venous calcifications and symptoms of phlebosclerotic colitis were enrolled. "Among these 12 patients, the mean age of the six males and the six females was 61.8 ± 11.5 years. All patients exhibited typical imaging characteristics, consisting of threadlike calcifications and colonic wall thickening in the standard abdominal radiographs and calcifications along the colonic and mesenteric vessels or associated with colonic wall thickening and adjacent fat stranding in the computed tomography images. The median score of the severity of the venous calcifications was 18 ± 13, and the median number of active disease episodes was 1 ± 1.75. Spearman's correlation analysis revealed that the number of episodes of active phlebosclerotic colitis disease significantly positively correlated with the severity of the calcification of the mesenteric veins ($r = 0.619$, $P < 0.05$)".

Calcification in the portal vein or its tributaries visible on abdominal radiography is a rare radiological finding, and almost always occurs in patients with long-standing portal hypertension, regardless of underlying etiology [53].

Tomography of the azygos vein may show enlargement as the collateral flow enters the azygos system. A widened left paravertebral shadow may be due to lateral displacement of the pleural reflection between the aorta and vertebral column by a dilated hemiazygos vein. Massively dilated paraoesophageal collaterals may be seen on the chest radiograph as a retrocardiac posterior mediastinal mass[14].

b) Barium Studies:

In 1993, Ginai et al[54] conducted a blind radiological/endoscopic comparative study using endoscopy as the gold standard was retrospectively carried out in 72 patients. A prospective study was then carried out in 47 patients to define the validity of the radiological criteria found by the first study. Out of the 72 patients in the first study, 33 cases had endoscopically absent or small varices , while 39 cases had larger varices. The results of both studies showed that the length and the width of the mucosal folds representing varices as measured on barium swallow radiographs have a significant relationship with the grade of the varices as determined by endoscopy. They conclude that barium swallow is a quick and reliable method for quantitative assessment of oesophageal varices.

In 2000, Chang et al[55] "reviewed eight cases who underwent upper gastrointestinal barium examinations of 118 patients with endoscopically diagnosed portal hypertensive gastropathy. Four of the eight patients underwent doublecontrast

examinations and the other four had single-contrast examinations. Five (63%) of the eight patients with portal hypertensive gastropathy had thickened gastric folds, which had a mean thickness of 10 mm (range, 8–12 mm). The enlarged folds involved only the fundus in four patients and the fundus and body in one. In all five patients, the thickened folds had a nodular appearance with undulating contours and indistinct borders. When the double-contrast and single-contrast studies were considered separately, thickened folds were detected in three (75%) of four patients on doublecontrast examinations and in two (50%) of four on single-contrast examinations. Finally, five (71%) of seven patients with esophageal varices at endoscopy had radiographic evidence of esophageal varices".

Barium studies can reveal varices of the esophagus, stomach and duodenum. However, these studies have been largely superseded by upper gastrointestinal endoscopy. Oesophageal varices show as filling defects in the regular contour of the oesophagus. They are most often in the lower third, but may spread upwards so that the entire oesophagus is involved. Widening and finally gross dilatation are helpful signs[10a]. Gastric varices pass through the cardia, line the fundus in a worm - like fashion and may be difficult to distinguish from mucosal folds. Occasionally gastric varices show as a lobulated mass in the gastric fundus simulating a carcinoma. Portal venography is useful in differentiation[14].

c) Endoscopic Ultrasound:

In 1996, Choudhuri et al[56] "conducted EUS examination was performed on the upper stomach, GE junction, and lower esophagus in 50 patients with liver cirrhosis, 20 of whom had small (grades 1 & 2) and 30 had large (grades 3 & 4) esophageal varices. Esophageal varices could be detected in all the 30 (100%) patients with large, but in 9

(45%) of patients with small varices. Gastric Varices were detected significantly more often by EUS (33; 66%) compared with endoscopy (17; 34%, $p < 0.005$). The mean number (2.8 +/- 1.4 and 4.7 +/- 1.78, $p < 0.0005$) and size 3.41 +/- 0.57 and 5.98 +/- 1.66, $p < 0.00001$) of paraesophageal veins were higher in patients with large varices compared with those with small varices. When the lower 5 cm of the esophagus was scanned in patients with small and large varices, perforating veins connecting the para-esophageal and the submucosal veins (varices) could be identified in 3 (15%) and 21 (70%, $p < 0.0005$) of patients, respectively".

In 2002, Konishi Y et al[57] "studied thirty consecutive patients with esophageal varices at high risk for bleeding using endoscopic ultrasound (EUS) and conventional endoscopy. EUS before endoscopic variceal ligation demonstrated cardial submucosal varices in all patients, whereas conventional endoscopy revealed cardial varices in only 21 patients (70.0%, NS). Patients with recurrent esophageal varices after endoscopic variceal ligation were more likely to have severe-grade perforating veins before treatment than those without recurrence (71.4% vs. 12.5%, $p < 0.01$). Patients with recurrent esophageal varices after endoscopic variceal ligation were more likely to have severe-grade perforating veins before treatment than those without recurrence (71.4% vs. 12.5%, $p < 0.01$). Patients with severe as opposed to mild-grade perforating veins before treatment had a significantly higher recurrence rate (90.9% vs. 21.0%, $p < 0.01$%).Hence, EUS findings for cardial vascular structures before treatment are useful for predicting the likelihood of recurrence of esophageal varices".

In 2002, Lee Y T et al[58] studied "a total of 52 cirrhotic and 166 dyspeptic patients. EUS identified esophageal varices (EV) endoscopically in 28 patients (53.8 %), which

showed a good correlation with EGD findings ($r = 0.855$, $P < 0.001$). The red color sign and portal hypertensive gastropathy were diagnosed in six and seven patients, respectively, by both methods. EUS detected gastric varices sonographically in 16 patients (30.8 %), compared with detection in nine patients by EGD. Extraluminal venous abnormalities were detected in 48 cirrhotic patients (92 %) and in only nine dyspeptic patients (5.4 %) ($P < 0.001$). The size of extraluminal adventitial venous dilatation was significantly correlated with the severity of GEV and cirrhosis ($P < 0.001$). Perforating veins were identified in all patients with GEV".

In 2009, Sato et al[59] "retrospectively evaluated hemodynamics of esophageal varices in 306 patients before and after endoscopic injection sclerotherapy (EIS) using endoscopic color Doppler ultrasonography (ECDUS). The patients were divided into three groups according to time of esophageal variceal recurrence: early recurrence within one year (Group A, n = 16), no recurrence over three years (Group B, n = 12), and recurrence between one and three years (Group C, n = 278). Before EIS, the frequency of detection of perforating veins and the inflowing type of perforating veins using ECDUS was significantly higher for Group A than Groups B or C. After EIS, the frequency of detection of cardiac intramural veins, perforating veins and the inflowing type of perforating veins using ECDUS was significantly higher in Group A than Groups B or C. Hence, Endoscopic ultrasonographic evaluation of the hemodynamics in esophageal varices before and after EIS enables prediction of early variceal recurrence".

Endoscopic ultrasound with its ability to provide both endoscopic and ultrasonographic visualization has expanded the diagnostic and therapeutic armamentarium in patients with portal hypertension. Endoscopic ultrasound has been used to study gastroesophageal

varices and to identify high risks of bleeding by determining the size of the varix on crosssectional imaging[60]. EUS can effectively measure the size of EV by using the sum of the cross-sectional surface area of all the EV in the distal third of the esophagus[60]. While upper gastrointestinal endoscopy continues to be the gold standard in detecting EV, EUS has better sensitivity in detecting gastric varices. Since EUS can detect vascular changes better, some experts believe that EUS can easily differentiate thickened gastric folds from small gastric varices that can be difficult to diagnose via EGD. EUS like EGD can not only diagnose esophageal and gastric varices but can also predict the risk of bleeding[60].

d) ULTRASOUND DOPPLER[61]:

Ultrasonography (US) is the first-line imaging technique recommended for the diagnosis and follow-up of patients with portal hypertension[62], since it is noninvasive, repeatable, inexpensive and can be performed at bedside. US is highly specific for the diagnosis of cirrhosis and portal hypertension.

In the work up of any patient with portal hypertension the following parameters are important:

- Portal vein diameter
- Response of portal vein to respiration
- Portal flow direction.
- Portal flow velocity and waveform.
- Portal and splenic venous flow.
- Splenic size.
- Collateral circulation.

PORTAL VEIN DIAMETER :

In 1990, Goyal et al[63] conducted a study on 100 normal healthy subjects and 50 patients with PH. Considering the fasting state, supine decubitus, and deep inspiration as suitable and standard variables, the diameters were compared in 100 healthy subjects and 50 patients with portal hypertension. The upper normal limits of portal, splenic, and superior mesenteric vein diameters were reported as 16, 12, and 11 mm, respectively, and the dimensions above these values provided an overall sensitivity of 72%, an accuracy of 91%, and a specificity of 100% in diagnosing the patients with suspected portal hypertension.

In 2001, F.Schepis et al[64] conducted Doppler study on one hundred forty-three compensated cirrhotic patients, using stepwise logistic regression, presence of esophageal varices was independently predicted by ultrasonographic portal vein diameter greater than 13 mm (OR: 2.92; 95% CI: 1.3-6.4). The discriminating ability of the prediction rule was relevant (area under the curve: 0.80) and did not change by replacing ultrasonographic portal vein diameter with congestion index of portal vein. We concluded that compensated cirrhotic patients should be screened by upper gastrointestinal endoscopy when platelet count less than 100 x 10(9)/L, and ultrasonographic portal vein diameter greater than 13 mm are observed, whereas those without any of these predictors should not undergo endoscopy.

In 2005, Perisic et al[65] conducted a dppler hemodynamic study in 30 patients with liver cirrhosis and portal hypertension, significant correlation was found between the diameters of the right liver lobe and the portal vein (p=0.01), mean portal vein diameter

significantly increases (p=0.01) in patients with HE (14.87 +/- 1.86mm), compared to those without HE (13.2 +/- 2.31mm).

In 2005, Rokni YH[66] conducted a study on 46 biopsy proven cases of cirrhosis and found that an increased diameter of portal vein (>13 mm) was noted in 32.5% of cases with a high specificity of 94% and specificity of 31%.

In 2008, Chung-Chieng Wu in his study[67] showed that the main portal vein with a dimension > 13 mm in the supine position, as a diagnostic indicator for portal hypertension, had a sensitivity of 40% or less, with an accuracy of around only 60% .

In 2009, Desmosthenes suggested that a portal vein diameter over 13 mm is indicative of portal hypertension with a specificity of 100% and a sensitivity of 45-50%[68].

In 2014, Aarti Anand et al[69] conducted a retrospective study to review the Doppler findings to evaluate its usefulness in patients of portal hypertension and found that, portal vein was dilated more than 13 mm in 67 (95%) of total 70 cases with portal hypertension.

In 2014, a study by MS Ahamed[70] showed during deep inspiration, diameter of portal vein was greater than 13 mm in 31 (52.54%), while equal to or less than 13 mm in 28 (47.46%) of portal hypertensive cases. Out of 45 controls, in 8 (17.78%) cases, maximum diameter of portal vein was over 13 mm, while in 37 (82.22%) cases, diameter of portal vein was equal to or less than 13 mm.

Other workers such as Bolondi[71], Zoli[72] and Kurol[73] "all found in their respective studies that an enlarged portal vein was present in cases of portal hypertension. The

average sensitivity of all these studies ranged from 60-80%. None of these studies focussed on respiratory variations. La fortune found in his study that dilated portal vein was not diagnostic of portal hypertension[74]. He correlated his findings with angiography to confirm his data. Bradley Koslin in his study also found that diameter alone was not diagnostic of portal hypertension[75]. Extensive review of literature conducted by Van Leeven also confirmed that diameter of portal vein was not a diagnostic criteria for portal hypertension[76]. Bellamy found that following food intake there was an increase in the diameter of the portal vein of upto 50% of its original diameter[77]. Rabin[78] found that the portal vein diameter varies considerably in supine and decubitus positions".

In 2014, Aly A. Elbarbarya[79] conducted a study on 50 patients with liver cirrhosis and 20 apparently healthy individuals as controls to evaluate the role of duplex Doppler ultrasound in portal vein and upper gastrointestinal endoscopy in the assessment of signs of portal hypertension in patientswith liver cirrhosis. PV diameter in all the 50 patients showed range of 12–17 mm whereas in control group the PV diameter was between 10-13 mm and PV flow velocity in all the 50 patients showed range of 12–20.250 cm/s whereas in control group the PV diameter was between 17.25-23.50 cm/s. Comparison between all the patients and the controls in the PV diameter and velocity showed a statistically significant difference ($P < 0.001$).

In 2017, Shikha Singh et al[80] "conducted a prospective observational study on 300 healthy adults. Portal vein diameter was measured in supine position and normal respiration by grey scale USG. PVD measurements ranged from 7.0 to 12.6 mm. Mean PVD measurement, standard deviation and median value were 9.495, 1.03 and 9.40 mm respectively. Males had significantly higher mean PVD values (9.70±1.02 mm) as

compared to females (9.10±0.94 mm). Mean PVD was maximum in age group 21-25 years and minimum in age group 26-30 years. Statistically, a significant difference in mean PVD among different age groups was observed ($F=3.328$; $p=0.037$). For all the age groups males had significantly larger mean PVD ($p<0.05$) but within gender no significant effect on mean PVD was observed for increasing age ($p>0.05$).

The normal caliber of the portal vein is up to 13 mm during calm respiration. It increases up to 16 mm in deep inspiration, as well as postprandially[68,81]. On the contrary, the portal vein diameter decreases after exercise and in the erect position. The portal vein diameter should be measured at the level of the porta hepatis just before its entry into the liver and above the inferior vena cava (IVC) with the patient in quiet respiration in oblique, cranially angled sub-xiphoid view (recurrent subcostal oblique projection)[82,83]. Measurements were obtained lumen to lumen and in mm. It is important to recognize, however, that the portal vein is not always enlarged with portal hypertension. In some cases, portal flow may be primarily diverted through collateral channels, resulting in a small portal vein at the porta hepatis. This can be seen with diversion of flow through a large coronary vein, splenorenal shunt, or other similar channel"[62].

RESPONSE TO RESPIRATION :

In 2005, Rokni YH[66] "conducted a study on 46 biopsy proven cases of cirrhosis and found that reduced respiratory change of diameter of portal vein equal to or less than 20% had higher specificity and specificity of 89 % in diagnosing portal hypertension. Zoli in his study found that the respiratory variation in the portal vein calibre is reduced in portal hypertension[72]. The average variation between inspiration and expiration was

less than 20% in portal hypertensives, and the sensitivity of this sign in diagnosing portal hypertension was 82%. Kurol and Bolondi also found that the absence of variation of portal vein diameter during respiration was a sensitive indicator of portal hypertension and their studies revealed a sensitivity of 70-80% inthe diagnosis of portal hypertension using this criteria[71,73]. Later studies of Leveen and Bradley Koslin confirmed these observations[76,84].

In 2014, Chakenahalli N et al[85] conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. Loss of respiratory phasicity of portal vein was noted in 51 of the 58 cases (87.9%). There was significant association of portal hypertension with loss of portal vein respiratory phasicity (each $p<0.001$).

In 2016, Geleto et al[86] conducted a cross-sectional study on a total of 195 clients for sonographic assessment of normal mean portal vein diameter. Among these, 121(62.1%) were males and the median age of the participants was 35 years. The study revealed a normal mean portal vein diameter of 10.6 mm ±1.8 SD with a respirophasic variation of 25.6%.

The diameter of the portal vein increases during inspiration. Due to the reduced filling of the heart during inspiration and the downward excursion of the diaphragm there is increased intra abdominal pressure and stasis of blood in the liver and the portal venous system causing dilatation of the portal vein. In normal individuals the calibre of the portal vein changes from 20-200% between phases of respiration".

PORTAL BLOOD FLOW DIRECTION :

In 1986, H.Patriquin et al[87] studied 195 patients with chronic liver disease (1 50 adults and 45 children, aged 2 weeks to 18 years) and 20 normal controls, with real-time B-mode sonography and pulsed Doppler techniques. The portal vein was examined as it crosses the hepatic artery. At this point, the portal venous signal was easily obtained and the direction of flow could be compared with that of the hepatic artery. Flow direction in all portal vein branches was recorded using an intercostal or subcostal, transverse or oblique approach. The normal Doppler examination of the portal venous system consisted of the examination of orthograde, hepatopetal flow in the splenic vein and superior mesenteric vein, as well as in the portal vein and its intrahepatic branches. The flow in the portal and splenic veins is slightly modulated by cardiac systole in some patients.

In 1991, Gaiani et al[88] "evaluated the prevalence of spontaneous reversal of flow in the portal venous system non invasively by Doppler ultrasound in 228 patients with liver cirrhosis and portal hypertension. Reversed flow was detected in the portal vein in 7 patients (3.1%), in the splenic vein in 7 patients (3.1%), and in the superior mesenteric vein in 5 patients (2.1%), with an overall prevalence of 8.3% (19/228). This prevalence did not differ in relation to the etiology of liver cirrhosis, whereas hepatofugal flow was found in more patients classified as Child's C (15.4%) and B (12.5%) than those classified as Child's A (2.7%) ($P < 0.02$) and was associated with a higher frequency of hepatic encephalopathy (21% vs. 7.2%; $P < 0.05$). Endoscopic evaluation of esophageal varices did not reveal any correlation between the presence and size of varices and hepatofugal flow, whereas red signs were detected more frequently in patients with this hemodynamic pattern (42.1% vs. 24.4%; NS). The rate of previous variceal bleeding was

not significantly different in patients with and without hepatofugal flow (30.8% vs. 24.4%; NS). Conversely, the prospective evaluation of 15 patients with hepatofugal flow and 29 matched patients with hepatopetal flow, derived from the group of 228 patients, followed up for a period of 12–18 months, showed that variceal bleeding occurred in 9 of 29 patients with hepatopetal flow and in none of the 15 patients with hepatofugal flow ($P < 0.02$).

In 2000, *Von Herbay A et al*[89] conducted a study of color Doppler sonography on 109 patients of cirrhosis confirmed by liver biopsy. The direction of portal venous flow was normal (hepatopetal) in 80 patients (73%), hepatofugal in 10 (9%), and bidirectional in 7 (6%); 12 patients (11%) had partial portal vein thrombosis.

La Fortune studied a series of 65 cirrhotics and found that hepatofugal flow is an absolute sign of portal hypension with a sensitivity of 85% and specificity of 100%[74]. In Takayaso's study of 80 cases hepatofugal flow was only observed in 2 cases. According to him, reversal of flow in the portal vein is rare in the absence of surgical shunts[90].

In 2011, a study by Puneet M[91] showed overall six patients (12%) among a total of fifty cases of portal hypertension had non hepatopetal flow (hepatofugal/bidirectional), four of them (8%) showed continuous hepatofugal flow and two patients (4%) showed bidirectional flow. Hepatofugal or bidirectional flow was seen only in Child's C group patients.

In 2015, a study by Ahirwal S, out of 15 cases of cirrhosis with portal hypertension,10 cases (66.6%) had abnormal flow direction in the portal portal vein[92].

In 2015, a retrospective study by Kondo T et al[93] consisting of 222 cirrhotic patients showed that twenty-four patients (10.8%) demonstrated NFPF i.e, bidirectional flow and the reversed flow with associated portal hemodynamic features in the patients with NFPF were smaller diameter of the portal trunk; presence of short gastric vein, splenorenal shunt, or inferior mesenteric vein; and advanced collateral vessels (diameter > 8.7 mm, flow velocity > 10.2 cm/s, and flow volume > 310 mL/min).

Normal portal venous flow is continuous and hepatopetal on Doppler ultrasound with minimal variations due to the cardiac cycle and respiration. Flow normally varies with respiration and heart pulse. In portal hypertension, velocity diminishes and the waveform is dampened with decrease in amplitude of oscillations during breathing[68]. As portal pressure increases, flow may become biphasic, towards and away from the liver during the cardiac cycle. Finally it reverses, becoming monophasic and hepatofugal Reversed (hepatofugal) portal venous blood flow can be present when the intrahepatic resistance is greater than the resistance of portosystemic collaterals"[94].

PORTAL BLOOD FLOW VELOCITY AND VOLUME :

In 1987, a study by P. Mildenberger et al[95] in 50 normal subjects flow velocity and direction on the portal vein was measured by ultrasonic duplex system. The measurements revealed at a mean diameter of 9.7 mm, a mean flow velocity of 15.2 +/- 2.6 cm/s, corresponding to a volume flow of 693 +/- 235 ml/min. Postprandially this increased to 880 +/- 269 ml/min. Inter-observer and day to day measurements demonstrated good reproducibility. Thus, this simple non-invasive method is well suited

for quantitative assessment of the portal vein system in portal hypertension, thrombosis or after shunt operations.

In 1995, *Kuo CH et al*[93] measured the portal vein (PV) velocity by duplex Doppler ultrasound to predict the severity of portal hypertension in a total of 143 patients with liver cirrhosis The maximal PV velocity was significantly lower in patients with moderate and severe varices, cardiac varices, red-color signs on varix, esophagitis and congestive gastropathy. The patients with bleeding esophageal varices or upper gastrointestinal tract were found to have a significantly maximal PV velocity. Comparing patients without ascites or victims with controllable ascites. The maximal PV velocity in Child's C or mortality cases was also significantly lower than that in Child's A, Child's B and surviving cases. By setting the cut off value of PV velocity at 15 cm/sec, the accuracy of 67.8%, 62.2%, 67.8% and 73.5% in the prediction of massive ascites, varices severity, Child C class and mortality respectively could be established. In conclusion, PV velocity may reflect the severity of clinical portal hypertension in cirrhotic patients; it could be a prognostic factor in cirrhotic patients.

In 2011, a study was conducted by Puneet M[91] "to evaluate the association between color Doppler findings and the severity of portal hypertension in patients with cirrhosis. The study group included 50 patients divided into three groups (Child' A, B and C) based on Child Pugh classification. Using one way ANOVA, there was a significant fall in the average PVV from Child's A to Child's C group patients ($F = 29.87$, $P < 0.0001$). So there was a significant fall in PVV with the increasing severity of the grade of cirrhosis".

In 2014, Aarti Anand et al[69] conducted a retrospective study to review the Doppler findings to evaluate its usefulness in patients of portal hypertension and found that, portal vein flow velocities were found to be below 10 cm/sec in 62 (88%) of total 70 cases with portal hypertension.

In 2016, Riahinezhad M et al[96] conducted a cross-sectional study in 33 cirrhotic children with or without esophageal varices and compared with 19 healthy children as controls using color and spectral Doppler US. Portal vein mean velocities were 15.03 ± 7.3 cm/s in cirrhotics, 16.47 ± 6.4 cm/s in controls (P = 0.51), 11.6 ± 4.7 cm/s in patients with varices, and 17.9 ± 7.3 cm/s in patients without varices (P = 0.015). Mean diameters of caudate lobe, portal vein, and splenic vein, as well as the mean values of liver and spleen span, were significantly higher in cirrhotic children.

An index commonly used in the diagnosis of portal hypertension is the "Congestive Index", which is the ratio of the portal vein area divided by mean portal blood flow velocity. The index is useful as it takes into account two physiological changes that occur in portal hypertension into its computation[97].

C =Cross sectional area (cm^2)/ Mean velocity (cm/sec) of portal vein[97]

In 2014, a study by Elbarbary AA[97] involving 50 patients with portal hypertension and 20 healthy individuals as controls, showed that the CI ranged from 0.009 to 0.159 in patients, mean 0.104 ± 0.039, and from 0.050 to 0.090 in controls, mean 0.071 ± 0.014 with a statistically significant difference of $P < 0.05$.

In 2015, Mukhopadyay et al[98] conducted a study over 235 people consisisting of 100 Normal subjects (N), 10 patients with acute hepatitis (AH), 40 patients with chronic active hepatitis (CAH), 80 patients with liver cirrhosis (LC) and 5 patients with Idiopathic portal hypertension (IPH). Portal blood flow velocity was 15.5 ± 4.0 cm/sec in 100 N subjects, 15.1 ± 2.2 cm/sec in 10 AH cases, 12.5 ± 3.3 cm/sec in 40 CAH cases, 9.8 ± 2.8 cm/sec in 80 LC cases and 11.0 ± 3.5 cm/sec in 5 IPH cases and Congestion Indices (CI) of 0.070 ± 0.028 cm x sec, 0.072 ± 0.015 cm x sec, 0.122 ± 0.088 cm x sec, 0.180 ± 0.075 cm x sec and 0.188 ± 0.110 cm x sec respectively.

In 2015, a study by Ahirwal S, out of 15 cases of cirrhosis with portal hypertension,10 cases (66.6%) had abnormal flow velocity in the portal vein [92].

The velocity in the portal vein is approximately 15-18 cm/sec with a lot of variation in the range[83]. Portal flow velocity varies with the cardiac activity and respiration giving the portal waveform an undulating appearance[99].

The flow velocity increases in certain conditions like hypersplenism, arteriovenous fistulae, and hyperdynamic circulatory states. Portal vein flow velocity reduction is an accepted Doppler sign of cirrhosis and portal hypertension. A low flow velocity of <16 cm/sec in addition to a caliber increase in the MPV are diagnostic features of portal hypertension[228]. An averaged maximum velocity below 16 cm/s should be considered strongly suggestive of CSPH, whereas values < 24 cm/s more generally suggest cirrhosis[21b]. The velocity decreases in cases where there is increased resistance to the portal blood flow as postulated by Patriquin and Bradley Koslin[84,100]. With the development of portal hypertension the flow decreases and the velocity fluctuations

disappear (i.e., flow becomes continuous). Bradley Koslin in hisseries of 50 cirrhotics and 25 controls found the normal velocities ranging from 8-18cm/sec in adults and 10-30 cm/sec in children[75]. Mildenberger in his series found a mean velocity of 15.2 + 2.6 cm/sec[101]. Measurements of blood flow can be altered by factors such as collaterals, splenic size and site of obstruction. Gill in his study found that velocity was not very specific for the diagnosis of portal hypertension[72]. Most of the studies have found reduced flow velocities in cirrhotics. Data about flow volumes is even more variable. Burn stated that the serial velocity measurements can help in prognostic assessment of patients since progressive reduction in the blood velocity was a bad prognositc sign[102].

PORTAL VEIN THROMBOSIS:

In 2017, Stine J G et al[103] "conducted a study on one hundred subjects (50 matched pairs) with mean age 53.8±13.1 y and Model for End-stage Liver Disease (MELD) score 14.9±5.5 were included in our analysis. Sixty-four percent were male and 76% were Child-Turcotte-Pugh Class A or B. Baseline characteristics (prior to development of PVT) were similar, except for baseline PV velocity (16.9 cm/s, 95% CI 13.9-20.0 PVT vs 25.0, 95% CI 21.8-28.8 no PVT, P<.001). 30 PVT subjects had PV velocity <15 cm/s compared to five without PVT (P<.001). On adjusted multivariable analysis, PV velocity was the strongest independent risk factor predicting PVT development (HR 0.86, 95% CI 0.80-0.93). The predictive value for PVT development was greatest for flow <15 cm/s (c-statistic 0.77). PV velocity <15 cm/s had a highly significant association with future PVT (HR 6.00, 95% CI 2.20-16.40, P=<.001). Hence, decreased PV velocity is associated with increased risk of future PVT. Patients with

cirrhosis and decreased PV velocity are a high-risk subgroup that warrants further investigation with prospective study.

In 2017, Achar S[104] conducted a hospital-based cross-sectional study on twenty children with Extrahepatic portal vein obstruction (EHPVO) aged between 1 and 18 years over a period of 1 year. All the patients presented in chronic stage with portal cavernoma and only one patient (5%) had bland thrombus associated with cavernoma. The color Doppler ultrasonography (CDUSG) had a sensitivity of 66.6-90% and specificity of 91.5% with regard to the assessment of the extent of thrombus formation and flow in the portal venous system. It was found to help in preoperative assessment of EHPVO in detecting occlusion and identifying portosystemic collaterals and dilated intrahepatic biliary radicals.

With increasing portal venous pressure, there is a progressive decrease in the portal venous flow velocities approaching the level of stagnation. As this occurs, the phenomenon of a to-and-fro flow can be encountered whereby the nearly stagnant blood column in the portal veins is seen to shift into and out of the liver with the respiratory cycle. With worsening portal hypertension, stagnation of the blood column can lead to thrombosis or progress to a frank flow reversal. The secondary signs of portal vein thrombosis observed by Doppler include the presence of periportal collaterals, representing cavernous transformation, with a flow in the hepatopetal direction[105].

A sudden onset of ascites should prompt careful examination of the portal vein for thrombosis. When the portal vein is blocked multiple collaterals are formed. Subramanyam and Kauzlaric et al described in detail the collaterals formed[106]. They also

described the formation of a cavernoma. Wermke and Gansbeke found that 50% cases in their study with portal vein thrombosis had a cavernorma formation[107]. Ohinishi stated that the cavernoma formation can occur within 4 weeks of obstruction".

PORTO-SYSTEMIC COLLATERALS OR VARICES:

In 1990, Vilgrain et al [108] "assessed the sensitivity of ultrasonography (US) for the diagnosis of portal hypertension in 48 patients with known cirrhosis. These results were compared to the hemodynamic values obtained on the same day by hepatic vein catheterization. One or more portosystemic venous collaterals were present in 40 of 48 patients (83.3%). Splenorenal or gastrorenal veins were seen in 23 patients, paraumbilical vein in 22 patients, gastroesophageal veins or left gastric vein in 19 patients, and dilatation of presumed cystic veins in one patient. US detected one portosystemic route in 20 of 48 patients (41.6%), two in 14 of 48 patients (29.1%), and three in 6 patients (12.5%). The sensitivity of US in detecting portal hypertension was about 40% considering either a > 13 mm diameter of the portal vein or the lack of mild caliber variation of the superior mesenteric vein. The sensitivity was more than 80% considering the presence of portosystemic venous collaterals. Presence of numerous portosystemic shunts was significantly associated with high hepatic venous pressure gradients which reflected the severity of portal hypertension.

In 2000, *Von Herbay A et al*[89] conducted a study of color Doppler sonography on 109 patients of cirrhosis confirmed by liver biopsy. Spontaneous portosystemic shunts were found in 41 patients (38%), most often as splenorenal shunts (21%) and patent umbilical veins (14%). Less frequent were gastric collaterals, gallbladder varices, collaterals to thrombotic portal veins, mesoiliac shunts, and portorenal shunts to the right

kidney. The presence of shunts was associated with that of esophageal varices ($p < 0.01$), ascites ($p < 0.01$), and inversion of portal flow ($p < 0.001$) but not with splenomegaly.

In 2014, Chakenahalli N et al[55] conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. Collaterals were noted in 63% of the cases, Most frequent collateral were the splenorenal collaterals which were seen in 49.2% of cases. Anterior abdominal wall varices and paraumbilical veins were seen in 19% and 20% of cases respectively. Other visualised collaterals included perigastric (15.8%), coronal vein (7.9%), GE junction collaterals (7.9%) and GB wall varices (3.2%). Portal cavernoma was seen in 5 (7.9%) cases.

Doenner[109] with angiogaphic studies confirmed that these collaterals were small and thin walled and thus more likely to bleed. Collaterals draining towards the inferior vena cava are thick walled so bleeding episodes are rare whereas the incidence of encephalopathy is higher. This was also confirmed by Doehner and later again by Wexler.

In 2014, Minal Shastri et al[110] conducted a study on total of 50 adult patients with cirrhosis were included in the study. All subjects underwent a percutaneous liver biopsy, abdominal ultrasound and Esophagogastroduodenoscopy (EGD) along with other tests as part of the work up for cirrhosis. Association of portal vein diameter (PVD),portal vein velocity (PVV) and hepatic congestion index (HCI) with presence of Esophageal varices (EV) was statistically significant (p-value <0.01). PVV had the highest sensitivity 84% (95% CI 66.45%- 94.10%) for detecting the presence of EV. PVD and HCI had the highest specificity of 55% (95% CI 0.31-0.77) and the highest negative predictive value of 38%(95% CI 0.24-0.52). Positive predictive value was highest PVV at 76%. (95% CI

0.61-0.86). In resources- constricted settings where EGD is not available, PVI (PVV, PVD and HCI) on ultrasound abdomen can be used as non-invasive parameters to predict the presence of EV. Although EGD remains the gold standard for the diagnosis and management of EV, when this is not possible due to scarcity of resources, PVV may be used a tool to triage patients for referral for an EGD as it has the highest sensitivity of 84% (95% CI 66.45%-94.10%) and positive predictive value of 76% (95% CI 61.51%-86.47%) amongst the PVI studied for detecting the presence of EV.

Kim and Marchal stated that collaterals are seen along the bile ducts and gall bladder fossa. Subramanyam reported that the combined sensitivity of ultrasound for detection of coronary and gastoesophageal varices was 80%. The detection of the varices depended on their size as determined by endoscopy or barium studies, In patients with large varices the coronary vein was detected in 89% and the gastroesophageal veins in 68% in patients with small varices This sensitivity dropped to 63% and 18% respectively. Based on sonographic studies and previous angiographic observations Subramanyam concluded that the coronary vein > 5mm in diameter should be considered abnormal. Nordlinger correlated sonography and endoscopy and found that duplex sonography had a sensitivity of 85% and specificity of 95%. According to him 25% of bleeding varices were not detected on ultrasound and in this cases endoscopy was superior [111].

Dash in his study correlated angiographic with sonographic finding concluded that duplex sonography was superior to angiography in the detection of paraumbilical vein. Dockmeci found a similar result. Shadekhi stated that the patency of the paraumbilical vein could be seen in normal individuals but the lumen should not exceed 3

mm in diameter. A diameter more than 3 mm with hepatofugal flow was a sensitive indicator of portal hypertension[112].

Splenorenal collaterals are seen in 10-20% cases as observed by Kane and Burcharth[113]. Collaterals are also seen in the superior pole of the kidney passing into the retroperitoneum. The course of these collaterals has been documented by Van Leuson. Veins draining the retroperitoneal structures such as the duodenum, pancreas, ascending and descending colon, spleen and bare area of liver can establish collateral pathways with systemic circulation. These are called pancreatico-duodenal veins which eventually drain into the inferior vena cava. Subramanyam reported the presence of these collaterals in the region of the descending duodenum in 3 cases in his study.

In 2014, Bhattarai S[114] did a study on One hundred and fifty patients with clinical features, laboratory and sonological findings suggestive of cirrhosis of liver and endoscopic evidence of portal hypertension. They found that Average portal vein diameter of patients without gastro-esophageal varices was 10.800 ± 1.1402 mm, while it was 13.731 ± 1.061mm in patients with varices($p<0.001$). Average spleen size of patients without varices was 12.67 ± 2.35 cm and with varices was 15.367 ± 1.210 cm ($p < 0.001$). There was 92.72 % sensitivity and 90 % specificity for prediction for presence of esophageal varices when the cutoff value for portal vein diameter was 12.25 mm. There was 94.5 % sensitivity and 75 % specificity for prediction for presence of esophageal varices when the cutoff value for spleen size was 13.9 cm. In cirrhotic patients with portal hypertension, as portal vein diameter increases by > 12.25 mm, there is increased risk of development of gastro-esophageal varices; grades of varices increase with increment of portal vein size and as size of spleen increases by >13.9 cm, increased risk

of development of varices exist. They concluded that measurement of portal vein diameter and spleen size by ultrasonography can be recommended as a non invasive predictor for gastroesophageal varices in cirrhosis of liver.

In 2014, Aly A. Elbarbarya[79] conducted a study on 50 patients with liver cirrhosis and 20 apparently healthy individuals as controls to evaluate the role of duplex Doppler ultrasound in portal vein and upper gastrointestinal endoscopy in the assessment of signs of portal hypertension in patients with liver cirrhosis. There were no esophageal varices in eight patients, (16%), Grade I esophageal varices were present in 12 patients (24%). Grade II esophageal varices were present in eight patients (16%). Grade III esophageal varices were present in eight patients (16%). Grade IV esophageal varices were present in 14 patients (28%). In eight patients, there were no esophageal varices as the CI ranged from 0.06 to 0.09 (mean 0.07 ± 0.02). In 12 patients, there were grade I esophageal varices as the CI ranged from 0.01 to 0.09 (mean 0.06 ± 0.03). In eight patients, there were grade II esophageal varices as the CI ranged from 0.11 to 0.13 (mean 0.11 ± 0.01). In eight patients, there were grade III esophageal varices as the CI ranged from 0.13 to 0.14 (mean 0.13 ± 0.001). In 14 patients, there were grade IV esophageal varices as the CI ranged from 0.13 to 0.16 (mean 0.14 ± 0.01). There was a high statistically significant increase in the CI in relation to esophageal varices in all patients ($P < 0.001$). Comparison between all the patients and the controls in the arterial pulsatility index showed a statistically significant difference ($P < 0.001$).

When portal resistance is higher than that of small communicating channels between the portal and systemic circulation, portosystemic collaterals are formed[68]. This causes a subsequent decrease in the, initially dilated, caliber of the portal vein. Forming

of collateral vessels is a definitive finding of portal hypertension, ultrasonography (US) can reveal up to 65-90% of these vessels[115].

The common sites of portosystemic collateral veins include as follows[68]:

Gastroesophageal Junction: Whilst gastroesophageal collaterals are the most common type of collaterals found clinically they are less often seen on ultrasound than paraumbilical or splenorenal collaterals. This is due to the very deep location of the varices around the oesophagus, the close proximity between the left gastric vein and the gas filled gut, and the variability in the vascular anatomy. The coronary vein is imaged by locating the splenic vein in a midline sagittal view and moving the probe to the right. It is recognized as a small vessel coursing cephalad from the splenic vein near the portal-splenic confluence. Diagnosis of gastroesophageal collaterals by ultrasound depends on identification of an enlarged left gastric vein or demonstration of hepatofugal flow[68,116]. Reversed flow in the coronary vein is a useful sign of portal hypertension. The normal flow direction is toward the splenic/portal vein. This abnormal flow may be associated with esophageal varices and hemorrhage. Preservation of hepatopetal flow in the coronary vein may indicate a low risk of variceal hemorrhage.

Paraumbilical Vein: A recannalized paraumbilical vein with hepatofugal flow is another important collateral pathway. It is easily recognized sonographically as a tubular structure at the ligamentum teres and connects the left portal vein with the systemic epigastric vein close to the umbilicus[68]. It is very important to identify blood flow exiting the liver to ensure that a normal intrahepatic portal vein branch is not mistaken for a collateral. It is common to find reversal of flow (Hepatofugal) isolated to the right portal

vein due to the sump effect of the paraumbilical vein. This is a useful clue to the presence of a paraumbilical collateral. The left portal vein remains hepatopetal but may become enlarged as it feeds the paraumbilical vein. A high-frequency linear transducer can be used to follow the vessel to the level of the umbilicus, where it is seen to connect to a complex network of vessels know as the *caput medusa*[116].

Splenorenal-Gastrorenal Area: Tortuous veins arise close to the splenic and left renal hili, representing collaterals between the splenic, coronary and short gastric veins (portal system) and the left adrenal and renal veins (systemic venous system). Splenorenal collaterals have a more variable location and may be seen at the splenic hilum as well as more laterally between the spleen and left kidney. Reversal of flow in the splenic vein posterior to the pancreas indicates the presence of splenic (or rarely IMV) collaterals[68,116].

Other collaterals and varices include gastric, retroperitoneal, haemorrhoidal veins in the perianal region, between the liver and the abdominal wall, as well as in the wall of the gallbladder among others. Gastric varices may be seen around the stomach in the epigastrium, underneath the left lobe of the liver, and near the spleen. Retroperitoneal/paravertebral varices also may occur with portal hypertension but are more difficult to recognize with sonography. Careful scanning may reveal tortuous vessels between the liver and right kidney, near the left kidney or spine. Gallbladder varices may occur due to a backup of blood flow in the cystic vein. This can be recognized as a thickened gallbladder wall in which tubular structures (dilated veins) are present. Color and spectral Doppler will aid in the diagnosis by showing venous flow within the dilated vessels of the gallbladder wall[68,116].

Indirect sonographic markers of PH and esophageal varices (EV) include: ascites, portal vein diameter > or = 13 mm, spleen length, maximal and mean velocity of portal vein flow, respectively < 20 cm/sec and < 12 cm/ sec[236]. Ultrasound has supplanted the invasiveness, discomfort and expense of contrast angiography in the evaluation of many patients with advanced liver disease"[116].

SPLENIC SIZE:

In 2011, Mandal L et al[117] "conducted a study to find out the correlation of portal vein diameter and splenic size with gastro-oesophageal varices in 82 patients with cirrhosis of liver. In the study it was found that twenty patients had no varices (grade 0) and the rest sixty-two patients developed varices. Average portal vein diameter of patients without gastro-oesophageal varices was 11.545 ± 1.514 mm and of patients with varices 13.998 ± 1.123 mm with statistically significant difference ($p < 0.05$). Average spleen size of patients without gastro-oesophageal varices was 13.129 ± 1.102 cm and with varices 14.997 ± 1.992 cm with statistically significant variation ($p < 0.05$). There was a positive correlation between grading of oesophageal varices and portal vein diameter ($r = 0.707$; $p < 0.001$) and between splenic size with oesophageal grades ($r = 0.467$; $p < 0.001$).

In 2014, Aarti Anand et al[69] conducted a retrospective study on 70 cases with portal hypertension to review the Doppler findings and evaluate its usefulness in patients of portal hypertension, splenomegaly was noted in 60 (85%) cases and dilated splenic vein (>10 mm) was noted in 57 (81%) cases.

Splenomegaly is observed in most but not all patients with cirrhosis, more often when complicated by portal hypertension[118]. US shows a sensitivity of up to 95% and a

specificity of up to 98% in measuring the liver and spleen[118]. Mild to moderate splenomegaly (craniocaudal diameter of more than 13 cm) is a common finding of portal hypertension[239]. However, although there is no complete correlation between this finding and the pressure in the portal vein, monitoring of the spleen diameter may allow a prognostic stratification of cirrhotic patients[118]. Spleen size was measured ultrasonographically by placing the patient in supine position, using 2- 5 MHz curvilinear transducer in the coronal plane of section posteriorly in one of the lower left intercostal spaces. Splenomegaly commonly accompanies portal hypertension and is a noteworthy finding[117]. A maximum cephalo-caudal measurement exceeding 13 cm indicates enlargement with a high degree of reliability"[117].

SPLANCHNIC VEINS AND ARTERIES:

In 2002, F. Piscaglia[119] "assessed splanchnic haemodynamics in chronic liver diseases and various other disorders with splenomegaly. The study groups comprised: (i) patients with chronic liver disease (89 with cirrhosis, 35 with chronic hepatitis), (ii) patients with splenomegaly without relevant portal hypertension (14 with haematological splenomegaly and 25 liver transplant recipients without complications), (iii) 15 patients with arterial hypertension, (iv) 22 healthy controls. In all subjects, spleen size, portal flow parameters and splenic artery resistance index were measured using duplex-Doppler ultrasound. Splenic artery resistance index was significantly and selectively increased in patients with cirrhosis (0.63, whereas all other group means ranged between 0.53 and 0.56: $P < 0.01$). Portal flow velocity was significantly decreased in cirrhosis ($P < 0.01$). The combination of these two parameters provided an accuracy of 87.5% in distinguishing portal hypertensive from haematological splenomegaly. In patients with

cirrhosis, the degree of spleen enlargement was positively correlated with increasing portal flow volume, portal vein diameter and variceal size, whereas splenic resistance index and portal velocity did not differ in connection with spleen size. Hence, it was concluded that Splenoportal Doppler sonography provides specific findings in cirrhosis and may therefore be a useful tool in differentiating between splenomegaly of portal hypertensive of haematological origin. In patients with cirrhosis, the presence of splenomegaly is associated with the presence of larger oesophageal varices.

Enlarged splanchnic veins (e.g., a superior mesenteric vein (SMV) and splenic vein (SV) diameter of more than 1 cm) are suggestive of portal hypertension. Several studies have shown that the diameters of the SMV and SV are statistically different in control subjects and patients with cirrhosis with the expiration measurements being the most discriminating. Reversed flow may be detected in the SMV or SV at Doppler sonography, however this is a relatively rare finding, seen in less than 5% of cases of portal hypertension. Although reversed splanchnic vein flow is not related to the etiology of portal hypertension, it is seen more frequently in patients classified as Child's B and C than in those classified as Child's A[108]. Several studies have shown that blood flow increases and the resistance index falls in the superior mesenteric and splenic arteries in the setting of portal hypertension"[108].

ASCITES:

In 2014, Chakenahalli N et al[55 "]conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. Ascites was seen in 55 (87.3 %) of the 63 cases studied. Splenomegaly was noted in 50 (79.4 %) of the 63 cases. Loss of respiratory phasicity of portal vein was noted in

51 of the 58 cases (87.9%). There was significant association of portal hypertension with splenomegaly, ascites and loss of portal vein respiratory phasicity (each $p<0.001$).

In 2014, Aarti Anand et al[69] conducted a retrospective study on 70 cases with portal hypertension to review the Doppler findings and evaluate its usefulness in patients of portal hypertension, ascites was noted in 36 (51%) cases.

Normally, about 50-75 ml of free fluid is present in the peritoneum, acting as a lubricant[120]. An excess in this amount results in ascites, which is classified into transudate and exudate. Cirrhosis, peritoneal carcinomatosis, congestive heart failure and tuberculosis are the causes of over 90% of ascites. Pathophysiology of ascites in a cirrhotic patient includes portal hypertension, proteinaemia, increased hepatic lymph production and renal sodium retention. When the patient is in the supine position, fluid accumulates first in the paracolic gutters, Douglas and Morison's pouches"[68].

LIVER MORPHOLOGY:

In 2014, Chakenahalli N et al[55] "conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. It was found that most common etiology was cirrhosis seen in 48 cases (76.2%). Portal vein occlusion as the etiology was seen in 19% cases. Malignancy causing portal venous occlusion was seen in 3.2% cases.

In early stages of cirrhosis the liver may be enlarged, while in the chronic phase it is usually small with relative enlargement of the caudate and left lobes compared to the right[120]. Transverse diameters of the caudate and right lobes should be measured in the portal vein bifurcation inside the liver. A caudate/right lobe ratio of 0.65 or higher is indicative of cirrhosis with high specificity (100%) but low sensitivity (43-84%)[68].

Coarse echotexture is also a common finding in cirrhosis[68]. Nodular irregularity of the liver surface is a common sign of cirrhosis due to the presence of regenerating nodules. The latter represent regenerating hepatocytes surrounded by fibrotic septa. Micronodular cirrhosis can evolve into macronodular, thus producing the nodular hepatic surface, a feature which is more prominent when ascites is present"[68].

HEPATIC VEINS and ARTERY:

In 2015, Kim G et al[121] "conducted a systematic review of 14 studies by searching databases, including MEDLINE, EMBASE, and the Cochrane Library, for relevant studies The US indices were obtained in the portal vein (n = 9), hepatic artery (n = 6), hepatic vein (HV) (n = 4) and other vessels. Using hepatic venous pressure gradient (HVPG) as the reference, the sensitivity (Se) and specificity (Sp) of the portal venous indices were 69–88% and 67–75%, respectively. The correlation coefficients between HVPG and the portal venous indices were approximately 0.296–0.8. No studies assess the Se and Sp of the hepatic arterial indices. The correlation between HVPG and the hepatic arterial indices ranged from 0.01 to 0.83. The Se and Sp of the hepatic venous indices were 75.9–77.8% and 81.8–100%, respectively. In particular, the Se and Sp of HV arrival time for clinically significant PH were 92.7% and 86.7%, respectively. A statistically significant correlation between HVPG and the hepatic venous indices was observed (0.545–0.649). it was concluded that some US indices, such as HV, exhibited an increased accuracy for diagnosing PH. These indices may be useful in clinical practice for the detection of significant PH".

In 2016, Antil N et al[122] "conducted a study on 30 patients of chronic liver disease to evaluate hepatic venous waveform, damping index(DI) and splenoportal index (SPI) in patients of cirrhosis on Colour Doppler ultrasound, also predict severity of portal hypertension and presence of oesophageal varices. Twenty two (73.3%) patients had monophasic waveform. Biphasic and triphasic waveforms were seen in 4 (13.3%) cases. Twenty two patients (73.3%) had monophasic waveforms and majority of them were in class C. This distribution of hepatic vein waveform was statistically significantly with the Child Pugh's class ($p<0.05$). Twenty patients (66.7%) had value of Damping index more than >0.6 where majority of patients (18) belonged to class C and 2 in class B. There was a positive correlation between Child Pugh's total score and Damping index ($r=0.614$; $p<0.05$). There was weak positive correlation between splenoportal index and Child Pugh's score ($r=0.269$; $p=0.15$). It was concluded that change in triphasic to monophasic waveform and DI >0.6 suggests severe liver dysfunction and is associated with severe portal hypertension. Hepatic venous waveform pressure changes, DI and SPI have no value in predicting presence of oesophageal varices.

The hepatic vein normal waveform is triphasic, reflecting pressure from the right atrium in a normally compliant liver through the thin walls of the veins. Two antegrade diastolic and systolic waves are followed by a smaller retrograde wave which corresponds to the atrial "Kick" [120]. As fibrosis evolves, the liver parenchyma stiffens, not allowing the hepatic veins to reflect pressure alterations. This results into decreased amplitude of phasic oscillations, reversed flow loss and flattened waveform[68]. As cirrhosis progresses, the hepatic veins' lumen narrows and velocity increases with colour aliasing and turbulence. Therefore, in cirrhotic patients, a triphasic pattern has been

observed in about half of cases and a biphasic waveform in the remaining half. A completely flat waveform has been noted in up to 3% of cirrhotic patients. Mean hepatic vein velocity is higher in cirrhotics than non-cirrhotic controls. The poorer the grade of cirrhosis, the higher is the hepatic vein mean velocity, with very high values (20 cm/s) noted in patients with moderate to massive ascites[123].

The hepatic artery normally shows a typical splanchnic waveform, with normal maximum velocity measuring 55.2 ± 12.0 cm/s. In cirrhotic patients, especially when portal vein thrombosis may occur, this value can increase up to 64.4 ± 21.8 cm/s"[123].

ESTIMATION OF PORTAL PRESSURE BY THE MEASUREMENT OF LIVER STIFFNESS:

In 2007, Vizzutti et al[124] "conducted a study to evaluate the ability of LSM to predict severe portal hypertension compared with that of HVPG in 61 consecutive patients with HCV-related chronic liver disease. A strong relationship between LSM and HVPG measurements was found in the overall population (r=0.81, P<0.0001). However, although the correlation was excellent for HVPG values less than 10 or 12 mm Hg (r=0.81, P=0.0003 and r=0.91, P<0.0001, respectively), linear regression analysis was not optimal for HVPG values>or=10 mm Hg (r2=0.35, P<0.0001) or>or=12 mm Hg (r2=0.17, P=0.02). The AUROC for the prediction of HVPG>or=10 and >or=12 mm Hg were 0.99 and 0.92, respectively and at LSM cutoff values of 13.6 kPa and 17.6 kPa, sensitivity was 97% and 94%, respectively. In patients with cirrhosis, LSM positively correlated with the presence of esophageal varices (P=0.002), although no correlation between LSM and esophageal varices size was detected. The area under the ROC for the prediction of EV was 0.76 and at a LSM cutoff value of 17.6 kPa sensitivity was 90%. It

was concluded that LSM represents a non-invasive tool for the identification of chronic liver disease patients with clinically significant or severe portal hypertension and could be employed for screening patients to be subjected to standard investigations including upper GI endoscopy and hemodynamic studies.

Vizzutti *et al*[124] showed that the correlation between LS and portal pressure in cirrhosis is very good up to 10-12 mmHg, while it is substantially lacking for higher values. This finding has been explained by the fact that while in the early stages of the disease the main factor determining portal hypertension is liver fibrosis, therefore it is well related to portal pressure once CSPH is established, the progression of portal hypertension depends not only on liver fibrosis but also on other factors, especially those related to the hyperdynamic circulation, the splanchnic vasodilatation and the resistance in portosystemic collaterals. Unfortunately, these factors are not estimated by LS.

In 2008, Lemoine M et al[125] conducted a study on 92 patients (44 had HCV related-cirrhosis and 48 alcoholic cirrhosis) to assess the relationship between LSM and HVPG in patients with compensated cirrhosis related to hepatitis C virus (HCV) or alcohol and to define the performance and the best cut-off of LSM for the diagnosis of PHT in these patients. LSM was positively correlated to HVPG in both groups. The area under the receiver operating characteristic curve for the diagnosis of significant PHT was 0.76 +/- 0.07 in HCV patients (best cut-off at 20.5 kPa) and 0.94 +/- 0.03 (best cut-off at 34.9 kPa) in alcoholic patients. It was concluded that liver stiffness measurement and HVPG were significantly correlated in patients with compensated cirrhosis because of HCV infection or alcohol. LSM could predict significant PHT in both these groups of patients with a higher cut-off and a better performance in alcoholic patients.

In 2011, a study was conducted by *Robic MA et al*[126] to prospectively assess and compare the prognostic performances of LS and HVPG in 100 patients with chronic liver disease who underwent LS and HVPG measurements on the same day and were thereafter followed-up for 2 years or until they experienced a complication related to their liver disease. Within the two-year follow-up, 41 patients developed, at least, one liver disease related complication. The performances of HVPG and LS for predicting the occurrence of these complications were not significantly different: AUROC 0.815 [0.727-0.903] and 0.837 [0.754-0.920], respectively. When considering only complications related to PHT, both methods were found to be similarly accurate: AUROC 0.830 [0.751-0.910] and 0.845 [0.767-0.823], for HVPG and LS, respectively. When patients were divided in two groups according to a LS value below or above 21.1kPa, actuarial rates of remaining free of any complication at 2 years were 85.4% vs. 29.5%, respectively. When only PHT related complications were considered, these rates were 100% vs. 47.5%, respectively. The performances of LS and HVPG were also similar in the subgroup of 65 patients with cirrhosis. It was concluded that LS proved to be as effective as HVPG in predicting clinical decompensation and PHT related complications in patients with chronic liver disease. Therefore, LS could be a valuable clinical tool to avoid invasive procedures.

Another important advancement in the noninvasive assessment of portal hypertension has been the introduction of noninvasive measurement of liver stiffness (LS) by transient elastography (TE)[40]. TE has proven sensitive for estimating the absence of liver fibrosis or the presence of high degree liver fibrosis, yet patients with moderate fibrosis remain more difficult to assess. TE has also been shown to be related to the

degree of portal pressure. Such a correlation is somewhat expected because liver fibrosis is the first and main determinant both of tissue stiffness and of intrahepatic resistance to portal blood flow[127].

LS can increase independently of fibrosis due to food ingestion, inflammation, cholestasis and liver congestion. Even with the limitations cited above, a number of studies have demonstrated that the related method allows not only for estimation of liver fibrosis but also determination of CSPH presence[128].

In recent years, additional techniques have been proposed for the evaluation of LS, each of which appear to overcome some of the limitations presented by traditional TE; these include acoustic radiation force impulse imaging (ARFI) and shearwave velocity estimation. In particular, the realtime shearwave elastography (SWE) allows for realtime viewing of the area under investigation, contrary to TE which is done blindly, as well as integration of the assessment of TE with traditional ultrasound and Doppler"[129,130].

ESTIMATION OF PORTAL HYPERTENSION BY THE MEASUREMENT OF SPLEEN STIFFNESS (SS)[131]:

In 2012, Sharma P et al[132] "conducted a study on 65 patients with ExtraHepaticPortalVeinObstruction (EHPVO) and 50 age-matched healthy control subjects. Twenty-two (34%) had hypersplenism. SS (P = .01) were higher in patients with EHPVO (51.7 kPa ± 21.5) than in control subjects (16.0 kPa ± 3.0). Patients who had a bleed had higher SS than did those without a bleed (60.4 kPa ± 5.4 vs 30.3 kPa ±

14.2, P = .01). An SS cutoff of 42.8 kPa yielded sensitivity and specificity of 88% and 94%, respectively.

In 2013, Y. Takuma, et al[133] conducted a prospective single-center study on 60 patients with liver cirrhosis. The efficacy of the parameters for the evaluation of portal hypertension was analyzed by using the Spearman rank-order correlation coefficient and receiver operating characteristic (ROC) curve analysis. The correlation coefficient between SS and HVPG (r = 0.876) was significantly better than that between LS and HVPG (r = 0.609, P < .0001). The areas under the ROC curve of SS for the identification of clinically important portal hypertension (HVPG ≥ 10 mm Hg), severe portal hypertension (HVPG ≥ 12 mm Hg), esophageal varices (EVs), and high-risk EVs were significantly higher (0.943, 0.963, 0.937, and 0.955, respectively) than those of LS, spleen diameter, platelet count, and platelet count to spleen diameter ratio (P < .05 for all). SS could be used to accurately rule out the presence of clinically important portal hypertension, severe portal hypertension, EVs, and high-risk EVs (negative likelihood ratios, 0.051, 0.056, 0.054, and 0.074, respectively). It was concluded that SS is reliable and has better diagnostic performance than LS for identifying portal hypertension in liver cirrhosis.

In 2013, Y. Takuma, Nouro.K, et al[134] conducted a prospective study, measuring SS and liver stiffness (LS) in 340 patients with cirrhosis undergoing endoscopic screening for EVs and 16 healthy volunteers (controls). Patients with cirrhosis had significantly higher SS and LS values than controls (P < .0001 and P < .0001, respectively). Levels of SS were higher among patients with EVs (n = 132) than controls, and values were highest among patients with high-risk EVs (n = 87). SS had the greatest

diagnostic accuracy for the identification of patients with EVs or high-risk EVs compared with other noninvasive parameters, independent of the etiology of cirrhosis. An SS cutoff value of 3.18 m/s identified patients with EVs with a 98.4% negative predictive value, 98.5% sensitivity, 75.0% accuracy, and 0.025 negative likelihood ratio. An SS cutoff value of 3.30 m/s identified patients with high-risk EVs with a 99.4% negative predictive value, 98.9% sensitivity, 72.1% accuracy, and 0.018 negative likelihood ratio. SS values less than 3.3 m/s ruled out the presence of high-risk varices in patients with compensated or decompensated cirrhosis. SS could not be measured in 16 patients (4.5%). It was concluded that Measurements of SS can be used to identify patients with cirrhosis with EVs or high-risk EVs. A cutoff SS was identified that could rule out the presence of varices and could be used as an initial noninvasive screening test.

In 2014 Colecchia A[135] "conducted a prospective study to assess SS predictive value for clinical decompression (CD) compared to HVPG, liver stiffness (LS), and other non-invasive tests for portal hypertension in a cohort of patients with HCV-related compensated cirrhosis. From an initial cohort of 124 patients, 92 underwent baseline LS, SS, HVPG measurements and upper gastrointestinal endoscopy at enrolment and then followed-up for 2 years or until the occurrence of the first CD. During follow-up, 30 out 92 (32.6%) patients developed CD. At univariate analysis varices at enrolment, all non-invasive parameters, HVPG, and model for end-stage liver disease (MELD) resulted clinical predictors of CD. At multivariate analysis only SS (p=0.0001) and MELD (p=0.014) resulted as predictive factors. This study shows that in compensated cirrhotic patients a SS and MELD predictive model represents an accurate predictor of CD with accuracy at least equivalent to that of HVPG. If confirmed by further studies, SS and

MELD could represent valid alternatives to HVPG as prognostic indicator of CD in HCV-related cirrhosis. A value for SS of < 54 kPa ruled out the risk of complications in the subsequent 2 years".

In 2015, Procopet B[136] prospectively included 88 consecutive patients undergoing hepatic venous pressure gradient measurement (HVPG, reference standard) for portal hypertension. Liver stiffness (LS) was measured by RT-SWE and by transient elastography (TE). Spleen stiffness (SS) was measured by RT-SWE. Reliability criteria for RT-SWE were searched, and the accuracy of these techniques to identify HVPG ⩾10mmHg (clinically significant portal hypertension, CSPH) was tested and internally validated by bootstrapping analysis. LS and SS by RT-SWE were feasible respectively in 87 (99%) and 58 (66%) patients. Both correlated with HVPG (LS: R=0.611, p<0.0001 and SS: R=0.514, p<0.0001). LS performed well for diagnosing CSPH (optimism corrected AUROC=0.858). Reliability of measurements was influenced by standard deviation (SD)/median ratio and depth. SD/median ⩽0.10 and depth of measurement <5.6cm were associated to 96.3% well classified for CSPH, while when one or none of the criteria were fulfilled the rates were 76.4% and 44.4%, respectively. Measurements fulfilling at least one criterion were considered acceptable; in these patients, RT-SWE performance to detect CSPH was excellent (AUROC=0.939; 95% CI: 0.865-1.000; p<0.0001; best cut-off: 15.4kPa). LS by RT-SWE and by TE were strongly correlated (R=0.795, p<0.0001) and performed similarly both in "per protocol" and in "intention-to-diagnose" analysis after applying reliability criteria.

In 2016, Balakrishnan M et al[137] conducted a study on 177 patients to characterize the intraobserver and interobserver variability of ARFI-measured liver and spleen

stiffness. Intraobserver Intraclass correlation coefficients (ICC) were the same for both observers for liver stiffness (0.89; 95% confidence interval [CI], 0.85–0.92) and spleen stiffness (0.72; 95% CI, 0.61–0.80). Interobserver agreement was excellent for liver stiffness (ICC, 0.85; 95% CI, 0.76–0.90) but not as good for spleen stiffness (ICC, 0.73; 95% CI, 0.60–0.83). A body mass index of 30 kg/m^2 or greater, waist circumference of greater than 105 cm, and skin-to-capsule distance of 2 cm or greater negatively affected the ICC for liver stiffness; small spleen size negatively affected the ICC for spleen stiffness. This article is the first report of ARFI findings in a US population with chronic liver disease. Liver stiffness reproducibility was excellent, particularly in nonobese patients. Spleen stiffness reproducibility was excellent in those with larger spleens and therefore may be most useful in patients with cirrhosis and portal hypertension.

A meta-analysis of 16 studies that compared the accuracy of SSM with LSM for use in predicting the presence of EV, has shown that SSM was significantly superior to LSM[138].

In 2016, Ma X et al[138] conducted a meta-analysis of the 16 studies (ten studies using TE, three using pSWE-VTQ (point shear wave elastography), and three using 2D-SWE-SSI) including 1892 patients to evaluate the diagnostic performance of LS and SS measurement for detecting EV in patients with chronic liver disease (CLD), and compare their accuracy. In detection of any EV, for LS measurement, the summary sensitivity was 0.83 (95% confidence interval [CI]: 0.78–0.87), and the specificity was 0.66 (95% CI: 0.60–0.72). While for SS measurement, the pooled sensitivity and specificity was 0.88 (95% CI: 0.83–0.92) and 0.78 (95% CI: 0.73–0.83). The summary receiver operating characteristic (SROC) curve values of LS and SS were 0.81 (95% CI: 0.77–0.84) and

0.88 (95% CI: 0.85–0.91) respectively, and the results had statistical significance (P<0.01). The diagnostic odds ratio (DOR) of SS (25.73) was significantly higher than that of LS (9.54), with the relative DOR value was 2.48 (95%CI: 1.10–5.60), P<0.05. It was concluded that under above mentioned techniques, SS is significantly superior to LS for identifying the presence of EV in patients with CLD. SS measurement may help to select patients for endoscopic screening.

However, most of the published data were obtained in heterogeneous populations of patients, with either compensated (correct target) or decompensated cirrhosis, and therefore, the superiority of SSM versus LSM for the diagnosis of PH in compensated ACLD patients, has not been definitively proven[131].

TE applicability for SSM is limited to about 70% of cases and, for technical reasons, it is closely dependent on the presence of increased spleen size. Additionally, measurement of stiffness by TE currently reaches a maximum of 75 kPa. As the spleen is significantly stiffer than the liver, most patients with severe PH show maximal values of SSM, above which, risk cannot be stratified. Widening the measurement range up to 150 kPa with appropriate software modifications has been proposed and tested, and showed that patients with large varices, or varices which had already bled, often had an SSM well above 75 kPa. pSWE[133,134] and 2D-SWE[137] have been used more recently, and do not have the ceiling effect of TE. Assessment of SSM using 2D-SWE (SSI), like TE, is limited to patients with enlarged spleen[137]. However, SSM can be measured using pSWE (VTQ) in about 95% of cases.37 Higher variability has been observed in the measurement of this parameter compared to LSM using the same technique[137].

In 2016, Y. Takuma et al[139] conducted a study on 446 cirrhotic patients and followed them prospectively to evaluate SS determined by ARFI imaging as a predictor of oesophageal variceal bleeding (OVB). The areas under the ROC curve (AUROC) values for predicting OVB were 0.857 for SS, 0.756 for PSR, 0.746 for spleen diameter, 0.720 for platelet count and 0.668 for LS. SS had a significantly better AUROC value for predicting OVBs compared with all other parameters. An SS cut-off value of 3.64 m/s identified patients with OVBs with a 97.9% negative predictive value, 78.8% sensitivity and 79.8% accuracy. In subgroup analyses, the AUROCs of SS for predicting OVBs were 0.911 in compensated, 0.786 in decompensated and 0.727 in patients with OV, respectively. Optimal SS cut-off values for predicting OVBs were 3.48 m/s for compensated patients and 3.75 m/s for both decompensated and patients with OV, respectively. OVB is the major cause of death in cirrhotic patients. In recent cross sectional studies, SS has shown improved diagnostic accuracy for portal hypertension, including the hepatic venous pressure gradient and OV, as compared with other parameters reflecting portal hypertension, such as platelet count and spleen diameter. In particular, among the patients with OV or decompensated cirrhosis, those with an SS value ≧3.75 m/s had a higher incidence of OVB compared with those with an SS value >3.64 m/s. This was the first reported study to quantitatively analyse the role of SS as a risk factor for OVB alone in a longitudinal study. It was concluded that SS measured using ARFI imaging provides excellent diagnostic performance for predicting OVB, particularly in compensated cirrhosis.

The spleen undergoes parenchymal remodelling in patients with PH. This is partly attributable to passive congestion and increased arterial inflow, and partly because of

increased hyperactive splenic lymphoid tissue and enhanced angiogenesis and fibrogenesis, leading to the progressive development of splenomegaly in most patients. Ultrasound studies in the 1980s and 1990s showed that spleen vascular resistance (estimated by Doppler pulsatility and resistance indexes) is increased in patients with PH, and correlates with PH severity and complications[119].

Stiffness and haemodynamics of the spleen are probably sensitive sensors of portal pressure and of portal vein resistance. Therefore, the next route to follow will be the combination of SS with the Doppler splenic resistance indices, and possibly platelet count and spleen size. Indeed, individually, these parameters have shown better accuracy in the prediction of portal hypertension. SS is probably related to splenic congestion due to portal hypertension in an organ with a rigid capsule. The platelet count/spleen diameter ratio is probably the simplest index for determining the presence of portal hypertension and EV[40]. Doppler splenic resistance indices are related to portal blood flow resistance and to HVPG[40].

Therefore, it has been postulated that spleen stiffness measurement (SSM) by ultrasound elastography could be an accurate non-invasive surrogate for PH, and devoid of the limitations of LSM. Studies comparing LSM and SSM (measured by TE in an adequate left intercostal space using technical conditions similar to those used for LSM) showed that the spleen is substantially stiffer than the liver in both healthy subjects and patients with CLD. In some studies, SSM showed a closer correlation with HVPG, CSPH and presence and size of EV when compared to LSM[6].

Similarly to LS, SS measurement has also been reported as useful for predicting clinical complications in compensated cirrhosis[135].

In patients with suspected portal hypertension of unknown cause, and in patients with non-cirrhotic portal hypertension, LSM and SSM may help the clinician in this initial assessment. LSM is usually only moderately increased in idiopathic PH (mean value of 8.4 ± 3.3 kPa), showing a clear mismatch with the values expected in patients with cirrhosis; however, SSM in this population is elevated to values similar or even higher than those observed in patients with cirrhotic PH. Cirrhotic and idiopathic PH often appear similar when imaged, and therefore, the ratio between LSM and SSM could improve the clinicians' ability to identify idiopathic PH and avoid an incorrect diagnosis of cryptogenic cirrhosis[131].

In patients with extrahepatic portal vein obstruction (EHPVO) spleen stiffness is increased and SSM values are higher in patients who had already bled from varices, versus patients whose varices had not bled. Therefore, SSM might be a valuable tool used to stratify the severity of PH in patients with EHPVO, in whom HVPG is not reliable (prehepatic PH)[131].

However, the limitations of Elastograhy is that, TE cannot be performed in patients with ascites, and the failure rate of TE is generally higher in obese patients[129]. Aminotransferase flares, food intake, extrahepatic cholestasis, steatosis, increased central venous pressure and the use of beta blockers can influence the accuracy of Stiffness assessment by TE. SSM is not yet used routinely in clinical practice because of the limitations described above. In recent years, additional techniques have been proposed for the evaluation of LS, each of which appear to overcome some of the limitations presented by traditional TE; these include acoustic radiation force impulse imaging (ARFI) and shearwave velocity estimation. Moreover, LS and SS measurement are

considered reliable for estimating portal hypertension only when the coefficient of variation among the successful measurements in a single patient is low[136]. Further research is needed to establish whether the dynamics of SSM over time or in response to treatment could be a better indicator of HVPG changes"[131].

TECHNICAL ASPECTS:

ULTRASOUND - GENERAL PRINCIPLES[140-143]

Ultrasonic (Latin: Ultra = 'beyond' or 'excess' and sonic = 'sound') sound are the sounds of frequencies beyond audible range. Unlike conventional X-ray and CT which make use of transmitted energy for imaging, ultrasound makes use of reflected energy for imaging.It provides images in real-time and so can also be used to interrogate the movement of structures such as cardiac valves, interactive guidance of biopsies and drainage procedures and, using the Doppler mode, the patterns of blood flow in both large and small vessels Diagnostic ultrasound has been in use since 1950.

Ultrasound is produced by a transducer constructed of a piezoelectric material which has the property of changing thickness when a voltage is applied to it. This phenomenon is called reverse piezoelectric effect. Likewise a small electric signal is produced when an ultrasound wave strike it, which is called piezoelectric effect. Thus, transducers are the devices that convert electric signal into ultrasonic energy and convert back reflected ultrasonic energy into electric signal.

DOPPLER-BASIC PRINCIPLES [144,145] :

The Doppler effect, first described by the Austrian physicist Christian Johann Doppler (1805–53) in 1842, describes the effect of motion on the reflected frequency of waves, and originally described the light waves emitted from stars.

The Doppler effect is a change in the frequency of a detected wave, when the source or the detector ismoving[144].

In medical ultrasonography a Doppler shift occurs when reflectors move relative to the transducer. The frequency of echo signals from moving reflector is higher or lower than the frequency transmitted by the transducer depending onwhether the motion is towards or away from the transducer. The amount of change in the frequency (*Doppler shift*) is proportional to the speed of the object and so a measurement of flow can be made (fig.13)[145].

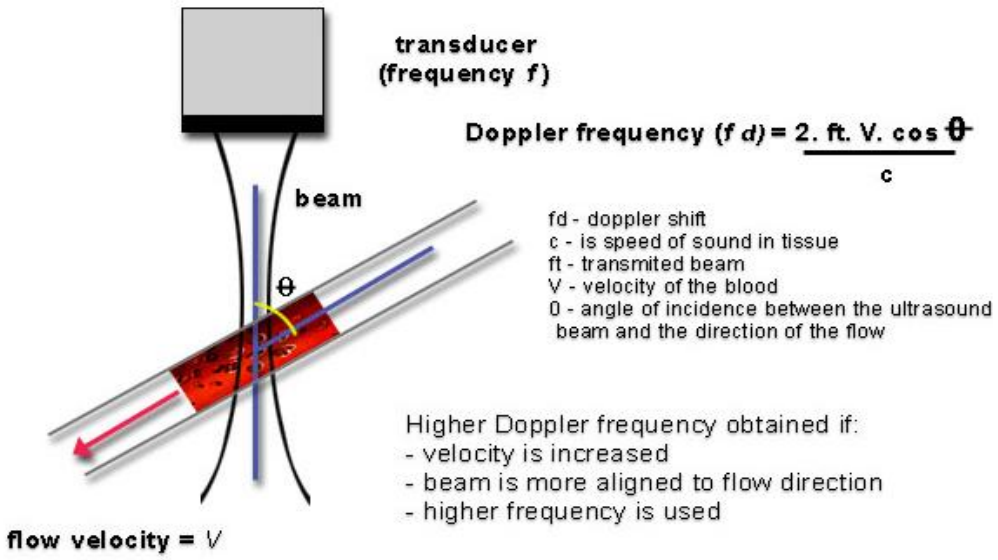


FIG13: The Doppler shift/equation[145]

"Ultrasound images of flow, whether color flow or spectral Doppler, are essentially obtained from measurements of movement. In ultrasound scanners, a series of pulses is transmitted to detect movement of blood. Echoes from stationary tissue are the same from pulse to pulse. Echoes from moving scatterers exhibit slight differences in the time for the signal to be returned to the receiver. These differences can be measured as a direct time difference or, more usually, in terms of a phase shift from which the 'Doppler frequency' is obtained. They are then processed to produce either a color flow display or a Doppler sonogram. In vessels, the major reflectors are the blood cells. The electronics allow the detection of the difference between normal reflections and reflections that have undergone Doppler shift. There are several different ways in which the Doppler image can be depicted.

Three basic levels of US can be performed, with each level adding information to the preceding level. At the first level is the traditional standard brightness mode (B-mode) gray-scale examination, in which no Doppler is used. The second level superimposes a color Doppler interrogation region of interest. This level produces an image that shows blood flow in vessels. The third level superimposes a small interrogation region, called a sample volume, over a vessel of interest. Targeted interrogation of the vessel produces a spectral Doppler waveform.

PRINCIPLES OF ELASTOGRAPHY[146]:

The elasticity of a material describes its tendency to resume its original size and shape after being subjected to a deforming force or stress. Fluids resist a change in volume, but not in shape: they possess only volume elasticity. Solids resist changes in

shape and volume: they possess rigidity or shear elasticity, as well as volume elasticity. The change in size or shape is known as the strain, which is expressed as a ratio (e.g. the change in length per unit length). The strain is produced by a system of forces; the force acting on unit area is known as the stress.

From a physics point of view, elastography aims to quantitatively image the Young's E modulus, the physical parameter corresponding to the stiffness. The Young's modulus, noted E, exhibits important variations between different biological tissues, which makes it ideal for the characterization of different tissues with an excellent contrast. The Young's modulus characterizes the stiffness of a tissue, which is exactly the quantitative reproduction of a clinician's palpation and has relevant diagnostic value.

To assess the Young's modulus of the tissue, all elastography techniques rely on the same basis: an external force is applied to the studied tissue and the resulting movements

are then followed. The external force can be classified according to two means of excitation: the static methods (or the quasi-static method) and the dynamic methods.

Quasi-static elastography cannot give a quantitative value for the Young's modulus since only the strain can be estimated and the applied stress is unknown and dynamic elastography technique suffers from the overlapping of both compression and shear waves in the studied medium. In addition, the latter technique is very sensitive to boundary conditions (the waves rebound at the interfaces and are mixed together), which makes it very difficult to distinguish between compression and shear waves.

Faced with these limitations, transient elastography was developed at the same time and provides several technological improvements. The main advantage of transient excitation is to naturally separate shear waves from compression waves, since shear waves are three times slower than compression waves. Thus measurements of the propagation speed become relatively more straightforward. By studying the propagation of only the shear waves induced by a specific mechanical excitation, it is possible to estimate the viscoelastic properties of the investigated tissues.

Acoustic Radiation Force Impulse Imaging (ARFI) or ‘‘Acoustic Radiation Force Imaging’’, is a method developed by the American team of Kathy Nightingale. This technique uses the acoustic radiation force but, unlike vibro-acoustography, ARFI only uses one focalized ultrasound beam. The radiation force slightly displaces the tissue at the focal spot according to Hooke’s law. Then the transducer switches into imaging mode and detect displacements of the focal spot by tracking of the ultrasound signal (called ‘‘speckle’’). It is therefore possible to follow the displacement and the relaxation of tissue depending on the radiation force. The temporal properties of these relaxation curves allow the deduction of elasticity and viscosity at the focal spot only.

The ARFI technique also allows reconstructing a complete image by sweeping the zone, like vibro-acoustography. However, this has the disadvantage to increase the acquisition time in order to recover an entire image of the medium, and the deposited energy in the medium, which can cause consequent heating. This technique has been tested in vivo in the breast and ex vivo in the prostate. Here again, the measured parameters (displacements, relaxation times, etc.) depend on the Young’s modulus of the investigated region, but also on many other parameters, such as the geometries of the

beam and of the medium. The technique therefore cannot be used to quantitatively estimate tissue Young's modulus, though the measured parameters strongly depend on it. However, it has been implemented in many commercial ultrasound systems. Nightingale's team is interested in the propagation of shear waves generated by the radiation force and has recently proposed a new ARFI model called ''ARFI-SWS''.

Based on this concept, it allows to quantitatively measure the Young's modulus in a small region of interest. This variation is currently being evaluated for the liver staging and is available on commercial ultrasound systems.

Shear wave based techniques have strong advantages over quasi-static techniques, as they are more reproducible, quantitative, rely on automatic shear wave generation and provide good elasticity contrast"[146].

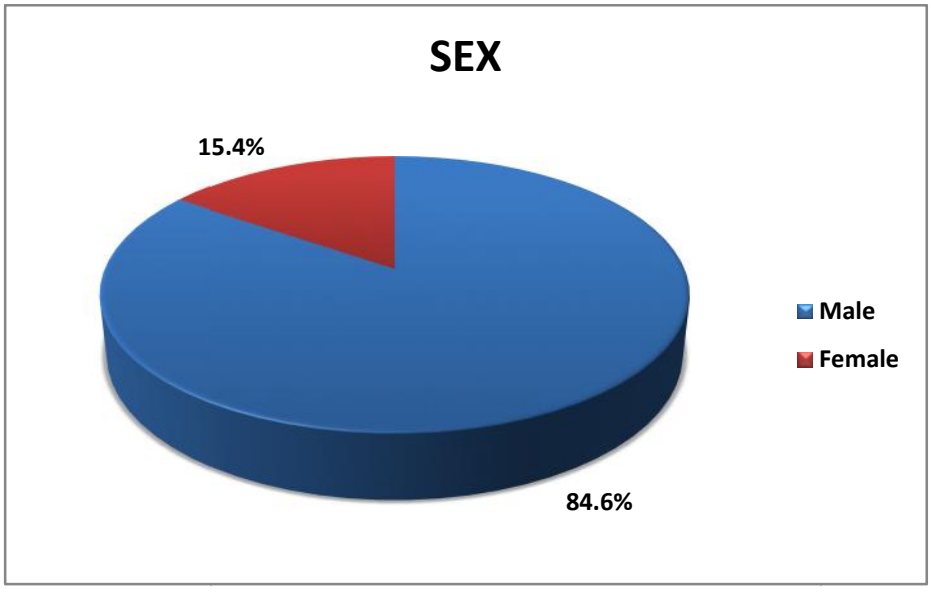
OBSERVATIONS AND RESULTS

TABLE 3: DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (yrs)	N	%
31-40	23	35.4
41-50	25	38.5
51-60	8	12.3
>60	9	13.8
Total	65	100

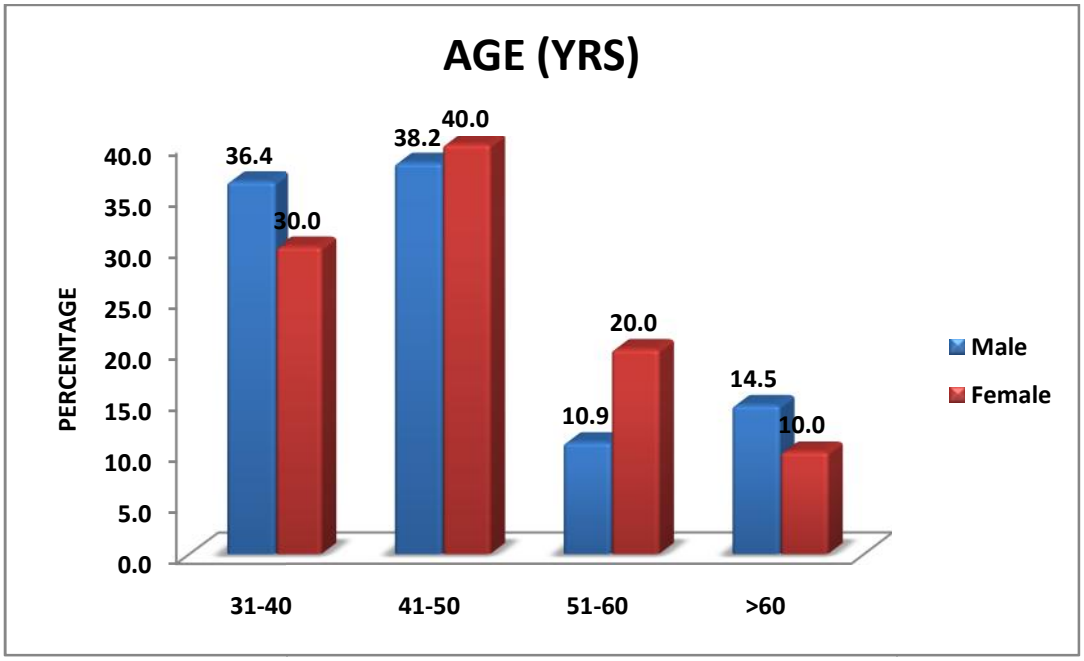
In a total of 65 patients included in the study with age group ranging from 30 to 70 years, the most common age groups presenting with portal hypertension were between 41-50 years (38.5%) and between 31-40 years (35.4%).

FIG. 14: DISTRIBUTION OF CASES ACCORDING TO SEX



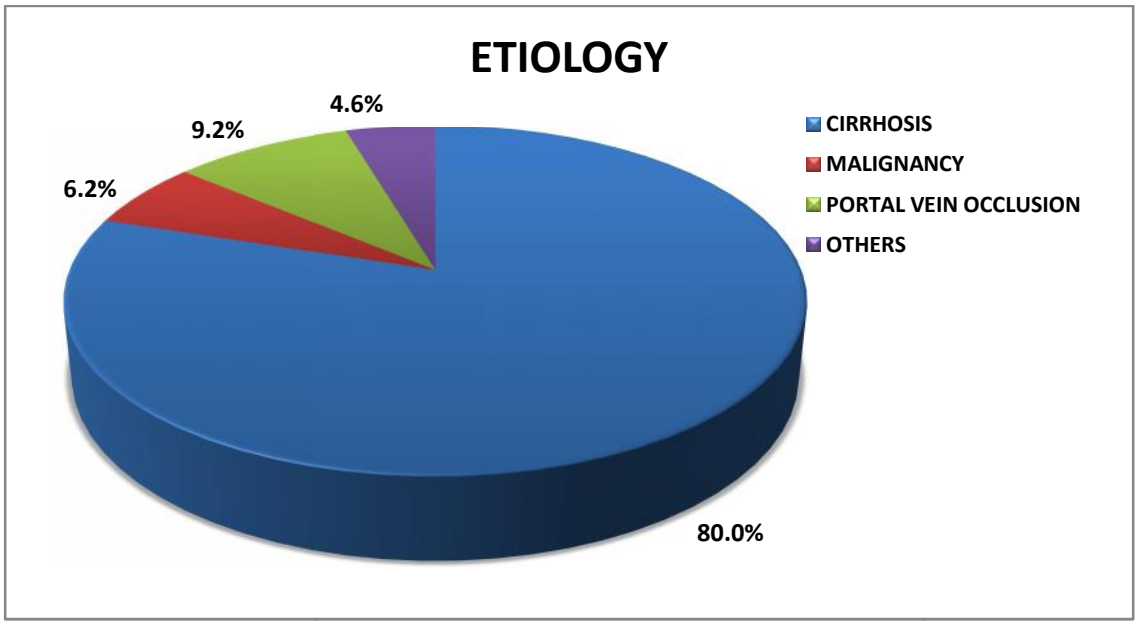
Our study group included 55 males and 10 females comprising 84.6 % and 15.4 % of the total cases respectively.

FIG. 15: ASSOCIATION OF AGE AND SEX



Male patients exceeded the number of female patients in all the age groups of our study.

FIG. 16: DISTRIBUTION OF CASES ACCORDING TO ETIOLOGY



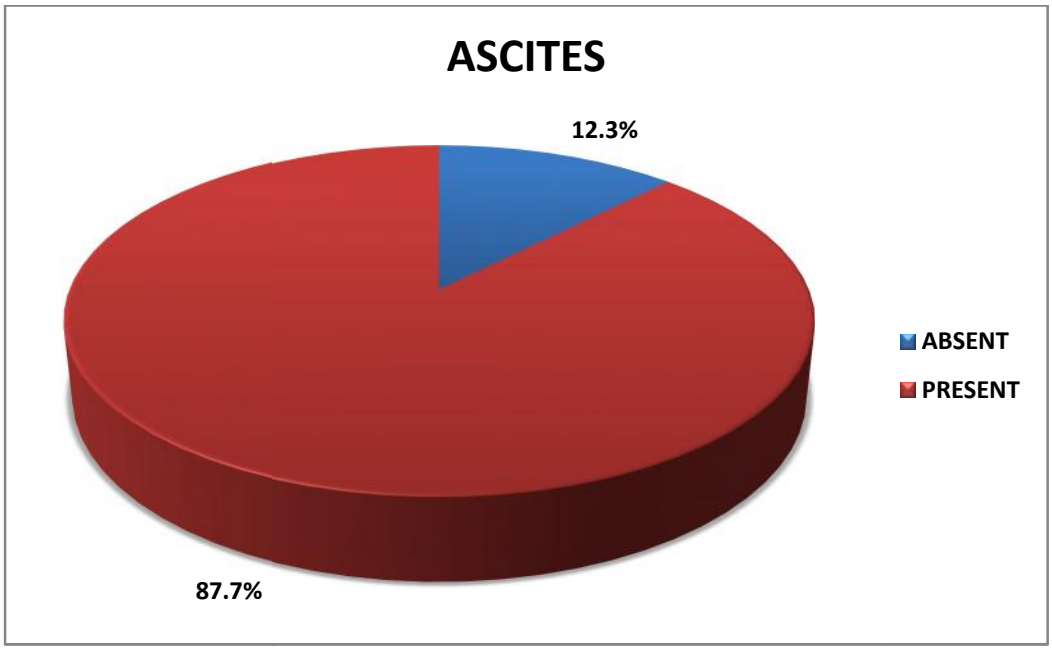
In our study, most common etiology was cirrhosis seen in 52 cases (80%). Second common etiology included Portal vein occlusion comprising 9.2 % cases. Malignancy causing portal venous thrombosis was seen in 6.2% cases.

TABLE 17: DISTRIBUTION OF CASES ACCORDING TO SPLEEN SPAN

SPLEEN SPAN (cm)	N	%
<13	10	15.4
≥13	55	84.6
Total	65	100

Splenomegaly (spleen span more than 13cm) was seen in 55 of the 65 cases corresponding to 84.6% of total cases, suggesting a significant association between portal hypertension and splenomegaly.

FIG. 17: DISTRIBUTION OF CASES ACCORDING TO ASCITES



Ascites was seen in 57 (87.7%) of the 65 cases studied revealing significant association between portal hypertension and ascites.

TABLE 5: DISTRIBUTION OF CASES ACCORDING TO DIAMETER OF PORTAL VEIN

DIAMETER OF PORTAL VEIN (mm)	N	%
<13	21	33.9
≥13	41	66.1
Total	62	100.0

Diameter of portal vein could not be measured in 3 cases where portal vein was not delineated due to cavernoma formation. Dilated portal vein was noted in 41 of 62 cases (66.1%).

TABLE 6: DISTRIBUTION OF CASES ACCORDING TO RESPIRATORY PHASICITY

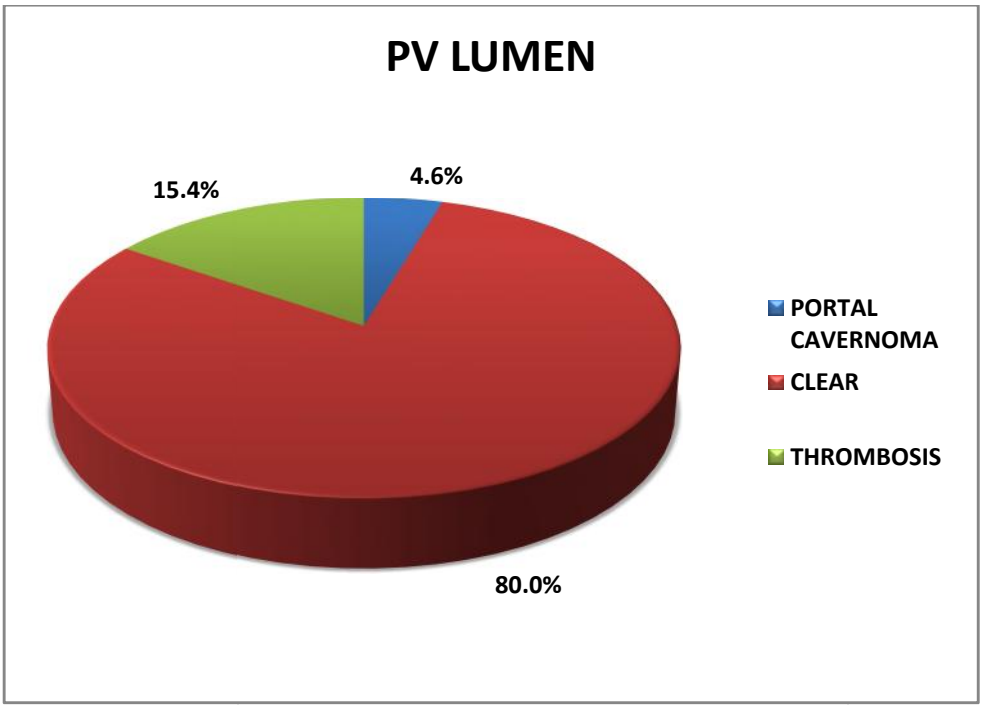
RESPIRATORY PHASICITY (%)	N	%
<20	49	79.0
≥20	13	21.0
Total	62	100.0

Loss of respiratory phasicity of portal vein was noted in 49 of the 62 cases (79 %). Loss of respiratory phasicity could not be assessed in 3 cases where portal vein was not delineated due to cavernoma formation.

TABLE 7: DISTRIBUTION OF CASES ACCORDING TO PV LUMEN

PV LUMEN	N	%
CLEAR	52	80
THROMBOSIS	10	15.4
PORTAL CAVERNOMA	3	4.6
Total	65	100

FIG. 18: DISTRIBUTION OF CASES ACCORDING TO PV LUMEN

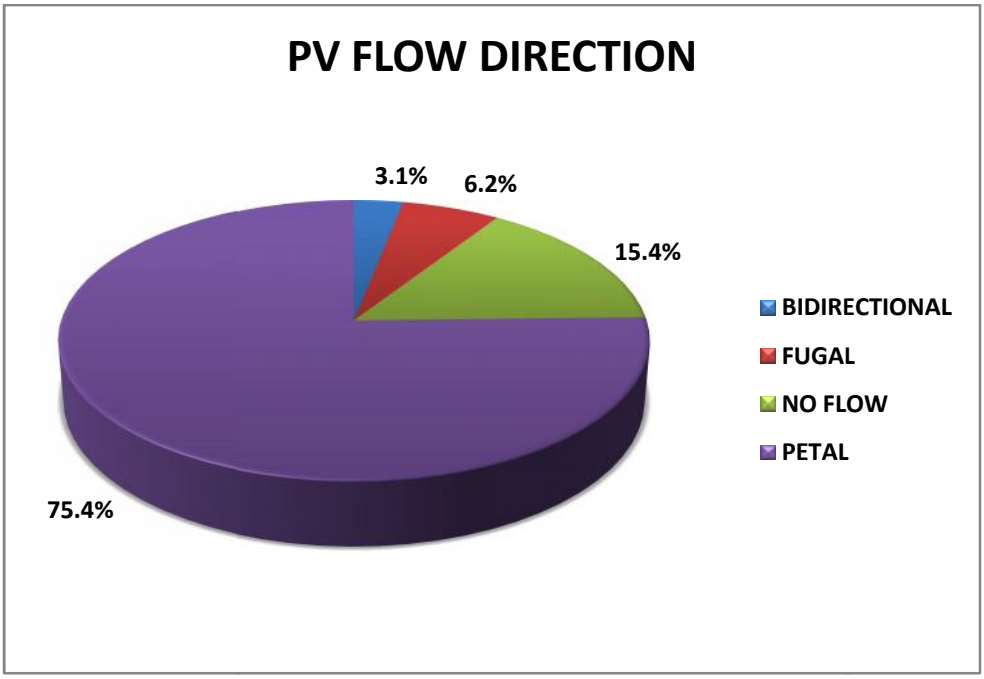


Intraluminal thrombus was noted in 10 of the 65 cases. An additional 3 cases showed cavernoma formation in the porta hepatis where PV was not delineated. In 52 cases (80%) the lumen was clear.

TABLE 8: DISTRIBUTION OF CASES ACCORDING TO PV FLOW DIRECTION

PV FLOW DIRECTION	N	%
PETAL	49	75.4
FUGAL	4	6.2
BIDIRECTIONAL	2	3.1
NO FLOW	10	15.4
TOTAL	65	100

FIG. 19: DISTRIBUTION OF CASES ACCORDING TO PV FLOW DIRECTION

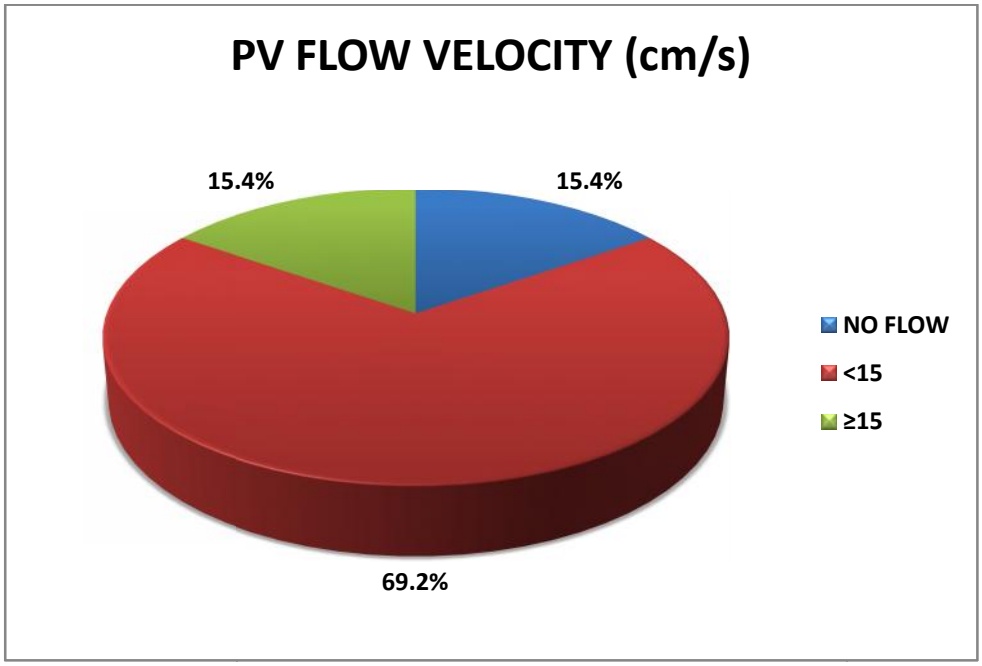


The direction of flow was hepatopetal in majority (75.4%) of the cases. Hepatofugal flow was noted in only 4 cases. Bidirectional flow was noted in 2 cases and no flow was noted in 10 cases due to thrombosis.

TABLE 9: DISTRIBUTION OF CASES ACCORDING TO PV FLOW VELOCITY

PV FLOW VELOCITY (cm/s)	N	%
NO FLOW	10	15.4
<15	45	69.2
≥15	10	15.4
Total	65	100

FIG. 20: DISTRIBUTION OF CASES ACCORDING TO PV FLOW VELOCITY

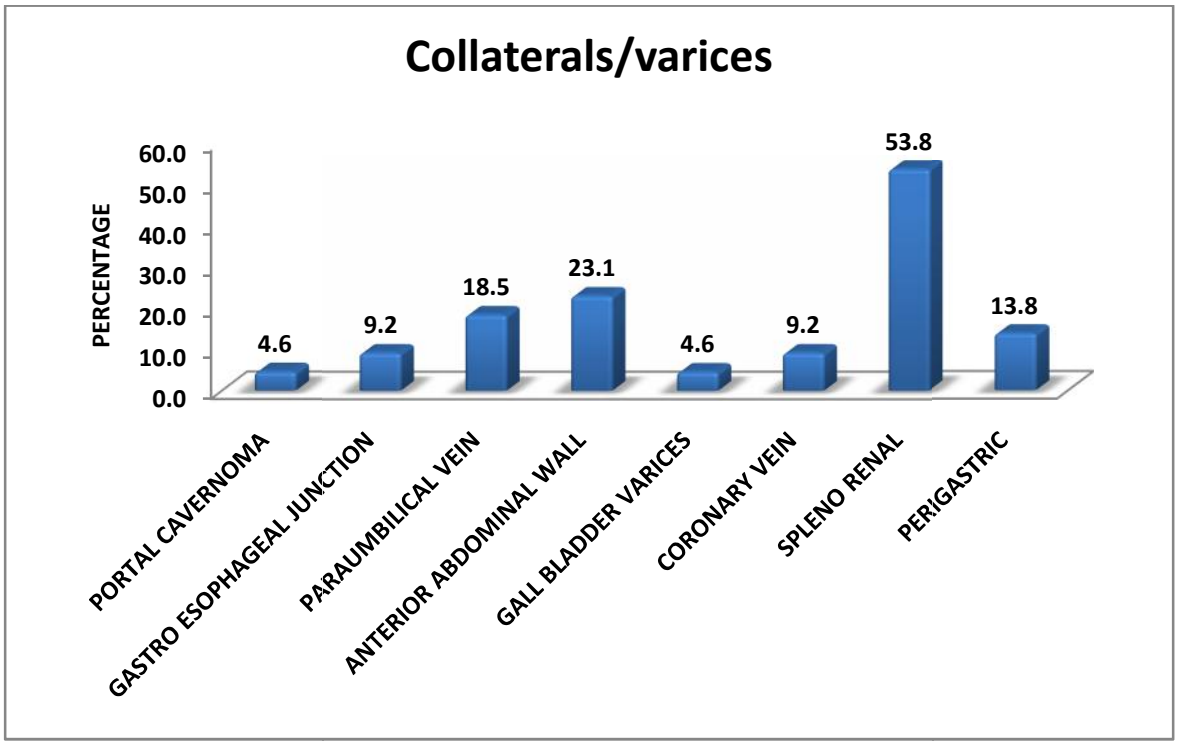


Out of total 65 cases studied, no flow was noted in 10 cases due to thrombosis. In the rest of the 55 cases, decreased velocity (<15cm/sec) was noted in 69.2 % cases and 15.4 % cases had velocity ≥15cm/sec.

TABLE 10: DISTRIBUTION OF CASES ACCORDING TO PORTOSYSTEMIC COLLATERALS/VARICES

COLLATERALS/VARICES	N	%
PORTAL CAVERNOMA	3	4.6
GASTRO ESOPHAGEAL JUNCTION	6	9.2
PARAUMBILICAL VEIN	12	18.5
ANTERIOR ABDOMINAL WALL	15	23.1
GALL BLADDER VARICES	3	4.6
CORONARY VEIN	6	9.2
SPLENO RENAL	35	53.8
PERIGASTRIC	9	13.8

FIG. 21: DISTRIBUTION OF CASES ACCORDING TO PORTOSYSTEMIC COLLATERALS/VARICES

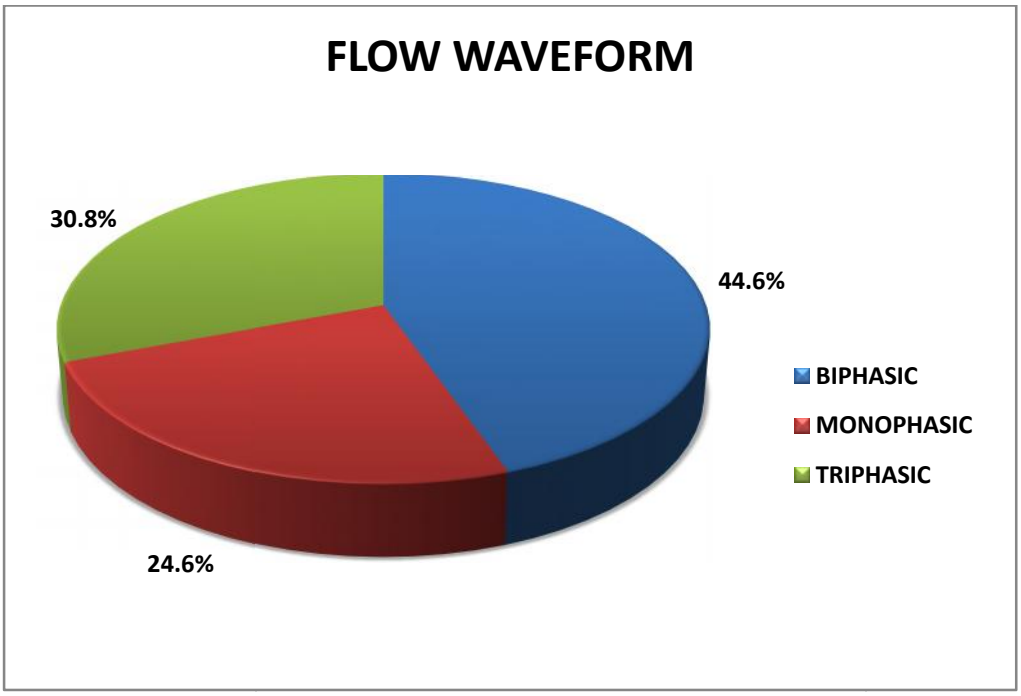


Most frequent collateral was the splenorenal collateral which comprised 53.8% of cases.

TABLE 11: DISTRIBUTION OF CASES ACCORDING TO HEPATIC VEIN FLOW WAVEFORM

FLOW WAVEFORM	N	%
BIPHASIC	29	44.6
MONOPHASIC	16	24.6
TRIPHASIC	20	30.8
Total	65	100

FIG. 22: DISTRIBUTION OF CASES ACCORDING TO HEPATIC VEIN FLOW WAVEFORM

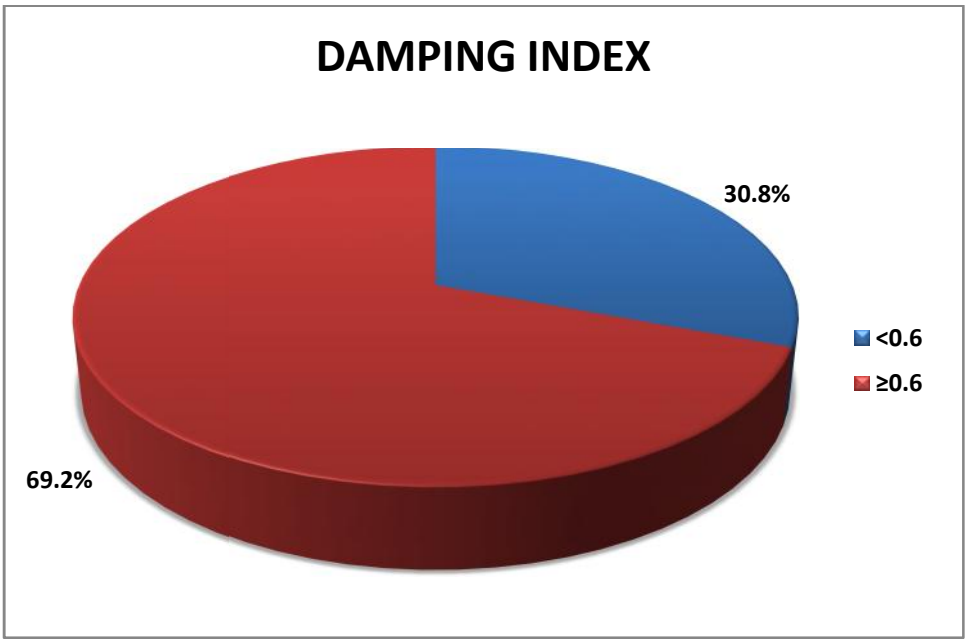


Out of 65 cases in the study group, 44.6% of cases showed biphasic hepatic vein waveform followed by triphasic and monophasic waveforms.

TABLE 12: DISTRIBUTION OF CASES ACCORDING TO DAMPING INDEX OF HEPATIC VEIN

DAMPING INDEX	N	%
<0.6	20	30.8
≥0.6	45	69.2
Total	65	100

FIG. 23: DISTRIBUTION OF CASES ACCORDING TO DAMPING INDEX OF HEPATIC VEIN

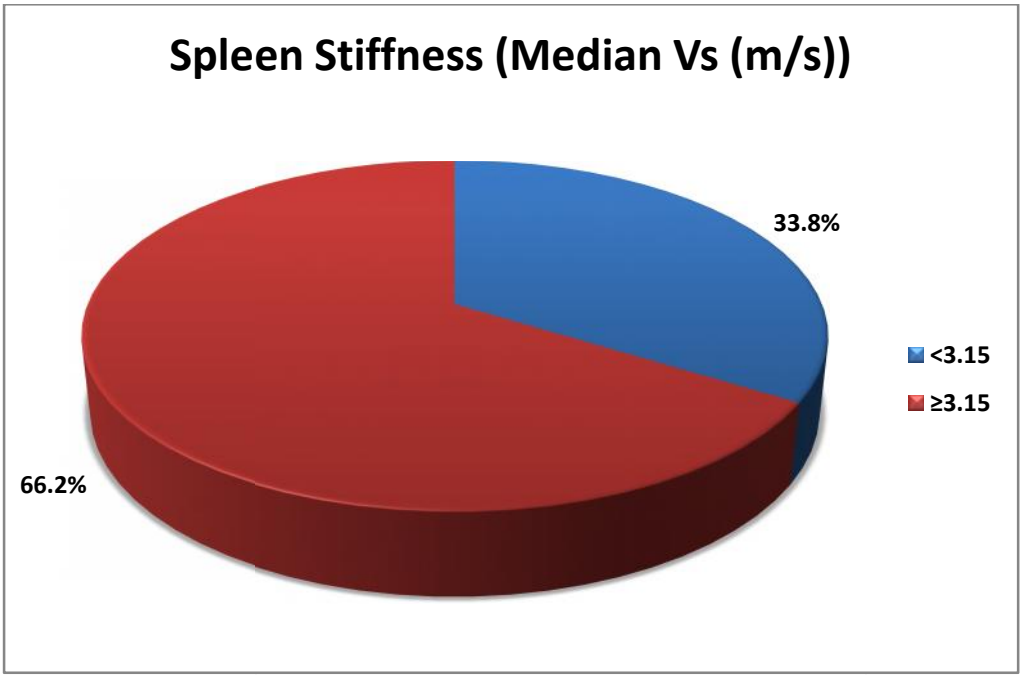


Damping index as calculated by the ratio of minimum by maximum velocity of hepatic vein was calculated in all the 65 cases of the study group. DI ranged between 0.36-0.92 with a mean value of 0.65± 0.15. Majority of the cases (69.2 %) showed DI>0.6 suggesting severe portal hypertension.

TABLE 13: DISTRIBUTION OF CASES ACCORDING TO SHEAR WAVE VELOCITY OF ARFI CUT OFFS SUGGESTED FOR SPLEEN STIFFNESS [133]

SPLEEN STIFFNESS: Median Vs (m/s)	N	%
<3.15	22	33.8
≥3.15	43	66.2
Total	65	100

FIG. 24: DISTRIBUTION OF CASES ACCORDING TO SHEAR WAVE VELOCITY OF ARFI CUT OFFS SUGGESTED FOR SPLEEN STIFFNESS [133]



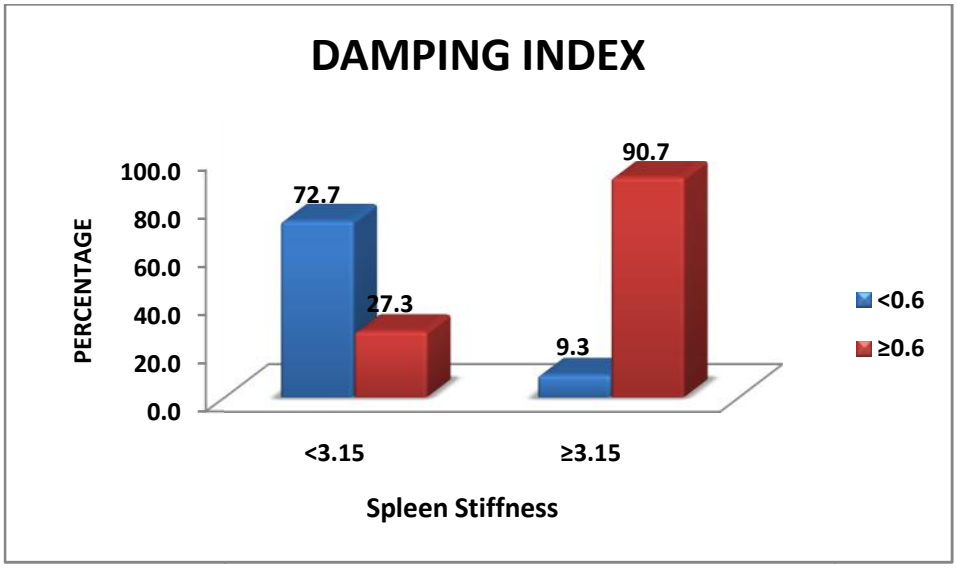
Spleen stiffness as measured by shear wave velocity using ARFI method was calculated in all 65 cases of the study group. Majority of the cases (66.2 %) showed median Vs >3.15 m/s.

TABLE 14: ASSOCIATION BETWEEN SUGGESTED CUT OFFS[133] FOR SHEAR WAVE VELOCITY OF SPLEEN AND DAMPING INDEX

DAMPING INDEX	SPLEEN STIFFNESS (Median Vs (m/s))				p value
	<3.15		≥3.15		
	N	%	N	%	
<0.6	16	72.7	4	9.3	<0.001*
≥0.6	6	27.3	39	90.7	
Total	22	100.0	43	100.0	

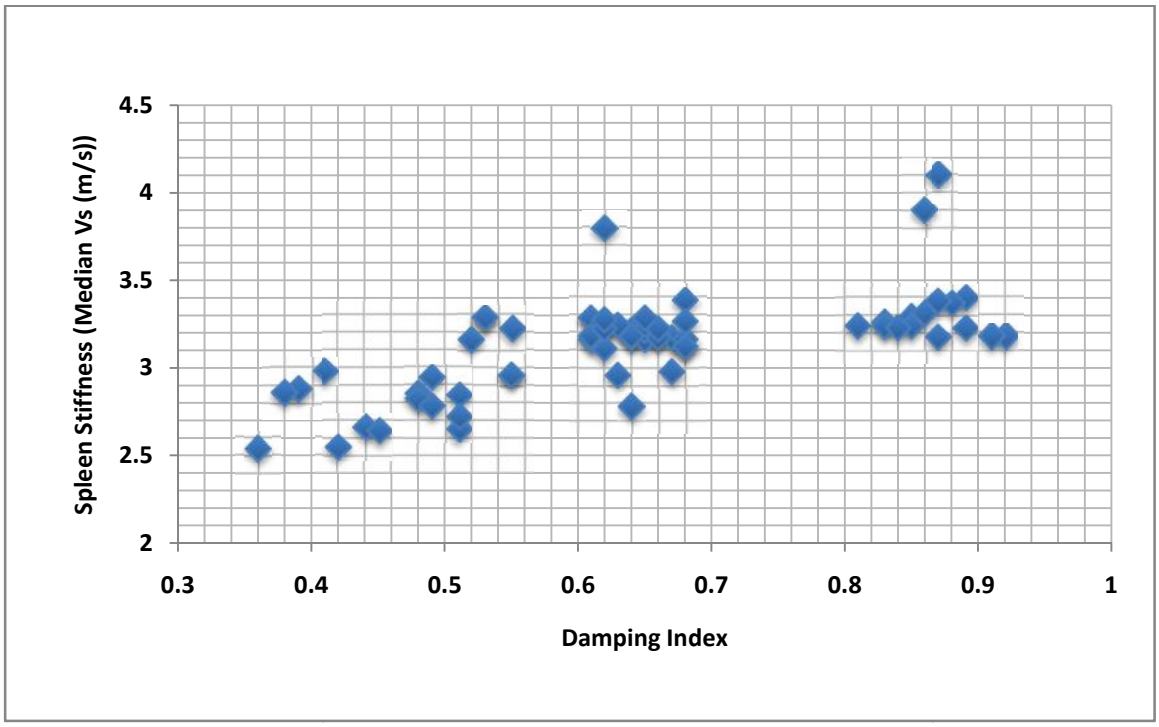
Note: * significant at 5% level of significance (p<0.05)

FIG. 25: ASSOCIATION BETWEEN SUGGESTED CUT OFFS[133] FOR SHEAR WAVE VELOCITY OF SPLEEN AND DAMPING INDEX



Out of 45 cases with DI>0.6 in the study group (severe portal hypertension), 39 cases (90.7 %) showed median Vs >3.15 m/s with significant p value (<0.001) reflecting a strong association between spleen stiffness and severity of portal hypertension.

FIG. 26: CORRELATION OF SHEAR WAVE VELOCITY OF SPLEEN WITH DAMPING INDEX



In the study group, DI ranged between 0.36 – 0.92 with mean value of 0.65 ± 0.15. Majority of the cases (69.2 %) showed DI>0.6 suggesting severe portal hypertension. ARFI shear wave velocity of spleen ranged between 2.54 – 4.1 m/s with mean SS of 3.14 ± 0.28 m/s.

TABLE 15: ASSOCIATION BETWEEN SUGGESTED CUT OFFS FOR SHEAR WAVE VELOCITY OF SPLEEN AND DAMPING INDEX

Damping Index	Spleen Stiffness (Median Vs (m/s))				p value
	<3.11		≥3.11		
	N	%	N	%	
<0.6	16	80.0	3	6.7	<0.001*
≥0.6	4	20.0	42	93.3	
Total	20	100.0	45	100.0	

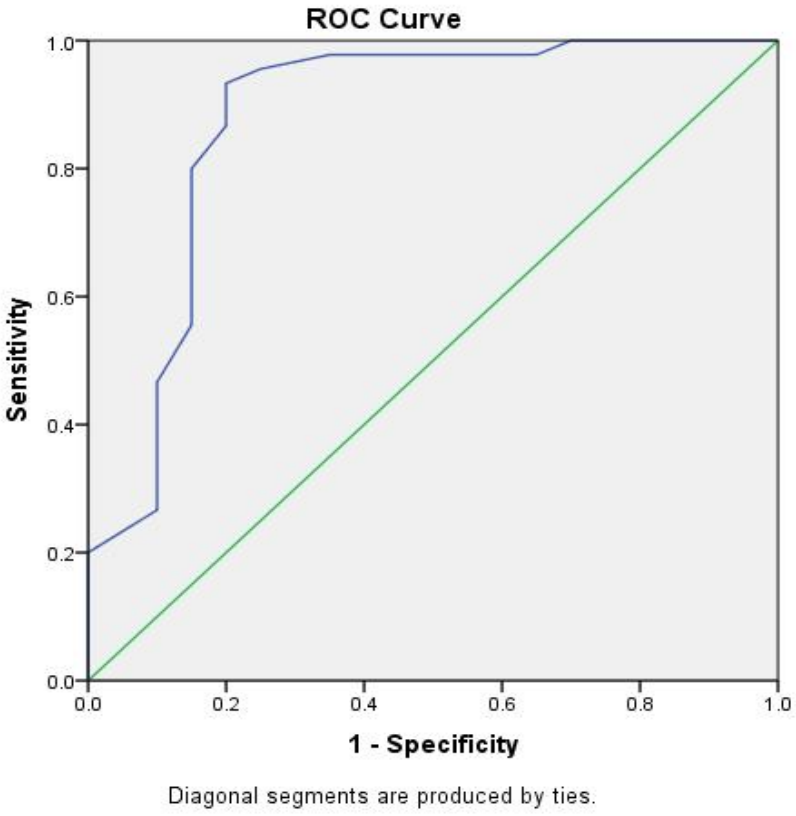
Note: * significant at 5% level of significance (p<0.05)

TABLE 16 : ROC ANALYSIS OF SHEAR WAVE VELOCITY OF SPLEEN TO DETECT DAMPING INDEX >0.6

Area Under the Curve	Std. Error	p value	95% Confidence Interval	
			Lower Bound	Upper Bound
0.877	0.056	<0.001*	0.767	0.988

Note: * significant at 5% level of significance (p<0.05)

FIG. 27: ROC ANALYSIS OF SHEAR WAVE VELOCITY OF SPLEEN TO DETECT DAMPING INDEX >0.6 (SEVERE PORTAL HYPERTENSION)



Area under the receiver operating curve (AUROC) analyses of spleen stiffness (SS) and DI in predicting the presence of severe portal hypertension. AUROC: 0.877.

TABLE 17: DIAGNOSTIC EFFICACY OF SHEAR WAVE VELOCITIES OF SPLEEN IN PREDICTING THE SEVERITY OF PORTAL HYPERTENSION BASED ON DAMPING INDEX (>0.6)

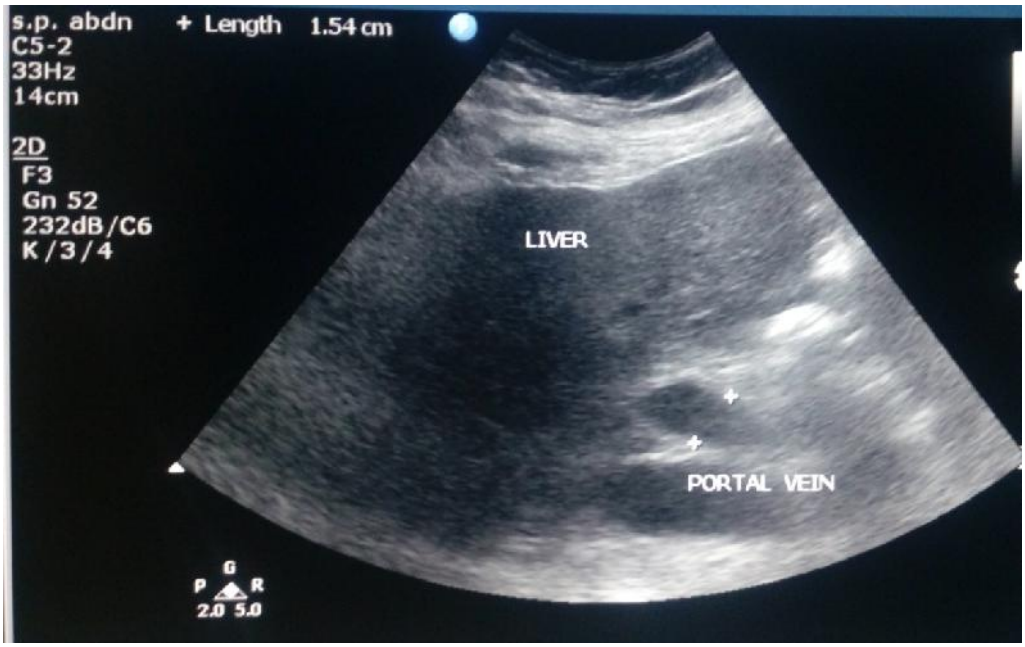
	WITH CUT OFF 3.15 m/s[133]	WITH CUT-OFF 3.11 m/s
TP (true positive)	6	42
FN (false negative)	16	3
FP (false positive)	0	4
TN (true negative)	0	16
Sensitivity	86.7%	93.33%
Specificity	80.0%	80.00%
PPV	90.7%	91.30%
NPV	72.7%	84.21%
Accuracy	84.6%	89.23%

TABLE 18: DIAGNOSTIC ABILITY OF SPLEEN STIFFNESS BY ARFI FOR IDENTIFYING SEVERE PORTAL HYPERTENSION

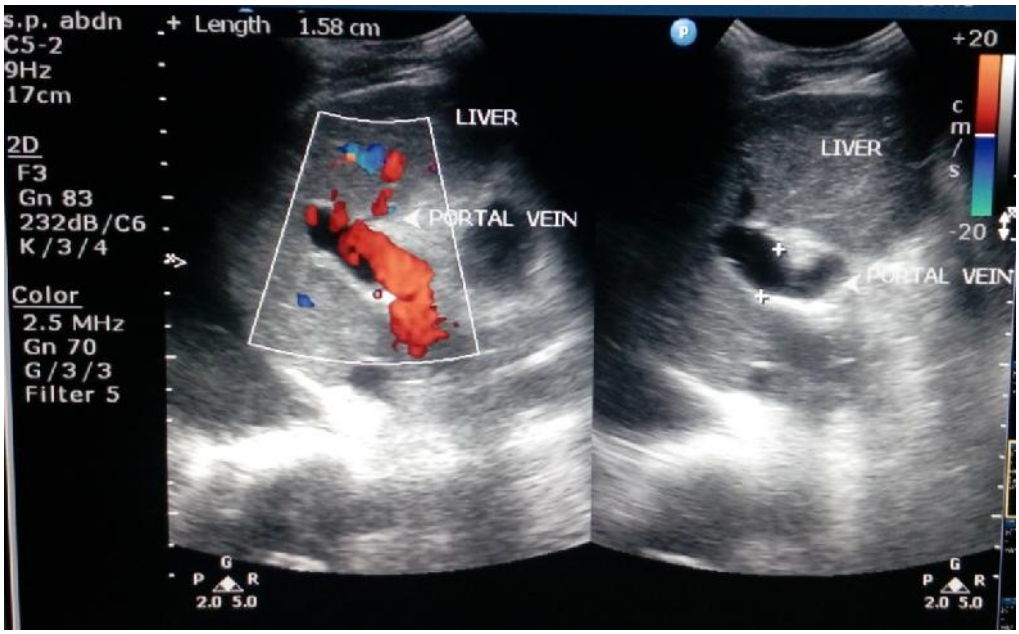
Cutoff value for severe PH (m/s)	**Sensitivity**	**Specificity**
2.75	100.0%	30.0%
3.11	**93.3%**	**80.0%**
3.15	**86.7%**	**80.0%**
3.20	60.0%	85.0%
3.28	26.7%	90.0%

The SS cutoff value of 3.11 m/sec was selected to rule out the presence of severe portal hypertension with a highest sensitivity of 93.3% and specificity of 80%.

IMAGING GALLERY



(a)



(b)

FIG. 28 : a) Grey scale & b) colour Doppler USG Image showing dilated portal vein

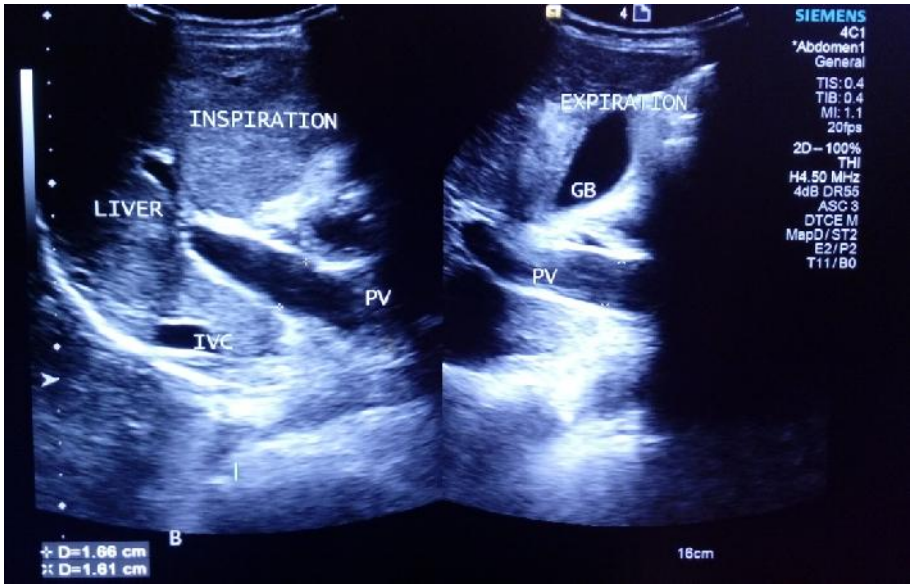


FIG. 29 : USG Image showing loss of respiratory phasicity in portal vein

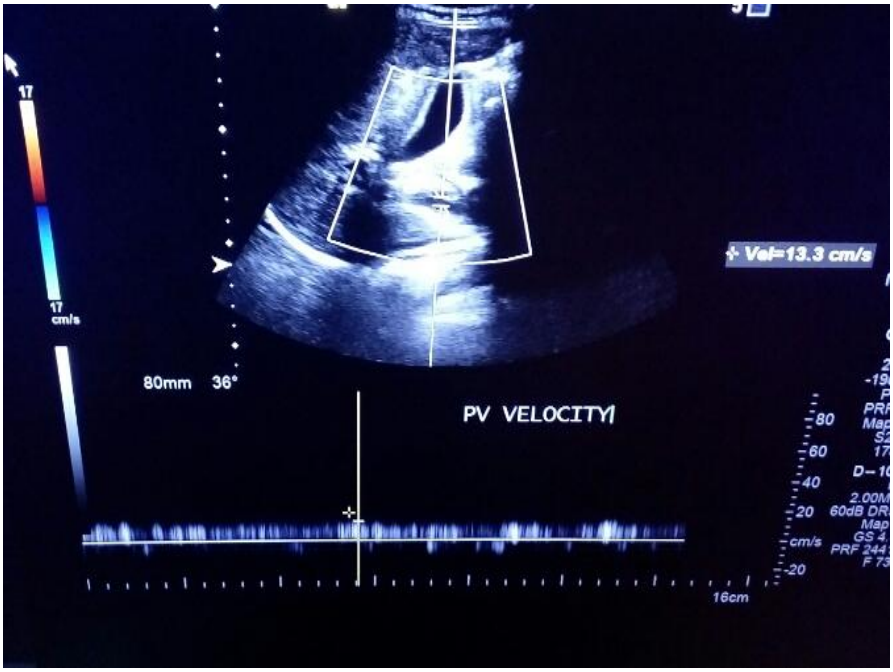


FIG. 30 : Spectral Doppler USG Image showing reduced portal vein velocity

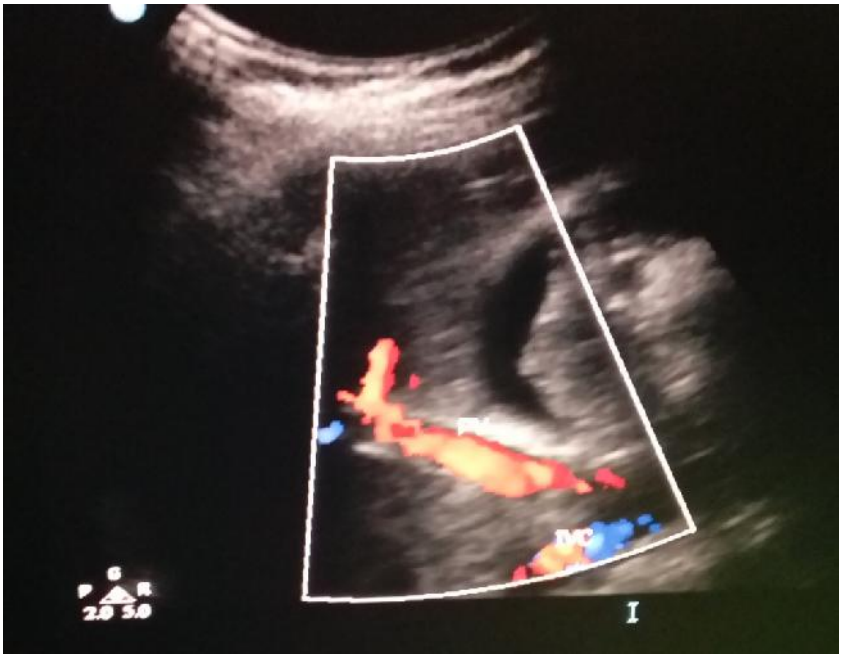


FIG. 31 : Colour Doppler USG Image showing hepatopetal flow in portal vein

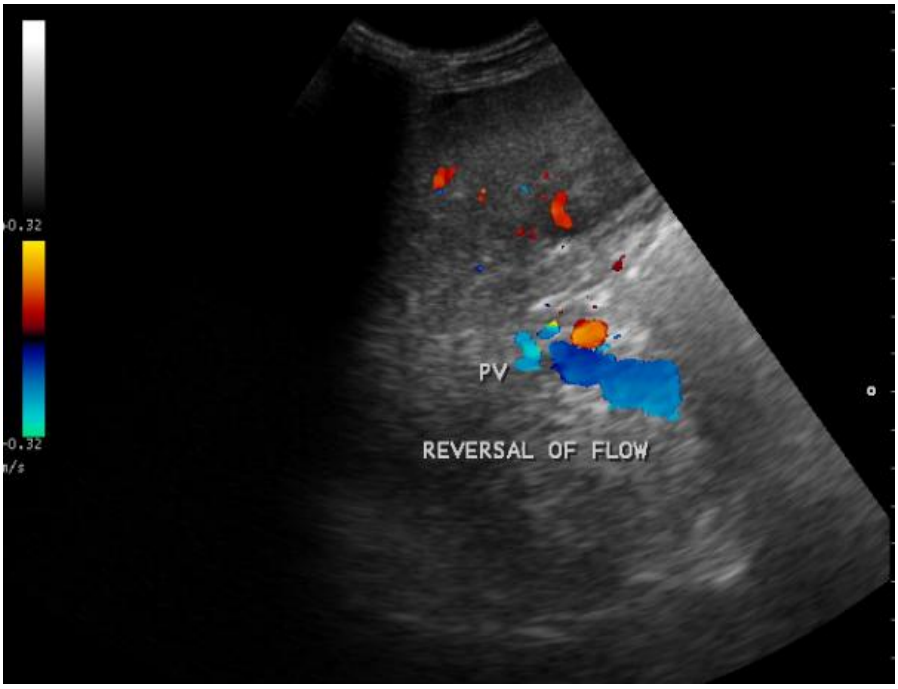
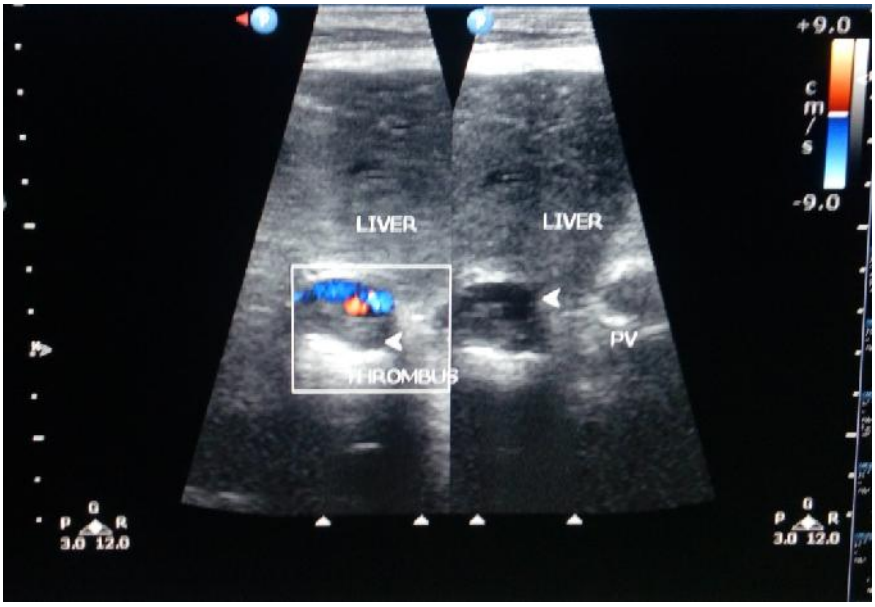
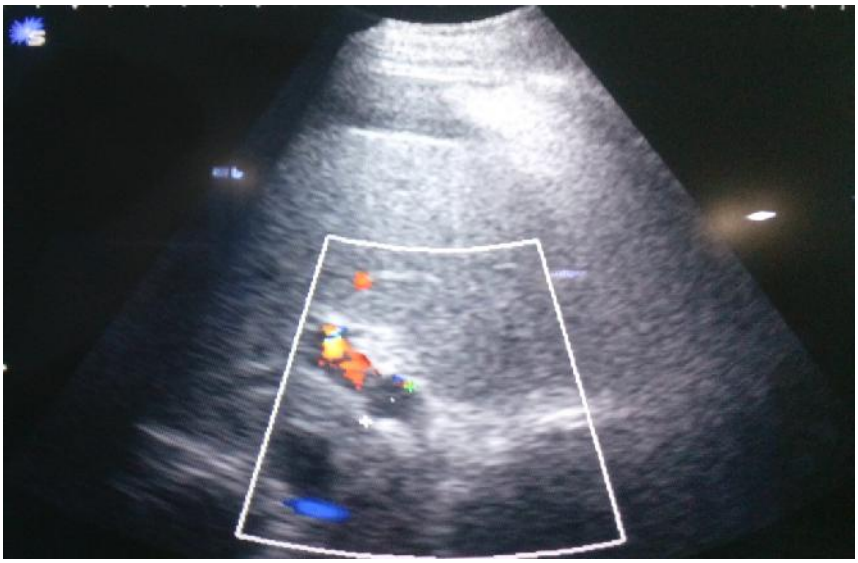


FIG. 32 : Colour Doppler USG Image showing reversal of flow in portal vein



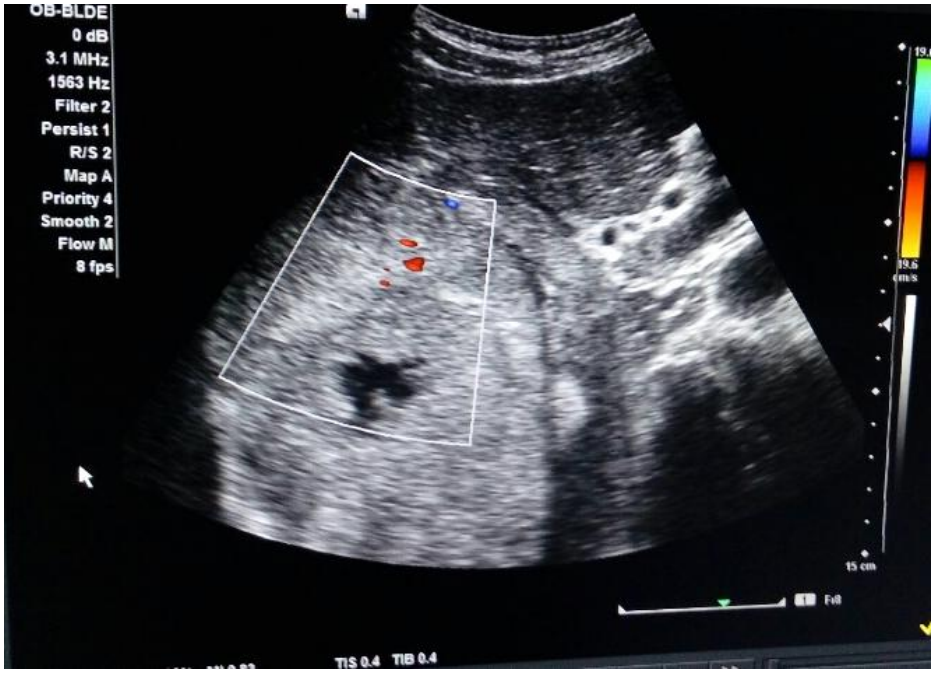
(a)



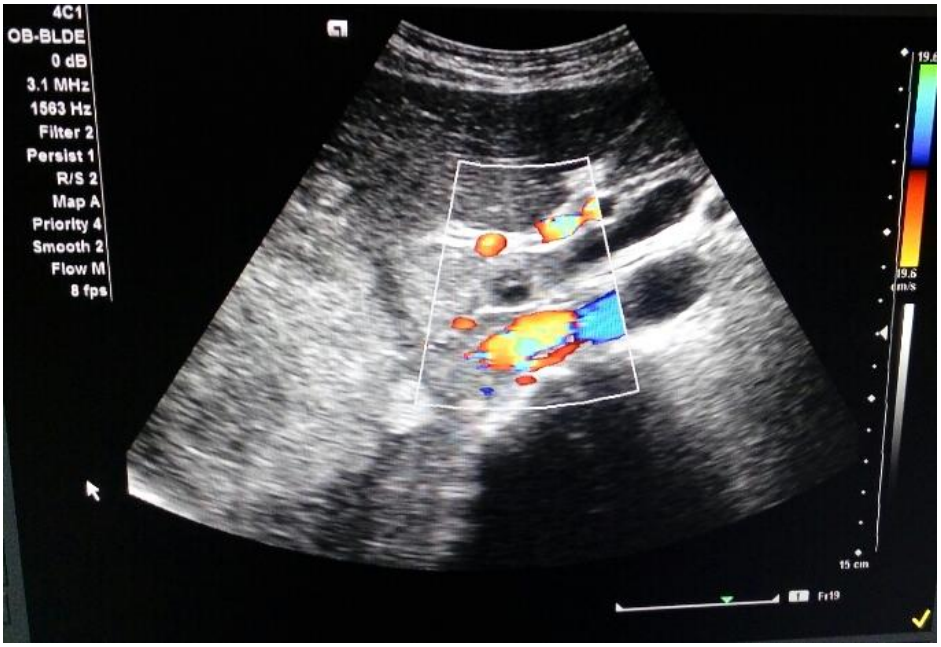
(b)

FIG. 33 : a) USG Image showing echogenic thrombus in the portal vein.

b)Colour Doppler USG Image showing filling defect in the portal vein suggestive of thrombosis.



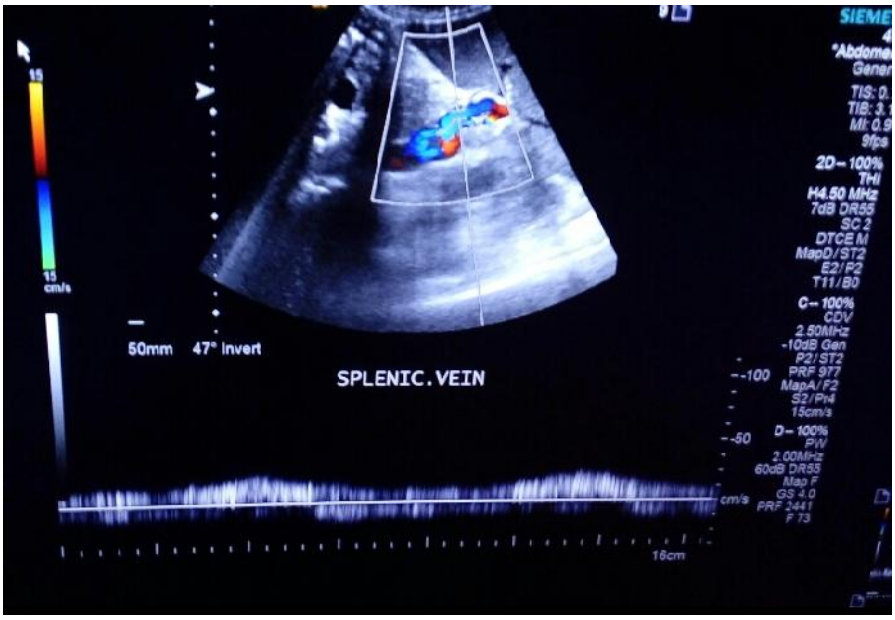
(a)



(b)

FIG. 34 : a)USG Image showing heterogenous mass in the liver with internal vascularity and anechoic necrotic area within suggestive of Malignant Lesion.

b)Colour Doppler USG image showing echogenic foci with filling defect in portal vein suggestive of Tumoral Thrombosis.



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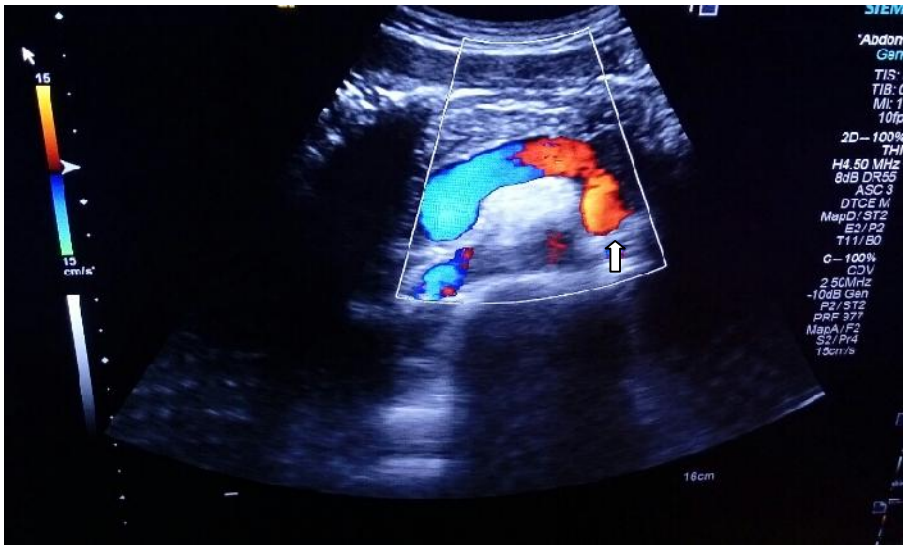


(b)

FIG. 35 : a)Spectral Doppler USG Image of Splenic vein.

b)Colour Doppler USG Image showing flow reversal in Splenic vein (arrow).

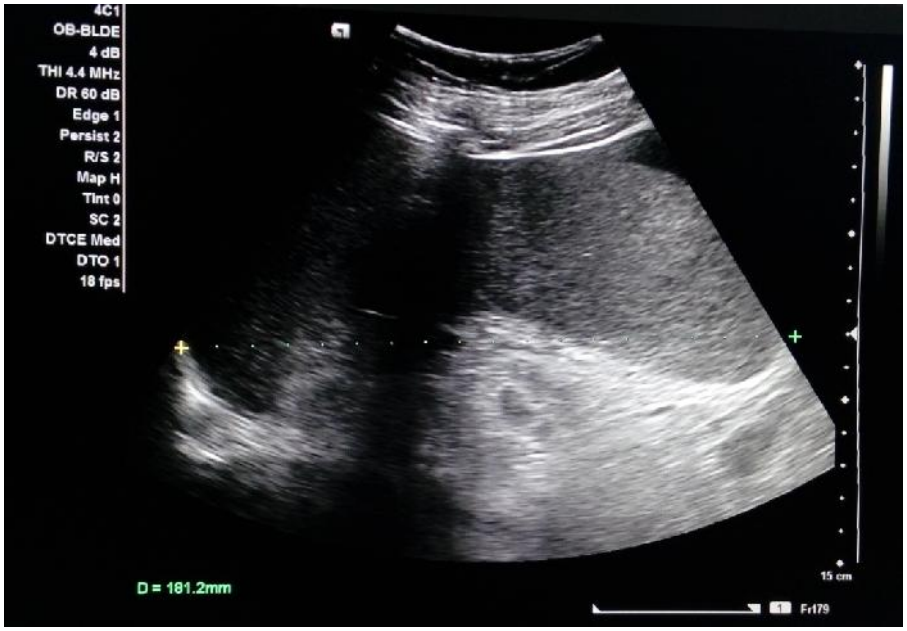


FIG. 36 : USG Image showing enlarged spleen.

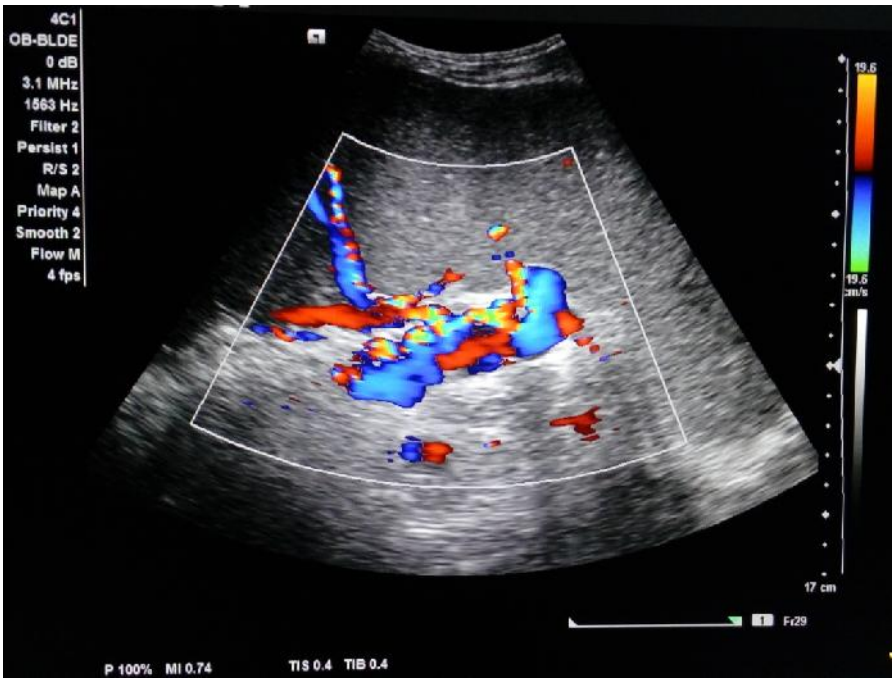


FIG. 37 : Colour Doppler USG Image showing splenomegaly with multiple collaterals at splenic hilum

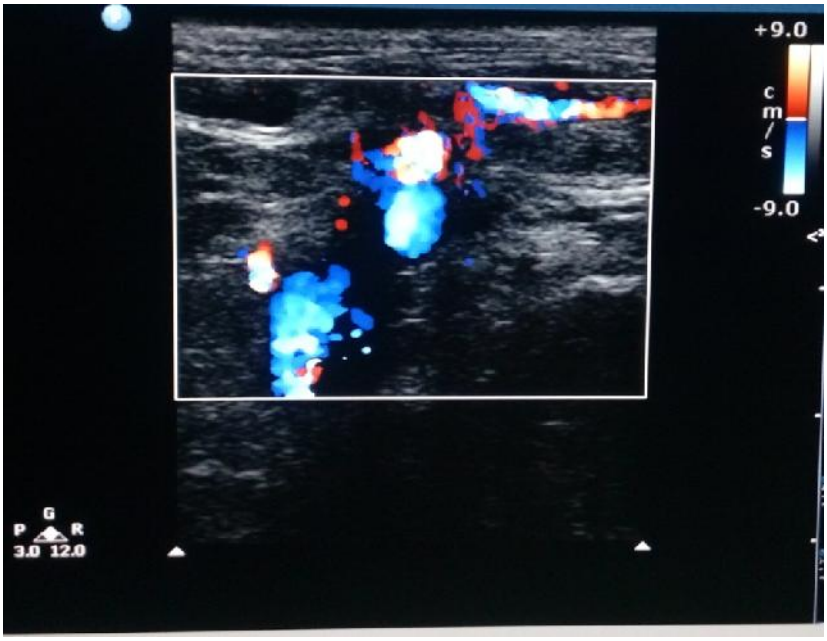


FIG. 38 : Colour Doppler USG Image showing anterior abdominal wall varices.

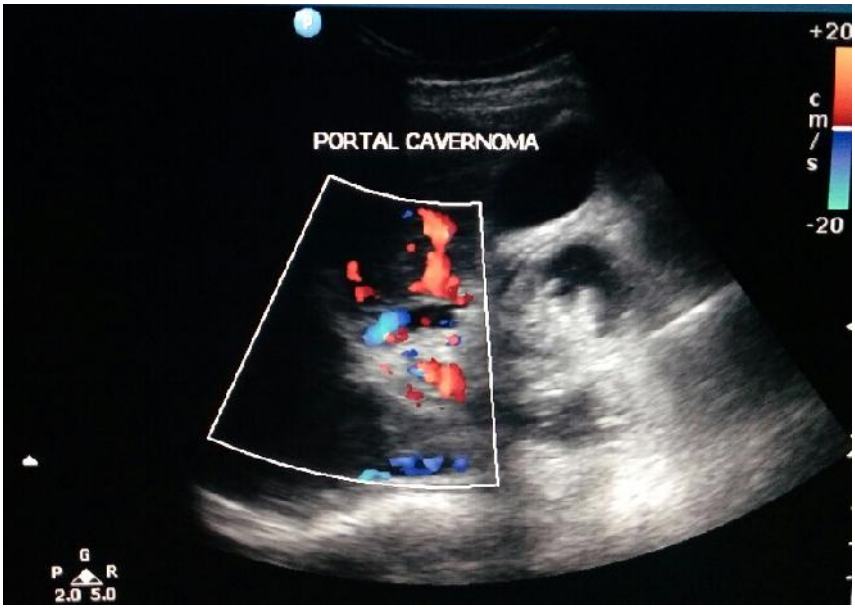


FIG. 39 : Colour Doppler USG Image showing cavernomatous transformation of portal vein/portal cavernoma

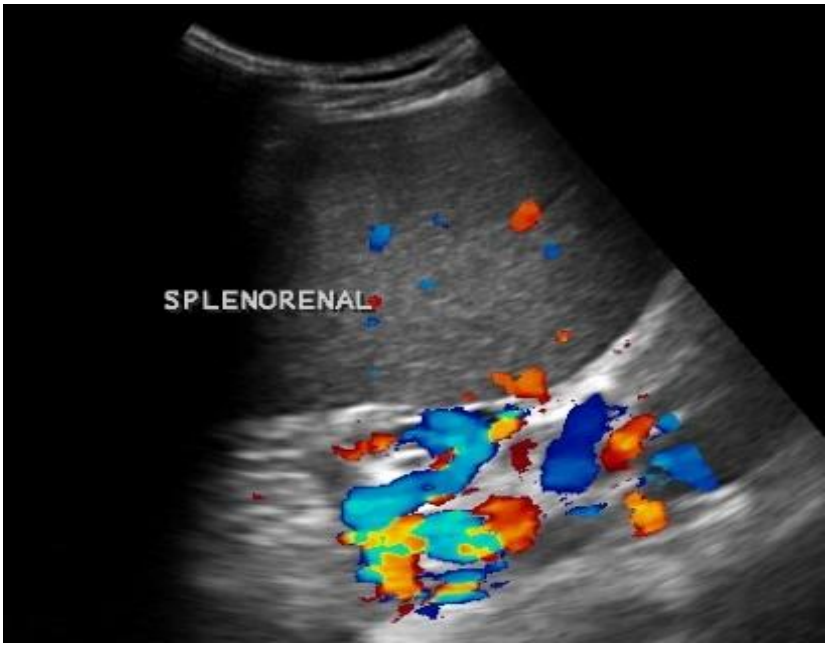


FIG. 40 : Colour Doppler USG Image showing Splenorenal collaterals.

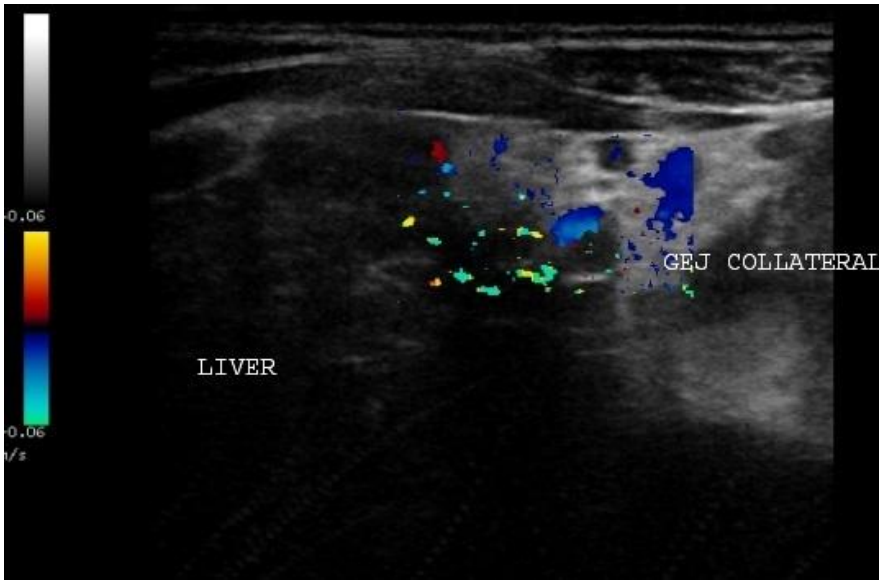


FIG. 41 : Colour Doppler USG Image showing Gastro-Esophageal Junction (GEJ) collaterals.

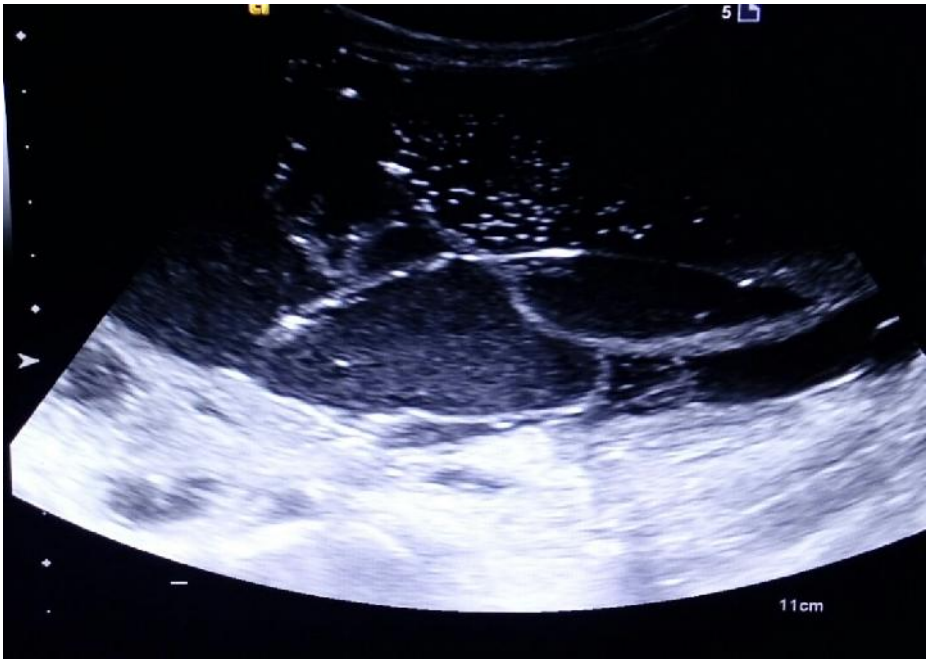


FIG. 42 : USG Image showing fluid in the peritoneum with internal echoes and septations suggestive of Complicated Ascites.

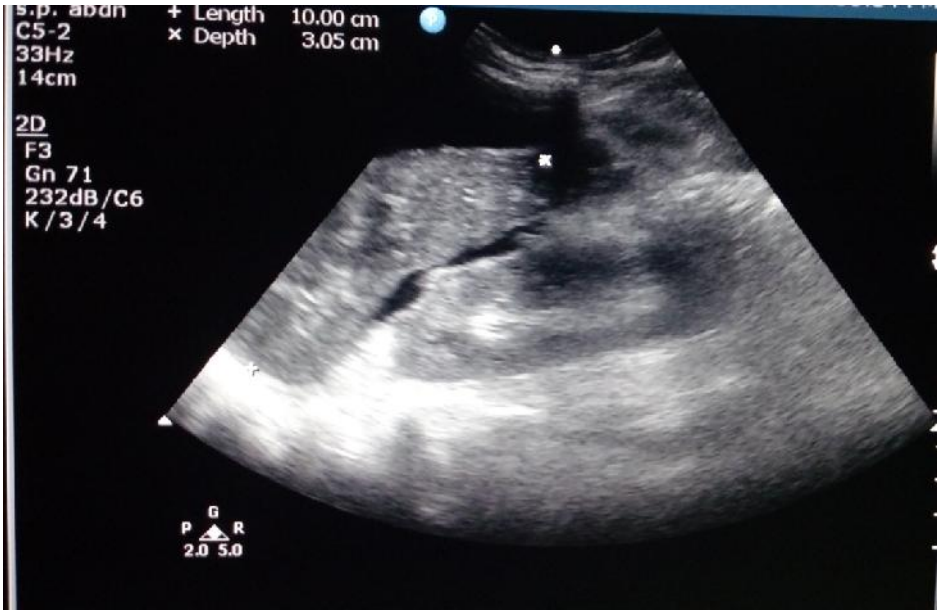
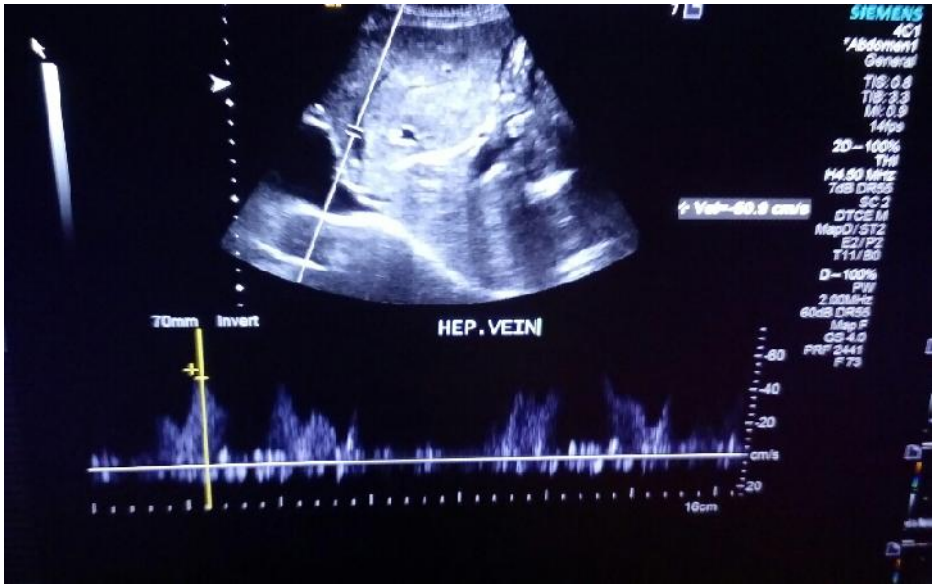
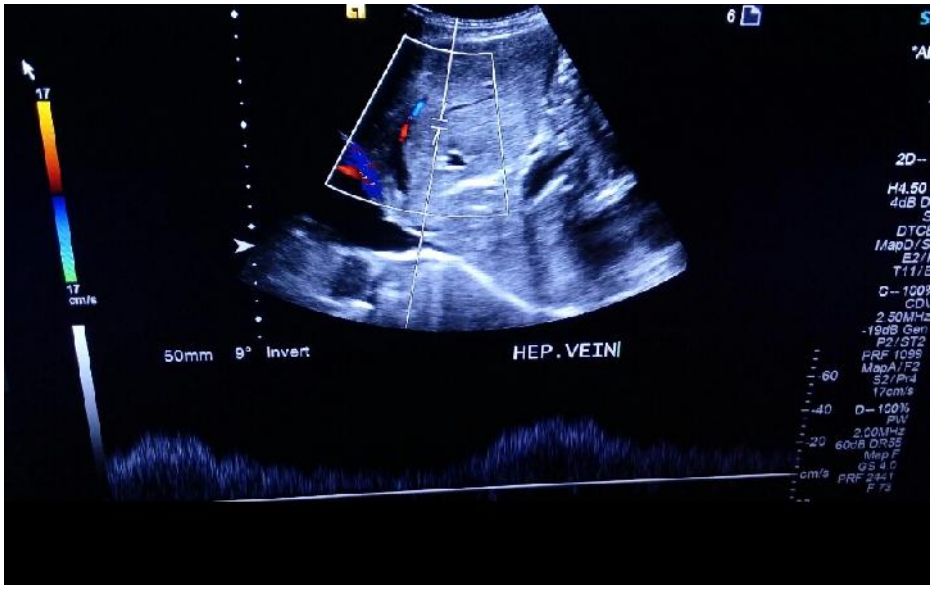


FIG. 43 : USG Image showing shrunken liver with coarse hepatic echotexture and surface nodularity suggestive of Cirrhosis.

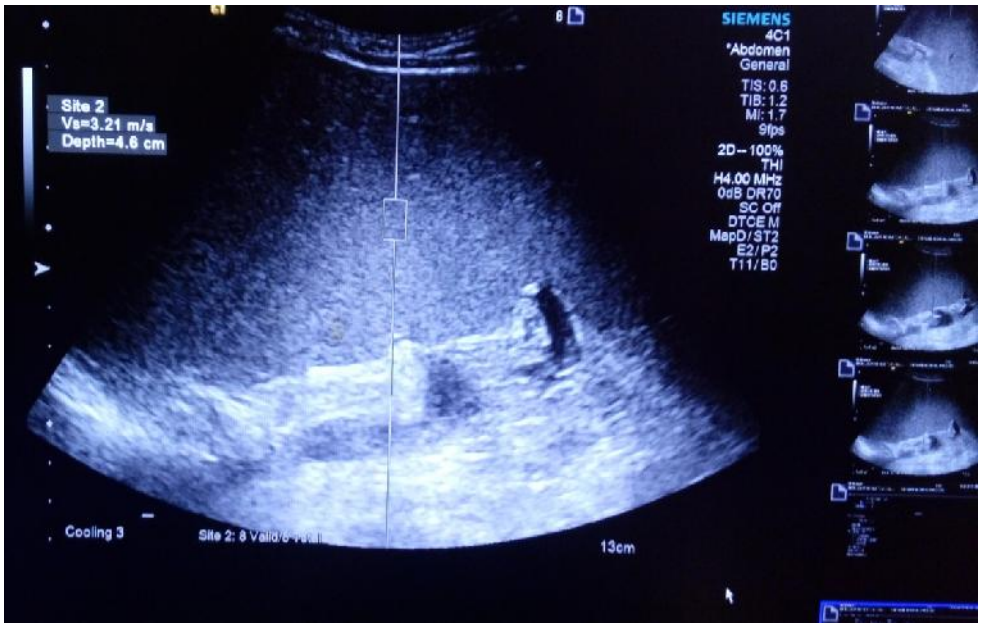


(a)

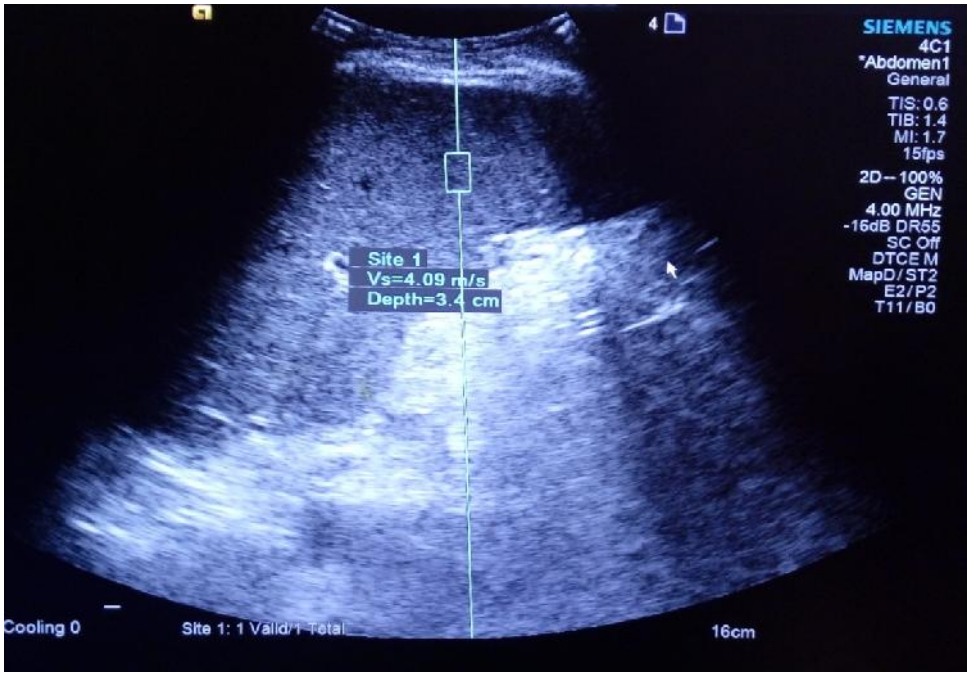


(b)

FIG. 44 (a&b): Spectral Doppler USG Image of Hepatic vein

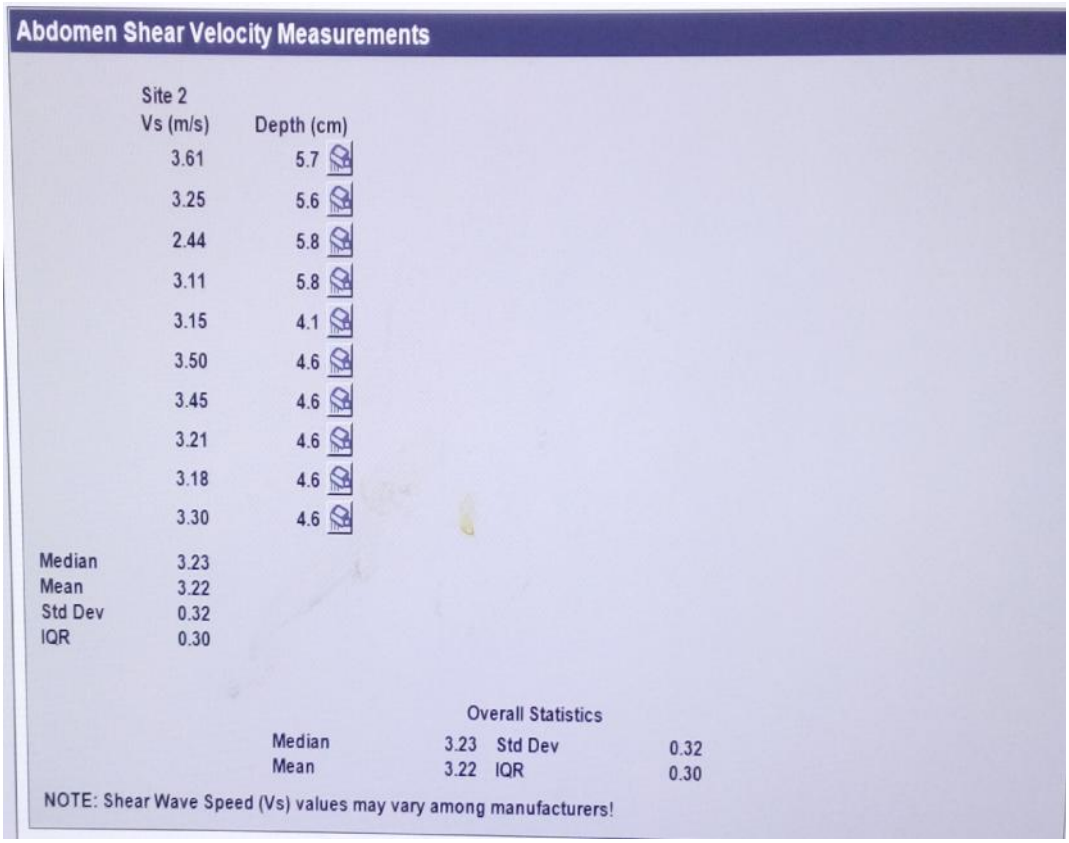


(a)



(b)

FIG. 45 (a&b): Spleen stiffness measured through shear wave velocity by ARFI method



Abdomen Shear Velocity Measurements

Site 2 Vs (m/s)	Depth (cm)
3.61	5.7
3.25	5.6
2.44	5.8
3.11	5.8
3.15	4.1
3.50	4.6
3.45	4.6
3.21	4.6
3.18	4.6
3.30	4.6

Median	3.23
Mean	3.22
Std Dev	0.32
IQR	0.30

Overall Statistics

Median	3.23	Std Dev	0.32
Mean	3.22	IQR	0.30

NOTE: Shear Wave Speed (Vs) values may vary among manufacturers!

FIG. 46 : Display of Median and Mean shear wave velocities of Spleen stiffness

DISCUSSION

Portal hypertension is a common clinical syndrome, characterized by an increase in portal venous pressure due to increased flow resistance in the hepatic sinusoids as well as an increase in total amount of blood flowing through the portal system[82]. It is defined as an increase in portal pressure above the normal range of 6-10 mmHg or an increased hepatic venous pressure gradient (HVPG) of more than 5 mmHg[2]. It results from various causes, cirrhosis being the most common cause. The evaluation of portal hypertension includes the assessment of the pathogenic factors, severity, clinical complications and to decide the therapeutic measures.

HVPG measurement and endoscopy are the backbone for the assessment of PH in CLD. However, they are invasive and may (in rare cases) lead to complications; in addition, a specialized clinical setting and specific expertise are required to carry out these tests, limiting their availability and increasing the cost to health care systems[252].

Among the various possible evaluations, in clinical practice, Ultrasonography (US) is a mainstay in the assessment of patients with portal hypertension; a noninvasive, widely available, and inexpensive technique that allows the evaluation of liver morphology as well as of functional parameters with Doppler US[2].

The development of newer noninvasive methodology like measurement of spleen stiffness by ARFI method has enabled early identification of low risk and at-risk patients, thereby, predicting the severity of PH (ie, not clinically significant, significant, and severe) that helps in identifying patients who could avoid invasive tests and who needs to be subjected to further invasive testing, which, ultimately, optimize the

diagnostic management of portal hypertension patients[255]. SSM might be a valuable tool used to stratify the severity of PH in patients with EHPVO, in whom HVPG is not reliable (prehepatic PH)[130].

A cross sectional study of 65 patients with clinical suspicion of portal hypertension was carried out over a period of 16 months using Gray scale and Colour Doppler Ultrasonography in correlation with spleen stiffness measurement.

AGE &SEX DISTRIBUTION:

The age group included in our study ranged from 30 to 70 years with mean age of 46 years. The most common age groups presenting with portal hypertension were between 41-50 years (38.5%) and between 31-40 years (35.4%).

There were 55 males and 10 females in this study with a male to female ratio of 5.5:1. Males comprised 84.6% and females comprised 15.4% of the study group. Male patients exceeded the number of female patients in all the age groups. The higher incidence in males is explained by the higher incidence of alcoholism in males leading to liver cirrhosis.

In 2005, Rokni Yazdi et al[65] studied 36 patients of portal hypertension. The mean age in their study was 45 years with a male to female ratio of 1.57:1.

In 2011, Puneet Mittal et al[90] studied 50 patients with cirrhosis and portal hypertension. The mean age of the patients in their study was 45 years. Maximum of the patients were in the 31-40 years age group. 66% of the patients were men with a male to female ratio of 1.94:1[74].

ETIOLOGY:

In our study, most common etiology was cirrhosis seen in 52 cases (80%). Portal vein occlusion as the cause was seen in 9.2 % cases. Malignancy causing portal venous thrombosis was seen in 6.2% cases.

In 2014, Chakenahalli N et al[84] conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. It was found that most common aetiology was cirrhosis seen in 48 cases (76.2%) followed by Portal vein occlusion (19%) and Malignancy causing portal venous occlusion (3.2%).

SPLENOMEGALY:

In our study, Splenomegaly (span more than 13cm) was seen in 55 of the 65 cases comprising 84.6% of the study group.

In 2009, Desmosthenes[67] "suggested that mild to moderate splenomegaly (craniocaudal diameter of more than 13 cm) is a common finding of portal hypertension with ultraonography having a sensitivity of up to 95% and a specificity of up to 98% in measuring the liver and spleen.

In 2011, Mandal L et al[116] conducted a study on 82 patients with cirrhosis of liver. In the study it was found that average spleen size of patients without gastro-oesophageal varices was 13.129 ± 1.102 cm and with varices was 14.997 ± 1.992 cm. This variation was also statistically significant ($p < 0.05$). There was a positive correlation between splenic size and oesophageal varices grades ($r = 0.467$; $p < 0.001$)".

In 2014, Aarti Anand et al[68] in her retrospective study on 70 cases with portal hypertension, found splenomegaly in 60 (85%) cases.

ASCITES:

It is frequently seen in portal hypertension. Ascites was seen in 57 of the 65 cases comprising 87.7% of the study group.

In a study by Puneet Mittal et al[90] in 2014, "ascites was reported in all the cases with hepatofugal flow and 74.4% of the cases with hepatopetal flow.

In 2014, Chakenahalli N et al[84] conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. Ascites was seen in (87.3 %) of the cases studied. There was significant association of portal hypertension with ascites ($p<0.001$)".

PORTAL VEIN DIAMETER:

In normal individuals the portal vein diameter can vary from < 13mm in quiet respiration to 16 mm in deep inspiration, as measured where the portal vein crossed anteriorly to the inferior vena cava.

In our study diameter of portal vein could not be measured in 5 cases where portal vein was not delineated due to cavernoma formation. Dilated portal vein in quiet respiration (>13 mm) was noted in 41 of 62 cases(66.1%).

In 2009, Desmosthenes[67] "suggested that a portal vein diameter over 13 mm is indicative of portal hypertension with a specificity of 100% and a sensitivity of 45-50%.

In 2014, a study by MS Ahamed[69] showed during deep inspiration, diameter of portal vein was greater than 13 mm in 31 (52.54%), while equal to or less than 13 mm in 28 (47.46%) of portal hypertensive cases. Out of 45 controls, in 8 (17.78%) cases, maximum diameter of portal vein was over 13 mm, while in 37 (82.22%) cases, diameter of portal vein was equal to or less than 13 mm.

Bolondi et al studied 79 cases with portal hypertension and 45 controls. They concluded that portal vein diameter > 13 mm can be considered fairly characteristic sign of portal hypertension. Ditchfield et al studied 118 patients diagnosed as portal hypertension using endoscopy, sonography and Doppler signs. They found that portal vein diameter of <13mm was seen in 42% patients and > 13mm in 59%"[112].

LOSS OF RESPIRATORY PHASICITY :

The diameter of the portal vein increases during inspiration. Due to the reduced filling of the heart during inspiration and the downward excursion of the diaphragm there is increased intra abdominal pressure and stasis of blood in the liver and the portal venous system causing dilatation of the portal vein. In normal individuals the caliber of the portal vein changes from 20-200% between phases of respiration.

In our study, loss of respiratory phasicity (<20%) of portal vein was noted in 49 of the 62 cases(79%).

In 2005, Rokni YH[65] "conducted a study on 46 biopsy proven cases of cirrhosis and found that reduced respiratory change of diameter of portal vein equal to or less than 20% had higher specificity and specificity of 89 % in diagnosing portal hypertension.

In 2016, Geleto et al[85] conducted a cross-sectional study on a total of 195 clients for sonographic assessment of normal mean portal vein diameter. Among these,

121(62.1%) were males and the median age of the participants was 35 years. The study revealed a normal mean portal vein diameter of 10.6 mm ±1.8 SD with a respirophasic variation of 25.6%".

DIRECTION OF FLOW IN PORTAL VEIN:

Normal portal venous flow is continuous and hepatopetal on Doppler ultrasound with minimal variations due to the cardiac cycle and respiration. In portal hypertension, velocity diminishes and the waveform is dampened with decrease in amplitude of oscillations during breathing[67]. As portal pressure increases, flow may become biphasic, towards and away from the liver during the cardiac cycle. Finally it reverses, becoming monophasic and hepatofugal Reversed (hepatofugal) portal venous blood flow can be present when the intrahepatic resistance is greater than the resistance of portosystemic collaterals[93].

In our study, the direction of flow was normal hepatopetal in majority (75.4%) of the cases. Hepatofugal flow was noted in only 6.2% cases. Bidirectional flow was noted in 3.1% cases and no flow was noted in 15.4% cases due to thrombosis.

In 2000, Von Herbay A et al[88] "conducted a study of color Doppler sonography on 109 patients of cirrhosis confirmed by liver biopsy. The direction of portal venous flow was normal (hepatopetal) in 80 patients (73%), hepatofugal in 10 (9%), and bidirectional in 7 (6%); 12 patients (11%) had partial portal vein thrombosis.

In Takayaso's study of 80 cases hepatofugal flow was only observed in 2 cases. According to him, reversal of flow in the portal vein is rare in the absence of surgical shunts[89].

In 2011, a study by Puneet M et al[90] showed overall six patients (12%) among a total of fifty cases of portal hypertension had non hepatopetal flow (hepatofugal/bidirectional), four of them (8%) showed continuous hepatofugal flow and two patients (4%) showed bidirectional flow. Hepatofugal or bidirectional flow was seen only in Child's C group patients.

In 2015, a retrospective study by Kondo T et al[92] consisting of 222 cirrhotic patients showed that twenty-four patients (10.8%) demonstrated NFPF i.e, bidirectional flow and the reversed flow".

PORTAL BLOOD FLOW VELOCITY:

The velocity in the portal vein is approximately 15-18 cm/sec with a lot of variation in the range[82]. Portal vein flow velocity reduction is an accepted Doppler sign of cirrhosis and portal hypertension. A low flow velocity of <16 cm/sec in addition to a caliber increase in the main portal vein are diagnostic features of portal hypertension[107]. An averaged maximum velocity below 16 cm/s should be considered strongly suggestive of CSPH, whereas values < 24 cm/s more generally suggest cirrhosis[98]. The velocity decreases in cases where there is increased resistance to the portal blood flow as postulated by Patriquin and Bradley Koslin[83,99]. With the development of portal hypertension the flow decreases and the velocity fluctuations disappear (i.e., flow becomes continuous).

In our study, out of total 65 cases, no flow was noted in 10 cases. In the rest of the 55 cases decreased velocity (<15cm/sec) was noted in 69.2% cases. 15.4% cases had

velocity ≥15cm/sec. There was a wide range of velocities from 5 to 22 cm/sec with a mean of 11.85 cm/sec.

In 2011, a study was conducted by Puneet M[90] "to evaluate the association between color Doppler findings and the severity of portal hypertension in patients with cirrhosis. The study group included 50 patients divided into three groups (Child' A, B and C) based on Child Pugh classification. Using one way ANOVA, there was a significant fall in the average PVV from Child's A to Child's C group patients ($F = 29.87$, $P < 0.0001$). So there was a significant fall in PVV with the increasing severity of the grade of cirrhosis.

In 2014, Aarti Anand et al[68] conducted a retrospective study to review the Doppler findings to evaluate its usefulness in patients of portal hypertension and found that, portal vein flow velocities were found to be below 10 cm/sec in 62 (88%) of total 70 cases with portal hypertension.

In 2015, Mukhopadyay et al[97] conducted a study over 235 people consisisting of 100 Normal subjects (N), 10 patients with acute hepatitis (AH), 40 patients with chronic active hepatitis (CAH), 80 patients with liver cirrhosis (LC) and 5 patients with Idiopathic portal hypertension (IPH). Portal blood flow velocity was 15.5 ± 4.0 cm/sec in 100 N subjects, 15.1 ± 2.2 cm/sec in 10 AH cases, 12.5 ± 3.3 cm/sec in 40 CAH cases, 9.8 ± 2.8 cm/sec in 80 LC cases and 11.0 ± 3.5 cm/sec in 5 IPH cases.

In 2015, a study by Ahirwal S[91], out of 15 cases of cirrhosis with portal hypertension,10 cases (66.6%) had abnormal flow velocity in the portal vein.

In 2016, Riahinezhad M et al[95] conducted a cross-sectional study in 33 cirrhotic children with or without esophageal varices and compared with 19 healthy children as controls using color and spectral Doppler US. Portal vein mean velocities were 15.03 ± 7.3 cm/s in cirrhotics, 16.47 ± 6.4 cm/s in controls (P = 0.51), 11.6 ± 4.7 cm/s in patients with varices, and 17.9 ± 7.3 cm/s in patients without varices (P = 0.015)".

PORTAL VEIN THROMBOSIS AND CAVERNOMA FORMATION:

Portal hypertension can cause thrombosis of the portal vein due to stagnation of flow. Hypercoagulable states can result in thrombosis of the portal vein directly or indirectly through thrombosis in the splenic or superior mesenteric vein. The secondary signs of portal vein thrombosis observed by Doppler include the presence of periportal collaterals, representing cavernous transformation, with a flow in the hepatopetal direction. A sudden onset of ascites should prompt careful examination of the portal vein for thrombosis[104].

In our study intraluminal thrombus was noted in 10 (15.4%) of the 65 cases. An additional 3 cases showed cavernoma formation in the porta hepatis where PV was not delineated. Rest of the 52 cases showed clear lumen.

Subramanyam and Kauzlaric et al "described in detail the collaterals formed[105] .They also described the formation of a cavernoma. Wermke and Gansbeke found that 50% cases in their study with portal vein thrombosis had a cavernorma formation[106].

In a study conducted by Rokni Yazeli et al[65] in 2005, Portal vein thrombosis was noted in 17.3% of the patients.

In 2017, Stine J G et al[102] conducted a study on one hundred subjects (50 matched pairs) with Model for End-stage Liver Disease (MELD) score 14.9±5.5. 76% were Child-Turcotte-Pugh Class A or B. Baseline characteristics (prior to development of PVT) were similar, except for baseline PV velocity (16.9 cm/s, 95% CI 13.9-20.0 PVT vs 25.0, 95% CI 21.8-28.8 no PVT, P<.001). 30 PVT subjects had PV velocity <15 cm/s compared to five without PVT (P<.001). On adjusted multivariable analysis, PV velocity was the strongest independent risk factor predicting PVT development (HR 0.86, 95% CI 0.80-0.93). The predictive value for PVT development was greatest for flow <15 cm/s (c-statistic 0.77). PV velocity <15 cm/s had a highly significant association with future PVT (HR 6.00, 95% CI 2.20-16.40, P=<.001). Hence, decreased PV velocity is associated with increased risk of future PVT. Patients with cirrhosis and decreased PV velocity are a high-risk subgroup that warrants further investigation with prospective study.

In 2017, Achar S[103] conducted a hospital-based cross-sectional study on twenty children with Extrahepatic portal vein obstruction (EHPVO) aged between 1 and 18 years over a period of 1 year. All the patients presented in chronic stage with portal cavernoma and only one patient (5%) had bland thrombus associated with cavernoma. The color Doppler ultrasonography (CDUSG) had a sensitivity of 66.6-90% and specificity of 91.5% with regard to the assessment of the extent of thrombus formation and flow in the portal venous system. It was found to help in preoperative assessment of EHPVO in detecting occlusion and identifying portosystemic collaterals and dilated intrahepatic biliary radicals".

PORTOSYSTEMIC COLLATERALS/VARICES:

When portal resistance is higher than that of small communicating channels between the portal and systemic circulation, portosystemic collaterals are formed[67]. This causes a subsequent decrease in the, initially dilated, caliber of the portal vein. Forming of collateral vessels is a definitive finding of portal hypertension, US can reveal up to 65-90% of these vessels[114].

In our study, portosystemic collaterals were visualized in 75% of the cases. Most frequent collaterals visualized were the splenorenal collaterals which were seen in 53.8% of cases. Anterior abdominal wall varices and paraumbilical veins were seen in 23.1 and 18.5% of cases respectively. Other visualized collaterals included perigastric (13.8%),coronal vein(7.9%),GE junction collaterals (9.2%) and GB wall varices(4.6%). Portal cavernoma was seen in 4.6% cases.

The most common collateral in the study by Rokni Yazdi et al was splenorenal (47.6% of all collaterals)[65]. Chawla et al studied one hundred and two patients with different forms of portal hypertension and found that frequency of gallbladder varices was between 13- 24% in different forms of portal hypertension. Subramanyam et al studied 40 cases with portal hypertension and collaterals were seen in 88% of cases and GEJ collaterals were the most common, seen in 60% cases[105].

In 2000, *Von Herbay A et al*[88] "conducted a study of color Doppler sonography on 109 patients of cirrhosis confirmed by liver biopsy. Spontaneous portosystemic shunts were found in 41 patients (38%), most often as splenorenal shunts (21%) and patent umbilical veins (14%). Less frequent were gastric collaterals, gallbladder varices,

collaterals to thrombotic portal veins, mesoiliac shunts, and portorenal shunts to the right kidney. The presence of shunts was associated with that of esophageal varices ($p < 0.01$), ascites ($p < 0.01$), and inversion of portal flow ($p < 0.001$) but not with splenomegaly.

In 2014, Chakenahalli N et al[84] conducted a study on 63 patients with clinically suspected/diagnosed portal hypertension. Collaterals were noted in 63% of the cases, most frequent collateral were the splenorenal collaterals which were seen in 49.2% of cases. Anterior abdominal wall varices and paraumbilical veins were seen in 19% and 20% of cases respectively. Other visualized collaterals included perigastric (15.8%), coronal vein (7.9%), GE junction collaterals (7.9%) and GB wall varices (3.2%). Portal cavernoma was seen in 5 (7.9%) cases.

In 2014, Minal Shastri et al[109] conducted a study on total of 50 adult patients with cirrhosis. All subjects underwent a percutaneous liver biopsy, abdominal ultrasound and Esophagogastroduodenoscopy (EGD) along with other tests as part of the work up for cirrhosis. Association of portal vein diameter (PVD) and portal vein velocity (PVV) with presence of Esophageal varices (EV) was statistically significant (p-value <0.01). PVV had the highest sensitivity (84%) for detecting the presence of EV. PVD had the highest specificity of 55% and the highest negative predictive value of 38%. Positive predictive value was highest PVV at 76%. In resources- constricted settings where EGD is not available, PVV and PVD on ultrasound abdomen can be used as non-invasive parameters to predict the presence of EV.

Mc Cain found the patent paraumbilical vein in 33% of cases in his study.Dash in his study correlated angiographic with sonographic finding concluded that duplex sonography was superior to angiography in the detection of paraumbilical veins.

Dockmeci found a similar result. Shadekhi stated that the patency of the paraumbilical vein could be seen in normal individuals but the lumen should not exceed 3 mm in diameter. A diameter more than 3 mm with hepatofugal flow was a sensitive indicator of portal hypertension[112].

In 2014, Bhattarai S[114] did a study on One hundred and fifty patients with clinical features, laboratory and sonological findings suggestive of cirrhosis of liver and endoscopic evidence of portal hypertension. They found that Average portal vein diameter of patients without gastro-esophageal varices was 10.800 ± 1.1402 mm, while it was 13.731 ± 1.061mm in patients with varices($p<0.001$). Average spleen size of patients without varices was 12.67 ± 2.35 cm and with varices was 15.367 ± 1.210 cm ($p < 0.001$). There was 92.72 % sensitivity and 90 % specificity for prediction for presence of esophageal varices when the cutoff value for portal vein diameter was 12.25 mm. There was 94.5 % sensitivity and 75 % specificity for prediction for presence of esophageal varices when the cutoff value for spleen size was 13.9 cm. In cirrhotic patients with portal hypertension, as portal vein diameter increases by > 12.25 mm, there is increased risk of development of gastro-esophageal varices; grades of varices increase with increment of portal vein size and as size of spleen increases by >13.9 cm, increased risk of development of varices exist. They concluded that measurement of portal vein diameter and spleen size by ultrasonography can be recommended as a non invasive predictor for gastroesophageal varices in cirrhosis of liver".

HEPATIC VEIN FLOW WAVEFORM:

The hepatic vein normal waveform is triphasic, reflecting pressure from the right atrium in a normally compliant liver through the thin walls of the veins. As fibrosis

evolves, the liver parenchyma stiffens, resulting in decreased amplitude of phasic oscillations, reversed flow loss and flattened waveform[68]. Colour Doppler ultrasound of the hepatic veins has emerged as a non-invasive technique for the diagnosis of portal hypertension and to predict oesophageal varices. Biphasic and monophasic HVW are associated with severe portal hypertension[121].

In our study, out of 65 cases, hepatic veins showed biphasic waveform in 29 (44.6%) cases followed by triphasic in 20 (30.8%) cases and monophasic in 16 (24.6%) cases.

In 2006, Baik SK et al[147] "conducted a study on 78 patients with cirrhosis (70 men, eight women) and a history of variceal bleeding, to evaluate the correlation between abnormal Doppler ultrasonography (US) hepatic vein waveforms and the hepatic venous pressure gradient (HVPG). Abnormal hepatic vein waveforms were seen in 72 patients (92%). Forty-four patients (56%) had biphasic waveforms, 28 (36%) had monophasic waveforms, and six (8%) had triphasic waveforms. A positive correlation was found between the extent of abnormalities in hepatic vein waveforms and the increase in HVPG ($P < .05$). Monophasic waveforms were associated with severe portal hypertension, with a sensitivity of 74% and a specificity of 95%. It was concluded that Doppler US hepatic vein waveform assessment is useful in the noninvasive evaluation of the severity of portal hypertension.

In 2016, Antil N et al[122] conducted a study on 30 patients of chronic liver disease to evaluate hepatic venous waveform, damping index(DI) and splenoportal index (SPI) in patients of cirrhosis on Colour Doppler ultrasound, also predict severity of portal

hypertension and presence of oesophageal varices. Twenty two (73.3%) patients had monophasic waveform. Biphasic and triphasic waveforms were seen in 4 (13.3%) cases. Twenty two patients (73.3%) had monophasic waveforms and majority of them were in Child Pugh's class C. This distribution of hepatic vein waveform was statistically significantly with the Child Pugh's class ($p<0.05$)".

DAMPING INDEX:

Damping index (DI) is the ratio between the minimum velocity and maximum velocity of the hepatic venous flow. Damping index > 0.6 is considered significant for portal hypertension. Higher DI values tend to give flat hepatic venous waveforms.

In our study DI was between 0.36-0.92 (0.65± 0.15). Majority of the cases (69.2 %) showed DI>0.6 suggesting severe portal hypertension.

Parameter	Range		Mean	SD
	Minimum	Maximum		
Damping Index	0.36	0.92	0.65	0.15

In 2007, Kim MY et al[123 "] conducted a study on 76 patients with cirrhosis to evaluate the correlation between the extent of abnormal Doppler HV waveforms expressed as damping index (DI) and the hepatic venous pressure gradient (HVPG). Abnormal HV waveforms were seen in 66 of 76 patients (86.8%). DI significantly correlated with the grade of HVPG, i.e. with higher HVPG increased DI was observed ($P<0.01$). By logistic regression analysis, DI>0.6 was significantly more likely to be severe portal hypertension (odds ratio: 14.19, 95% confidence interval: 4.07-49.55). It was concluded that Damping

index of the HV waveform by Doppler ultrasonography might be a non-invasive supplementary tool in evaluating the severity of portal hypertension[268].

In 2011, Kim SY[125] et al performed spectral Doppler sonography of the hepatic vein on 22 consecutive patients who underwent HVPG measurement for portal hypertension with liver cirrhosis. He found that, when the DI was greater than 0.56, the sensitivity and specificity for high-grade portal hypertension were 66.7% and 100.0%, respectively. He concluded that DI of hepatic vein as a helpful predictor in assessing the severity of portal hypertension.

In 2015, Kim G et al[121] conducted a systematic review of 14 studies by searching databases, including MEDLINE, EMBASE, and the Cochrane Library, for relevant studies The US indices were obtained in the portal vein (n = 9), hepatic artery (n = 6), hepatic vein (HV) (n = 4) and other vessels. Using hepatic venous pressure gradient (HVPG) as the reference, the sensitivity and specificity of the hepatic venous indices were 75.9–77.8% and 81.8–100%, respectively. A statistically significant correlation between HVPG and the hepatic venous indices was observed (0.545–0.649). It was concluded that some US indices, such as HV, exhibited an increased accuracy for diagnosing PH. These indices may be useful in clinical practice for the detection of significant PH.

In 2016, Antil N et al[122] conducted a study on 30 patients of chronic liver disease to evaluate hepatic venous waveform, damping index(DI) and splenoportal index (SPI) in patients of cirrhosis on Colour Doppler ultrasound, also predict severity of portal hypertension and presence of oesophageal varices. Twenty two (73.3%) patients had monophasic waveform. Biphasic and triphasic waveforms were seen in 4 (13.3%) cases.

Twenty two patients (73.3%) had monophasic waveforms and majority of them were in class C. This distribution of hepatic vein waveform was statistically significantly with the Child Pugh's class ($p<0.05$). Twenty patients (66.7%) had value of Damping index more than >0.6 where majority of patients (18) belonged to class C and 2 in class B. There was a positive correlation between Child Pugh's total score and Damping index ($r=0.614$; $p<0.05$). There was weak positive correlation between splenoportal index and Child Pugh's score ($r=0.269$; $p=0.15$). It was concluded that change in triphasic to monophasic waveform and DI >0.6 suggests severe liver dysfunction and is associated with severe portal hypertension".

SPLEEN STIFFNESS (SS):

The spleen undergoes parenchymal remodelling in patients with PH. This is partly attributable to passive congestion and increased arterial inflow, and partly because of increased hyperactive splenic lymphoid tissue and enhanced angiogenesis and fibrogenesis, leading to the progressive development of splenomegaly in most patients. Stiffness and haemodynamics of the spleen are probably sensitive sensors of portal pressure and of portal vein resistance. Therefore, it has been postulated that spleen stiffness measurement (SSM) by ultrasound elastography could be an accurate non-invasive surrogate for PH, and devoid of the limitations of LSM. In some studies, SSM showed a closer correlation with HVPG, CSPH and presence and size of EV when compared to LSM[6,119].

The present study aimed to assess diagnostic performance of SS measurement using ARFI elastography for the presence of severe portal hypertension by evaluating their associations with DI values in PH patients.

In our study, median shear wave velocity (Vs) of spleen stiffness as measured by ARFI method ranged from 2.54 - 4.1 m/s with a mean value of 3.14 ± 0.28 m/s.

Parameter	Range		Mean	SD
	Minimum	Maximum		
ARFI (m/s)	2.54	4.1	3.14	0.28

Due to non-availability of invasive techniques like HVPG measurement and Endoscopy, diagnosis of severe portal hypertension was determined on the basis of the Damping index of hepatic vein as studied by Kim MY et al in 2007 and Antil N et al in 2016 who found that by linear correlations with HVPG, DI>0.6 was significantly associated with severe portal hypertension (odds ratio: 14.19, 95% confidence interval: 4.07-49.55). It was concluded that Damping index of the HV waveform by Doppler ultrasonography might be a non-invasive supplementary tool in evaluating the severity of portal hypertension[122].

Among 65 patients in our study group, we tried to analyze the correlation between ARFI shear wave velocity of spleen with the severity of portal hypertension by considering DI>0.6 as the reference value. We observed a statistically significant difference between SS in subjects with DI<0.6 and those with DI>0.6 ($p<0.001$). The best SS cut-off value for predicting severe portal hypertension was 3.11 m/s (AUROC 0.877, $p<0.001$, with 93.3% Se, 80% Sp, 91.30% PPV, 84.21% NPV and 89.23% accuracy).

Area under the receiver operating curve (AUROC) analyses of spleen stiffness (SS) and DI was plotted to predict the presence of severe portal hypertension (AUROC: 0.877).

Cutoff value for severe PH	Sensitivity	Specificity
2.75	100.0%	30.0%
3.11	**93.3%**	**80.0%**
3.15	**86.7%**	**80.0%**
3.20	60.0%	85.0%
3.28	26.7%	90.0%

In our study, among 45 cases who has been considered as severe portal hypertension based on DI>0.6, 39 cases (93.3 %) showed a median Vs of SS >3.11m/s.

The SS cutoff value of 3.11 m/sec was selected to rule out the presence of severe portal hypertension with a highest sensitivity of 93.3% and specificity of 80%($p<0.05$) compared to other cut off velocities in the study group.

Hence, SS was the most accurate diagnostic factor for severe portal hypertension (AUC, 0.877; 95% CI: 0.767, 0.988).

In a study by Y. Takuma et al[133] in 2013, "SS of 3.15 m/s had a higher sensitivity and specificity of 96.6% and 77.8% respectively to rule out severe portal hypertension. The correlation coefficient between SS and HVPG (r = 0.876) was significantly better than that between LS and HVPG (r = 0.609, P < .0001). The areas under the ROC curve of SS for the identification of clinically important portal hypertension (HVPG ≥ 10 mm Hg), severe portal hypertension (HVPG ≥ 12 mm Hg), esophageal varices (EVs), and high-risk EVs were significantly higher (0.943, 0.963, 0.937, and 0.955, respectively) than those of LS, spleen diameter, platelet count, and platelet count to spleen diameter ratio (P < .05 for all).

In 2013, Y. Takuma, Nouso.K, Morimoto.Y, et al[134] conducted a prospective study, measuring SS and liver stiffness (LS) in 340 patients with cirrhosis undergoing endoscopic screening for EVs and 16 healthy volunteers (controls). Patients with cirrhosis had significantly higher SS and LS values than controls ($P < .0001$ and $P < .0001$, respectively). Levels of SS were higher among patients with EVs (n = 132) than controls, and values were highest among patients with high-risk EVs (n = 87). SS had the greatest diagnostic accuracy for the identification of patients with EVs or high-risk EVs compared with other noninvasive parameters, independent of the etiology of cirrhosis. An SS cutoff value of 3.18 m/s identified patients with EVs with a 98.4% negative predictive value, 98.5% sensitivity, 75.0% accuracy, and 0.025 negative likelihood ratio. An SS cutoff value of 3.30 m/s identified patients with high-risk EVs with a 99.4% negative predictive value, 98.9% sensitivity, 72.1% accuracy, and 0.018 negative likelihood ratio. SS values less than 3.3 m/s ruled out the presence of high-risk varices in patients with compensated or decompensated cirrhosis and could be used as an initial noninvasive screening test.

In 2016, Ma X et al[138] conducted a meta-analysis of the 16 studies (ten studies using TE, three using pSWE-VTQ (point shear wave elastography), and three using 2D-SWE-SSI) including 1892 patients to evaluate the diagnostic performance of LS and SS measurement for detecting EV in patients with chronic liver disease (CLD), and compare their accuracy. In detection of any EV, for LS measurement, the summary sensitivity was 0.83 (95% confidence interval [CI]: 0.78–0.87), and the specificity was 0.66 (95% CI: 0.60–0.72). While for SS measurement, the pooled sensitivity and specificity was 0.88 (95% CI: 0.83–0.92) and 0.78 (95% CI: 0.73–0.83). The summary receiver operating

characteristic (SROC) curve values of LS and SS were 0.81 (95% CI: 0.77–0.84) and 0.88 (95% CI: 0.85–0.91) respectively, and the results had statistical significance (P<0.01). The diagnostic odds ratio (DOR) of SS (25.73) was significantly higher than that of LS (9.54), with the relative DOR value was 2.48 (95%CI: 1.10–5.60), P<0.05. It was concluded that under above mentioned techniques, SS is significantly superior to LS for identifying the presence of EV in patients with CLD. SS measurement may help to select patients for endoscopic screening.

In 2016, Y. Takuma, Tomokuni.J, Sahara.A, et al[139] conducted a study on 446 cirrhotic patients and followed them prospectively to evaluate SS determined by ARFI imaging as a predictor of oesophageal variceal bleeding (OVB). The areas under the ROC curve (AUROC) values for predicting OVB were 0.857 for SS, 0.756 for PSR, 0.746 for spleen diameter, 0.720 for platelet count and 0.668 for LS (figure 1). SS had a significantly better AUROC value for predicting OVBs compared with all other parameters. An SS cut-off value of 3.64 m/s identified patients with OVBs with a 97.9% negative predictive value, 78.8% sensitivity and 79.8% accuracy. In subgroup analyses, the AUROCs of SS for predicting OVBs were 0.911 in compensated, 0.786 in decompensated and 0.727 in patients with OV, respectively. Optimal SS cut-off values for predicting OVBs were 3.48 m/s for compensated patients and 3.75 m/s for both decompensated and patients with OV, respectively. In particular, among the patients with OV or decompensated cirrhosis, those with an SS value ≧3.75 m/s had a higher incidence of OVB compared with other SS value".

SUMMARY

65 patients with clinical suspicion and diagnosis of portal hypertension were studied using grey scale, colour Doppler and elastography techniques of Ultrasound. Various parameters of portal hypertension like colour Doppler sonographic findings, flowmetric changes, presence of various portosystemic collaterals, associated liver parenchymal disease, splenomegaly, ascites and Spleen Stiffness measurement by acoustic radiation force impulse (ARFI) imaging were evaluated in this study.

- The most common age group in our study was between 41-50 years constituting about 38.5% of the total cases.
- Males were most commonly affected than females owing to the higher incidence of alcoholism leading to liver cirrhosis.
- Cirrhosis was the most common etiology seen in 80% of cases.
- Dilated portal vein >13 mm was noted in 41 cases (62%).
- Loss of respiratory phasicity (<20%) was noted in 79% of cases which can be considered as a sensitive indicator.
- Hepatopetal flow was present in most of the cases (75.4%) with only minority of the cases showing NFPF i.e, bidirectional and hepatofugal flow.
- Decreased PV flow velocity (<15cm/s) was seen in 69.2 % cases showing significant association with portal hypertension.
- Portosystemic collaterals were noted in 69.2 % of the cases. Most frequent collateral were the splenorenal collaterals comprising 53.8% of cases.
- Thrombosis of portal vein was seen in 10 cases with portal cavernoma formation in 3 cases.

- Associated findings like Splenomegaly and Ascites were seen in 84.6% and 87.7% of the cases respectively suggesting a strong association with portal hypertension.
- Damping Index >0.6 was seen in 69% of cases suggesting severe portal hypertension.
- Spleen stiffness as measured by ARFI shear wave velocity ranged between 2.54 – 4.1 m/s with mean SS of 3.14 ± 0.28 m/s.
- The diagnostic accuracy of SS for the presence of severe portal hypertension was compared with that of another noninvasive parameter Damping Index.
- The Spleen stiffness cutoff value of 3.11 m/sec was considered as the better indicator to rule out the presence of severe portal hypertension with a highest sensitivity of 93.3% and specificity of 80% ($p<0.05$).

The grey scale and Doppler parameters like presence of splenomegaly, ascites, dilated portal vein, loss of respiratory phasicity, decreased PV flow velocity and formation of portosystemic collaterals were frequently seen in association with portal hypertension where as some parameters like flow direction, NFPF was seen less commonly than normal Hepatopetal flow. Damping Index and Spleen stiffness measurement by acoustic radiation force impulse (ARFI) imaging has showed a strong association with the severity of portal hypertension.

To summarize, Ultrasound Doppler is an accurate non-invasive investigation in assessing the etiology, severity and complications of portal hypertension. The various spectrum of findings, flowmetric changes, portosystemic collaterals and Spleen Stiffness measurement by acoustic radiation force impulse (ARFI) imaging can be accurately studied using ultrasound.

CONCLUSION

Hepatic Venous Pressure Gradient (HVPG) measurement and endoscopy are the Gold standard methods for the assessment of Portal hypertension in Chronic Liver Disease. However, these are invasive and may (in rare cases) lead to complications; in addition, a specialized clinical setting and specific expertise are required to carry out these tests, limiting their availability and increasing the cost to health care systems.

Hence there is a need for non-invasive methods to assess portal hypertension in patients with chronic liver disease.

Doppler ultrasonography is a commonly used, well established, cost effective and non-invasive method to assess abdominal organs and the portal system. It is the first choice among imaging modalities for evaluating the signs of portal hypertension and progression of anatomic changes in the course of this disease.

The present study demonstrates various benefits of Ultrasound in the assessment of portal hypertension. Because of a close relationship with impaired portal hemodynamics, Doppler measurement data are useful to understand the underlying pathogenesis in the portal system.

The development of simple, non-invasive methods like Spleen Elastography has enabled the accurate and rapid diagnosis of patients with a low risk of severe portal hypertension and varices requiring immediate treatment thereby minimizing the further complications and better management.

Spleen stiffness measurements has recently received considerable attention as an indicator of portal hypertension because it can be examined by non-invasive imaging systems such as transient elastography and acoustic radiation force impulse imaging and could predict the severity of PH more effectively than other noninvasive parameters. The measurement of Spleen Stiffness by acoustic radiation force impulse (ARFI) imaging could help in rapid risk stratification and identification of patients requiring further testing such as screening endoscopy or prophylactic treatment for decompensation.

If the present results can be confirmed in further studies with large patient population, this completely non-invasive method might prove to be a readily available and popular alternative to invasive methods such as measurement of HVPG in patients with cirrhosis and portal hypertension.

CHALLENGES AND FUTURE DIRECTIONS

- The available Doppler parameters are not definitive indicator for HVPG, continuous efforts are required to determine the appropriate Doppler markers or alternative parameters are required with a hard/software development.
- Noninvasive diagnosis of Esophageal Varices is facing poor diagnostic performance.
- The field of ultrasound elastography is rapidly evolving, and newer techniques are becoming widely available; their diagnostic performance for PH remains to be established.
- An establishment of reliability criteria and an improved assessment for patients with unreliable data should be considered in the field of Elastography.
- Further research is needed to establish whether the dynamics of SSM over time or in response to treatment could be a better indicator of HVPG changes.
- Head-to-head comparisons to select the best method for each clinical scenario in PH is certainly a field for future research.
- There are still challenges in the research field, suggesting our future directions for the improvement of diagnostic ability by achieving the international study with large patient population.

BIBLIOGRAPHY

1. Sarin SK, Sachdev G. Nanda R. Follow up of patients after variceal eradication. A comparison of patients with cirrhosis, non-cirrhotic portalfibrosis and extrahepatic obstruction. Ann Surg. 1986: 204; 78-82.
2. Ravaioli F, Montagnani M, Lisotti A, Festi D, Mazzella G, Azzaroli F. Noninvasive Assessment of Portal Hypertension in Advanced Chronic Liver Disease: An Update. Gastroenterology Research and Practice. 2018;2018.
3. Warren JV, Brannon ES. A method of obtaining blood samples directlyfrom hepatic vein in man. ProcSocExpBiol Med 1944;55:144-146.
4. A Berzigotti, Susana S, Enric R, Jaime B. Assessing portal hypertension in liver diseases. Expert Review of Gastroenterology &Hepatology. 2013;7(2):141-155.
5. Tomita H, Fuchimoto Y, Ohkuma K, Hoshino K, Fujino A, Kato M, et al. Spleen stiffness measurements by acoustic radiation force impulse imaging after living donor liver transplantation in children: a potential quantitative index for venous complications. Pediatric Radiology. 2015;45(5):658-66.
6. DeLeve L, Valla D, Garcia-Tsao G. Vascular disorders of the liver. Hepatology. 2008;49(5):1729-1764.
7. Zweibel WJ. Sonographic diagnosis of hepatic vascular disorders. Sem US, CT, MR 1995;16:34-48.
8. Bradley SE, Ingelfinger FJ, Bradley GP, Curry JJ. The estimation of hepatic blood flow in man. J Clin Invest 1945;24(6):890-897.
9. Bosch J, Abraldes J, Fernández M, García-Pagán J. Hepatic endothelial dysfunction and abnormal angiogenesis: New targets in the treatment of portal hypertension. Journal of Hepatology. 2010;53(3):558-567.
10. Sanyal A, Bosch J, Blei A, Arroyo V. Portal Hypertension and Its Complications. Gastroenterology. 2008;134(6):1715-1728.
11. Treiber G, Csepregi A, Malfertheiner P. The Pathophysiology of Portal Hypertension. Digestive Diseases. 2005;23(1):6-10.

12. Bessa X, Callaghan E, Balleste B et al. Applicability of the Rockall score in patients undergoing endoscopic therapy for upper gastrointestinal bleeding. Dig Liv Dis 2006; 38: 12-17.
13. Cichoz-Lach, H & Celinski, Krzysztof & Słomka, M & Kasztelan-Szczerbińska, Beata. Pathophysiology of portal hypertension. Journal of physiology and pharmacology : an official journal of the Polish Physiological Society. 2008; 59 Suppl 2. 231-8.
14. GuhaMazumdar DN, Gupta JD, Dasgupta JD. Arsenic and non-cirrhoticportal hypertension. J. Hepatol. 1991; 13: 376.
15. Habibullah CM. Rao GN. Murthy DK, et al. Non cirrhotic portal fibrosisin Andhra Pradesh. J Assoc Physicians India 1978; 26: 379-82.
16. Yeon Seok Seo, Vijay H Shah. Pathophysiology of Portal Hypertension and Its Clinical Links. Journal of Clinical and Experimental Hepatology 2011;1(2):87–93.
17. Yasuko Iwakiri, Pathophysiology of Portal Hypertension. Clin Liver Dis.2014; 18(2): 281–291.
18. Hennenberg M, Tebicka J, Sauerbruch T, Heller J. Mechanisms of extrahepatic vasodilation in portal hypertension. Gut 2008;57:1300–1314.
19. Huang HC, Haq O, Utsumi T, et al. Intestinal and plasma VEGF levels in cirrhosis: the role of portal pressure. J Cell Mol Med. 2012; 16:1125–33.
20. Bandali MF, Mirakhur A, Lee EW, Ferris MC, Sadler DJ, Gray RR, Wong JK. Portal hypertension: Imaging of portosystemic collateral pathways and associated image-guided therapy. World journal of gastroenterology. 2017;23(10):1735.
21. Plessier A, Darwish-Murad S, Hernandez-Guerra M, Consigny Y, Fabris F, Trebicka J et al. Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study. Hepatology 2010; 51: 210-218.
22. Bosch J, Abraldes JG, Berzigotti A, García-Pagan JC. The clinical use of HVPG measurements in chronic liver disease. Nat Rev Gastroenterol Hepatol 2009; 6: 573-582.
23. Bosch J, Abraldes JG, Fernández M, García-Pagán JC. Hepatic endothelial dysfunction and abnormal angiogenesis: new targets in the treatment of portal hypertension. J Hepatol 2010; 53: 558-567.

24. Stankovic Z, Csatari Z, Deibert P, Euringer W, Blanke P, Kreisel W, Abdullah Zadeh Z, Kallfass F, Langer M, Markl M. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. Radiology 2012; 262: 862-873.
25. Kim YJ, Raman SS, Yu NC, To'o KJ, Jutabha R, Lu DS. Esophageal varices in cirrhotic patients: evaluation with liver CT. AJR Am J Roentgenol 2007; 188: 139-144.
26. Al-Busafi SA, McNabb-Baltar J, Farag A, Hilzenrat N. Clinical manifestations of portal hypertension. International journal of hepatology. 2012;2012.
27. Sato T, Akaike J, Toyota J, Karino Y, Ohmura T. Clinicopathological features and treatment of ectopic varices with portal hypertension. International journal of hepatology. 2011;2011.
28. Iwakiri Y, Groszmann RJ. The hyperdynamic circulation of chronic liver diseases: from the patient to the molecule. Hepatology 2006; 43: S121-S131.
29. Watanabe N, Toyonaga A, Kojima S, Takashimizu S, Oho K, Kokubu S, et al. Current status of ectopic varices in Japan: Results of a survey by the Japan Society for Portal Hypertension. Hepatol Res 2010; 40: 763-776.
30. Leiva JG, Salgado JM, Estradas J, et al. Pathophysiology of ascites and dilutional hyponatremia: Contemporary use of aquaretic agents. Ann Hepatol 2007;6:214–221.
31. DeLeve L, Valla D, Garcia-Tsao G. Vascular disorders of the liver. Hepatology. 2008;49(5):1729-1764.
32. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol 2012; 18: 2009-2017.
33. Khanna R, Sarin SK. Non-cirrhotic portal hypertension–Diagnosis and management. Journal of hepatology. 2014;60(2):421-41.
34. Procopet B, Berzigotti A. Diagnosis of cirrhosis and portal hypertension: imaging, non-invasive markers of fibrosis and liver biopsy. Gastroenterology report. 2017;5(2):79-89.
35. Deng H, Qi X, Guo X. Diagnostic Accuracy of APRI, AAR, FIB-4,FI, King, Lok, Forns, and FibroIndex Scores in Predicting the Presence of Esophageal Varices in

Liver Cirrhosis: A Systematic Review and Meta-Analysis. Medicine (Baltimore) 2015; 94: e1795.

36. Berzigotti A, Gilabert R, Abraldes JG, Nicolau C, Bru C, Bosch J, García-Pagan JC. Noninvasive prediction of clinically significant portal hypertension and esophageal varices in patients with compensated liver cirrhosis. Am J Gastroenterol 2008; 103: 1159-1167.
37. Sebastiani G, Tempesta D, Fattovich G, Castera L, Halfon P, Bourliere M, Noventa F, Angeli P, Saggioro A, Alberti A. Prediction of oesophageal varices in hepatic cirrhosis by simple serum non-invasive markers: Results of a multicenter, largescale study. J Hepatol 2010; 53: 630-638.
38. Augustin S, Millán L, González A, Martell M, Gelabert A, Segarra A, Serres X, Esteban R, Genescà J. Detection of early portal hypertension with routine data and liver stiffness in patients with asymptomatic liver disease: a prospective study. J Hepatol 2014; 60: 561-569.
39. Bolognesi M, Di Pascoli M, Sacerdoti D. Clinical role of non-invasive assessment of portal hypertension. World journal of gastroenterology. 2017 Jan 7;23(1):1.
40. Sandblom P .The history of portal hypertension, Journal of the Royal Society of Medicine 1993; 86:544-546
41. Thompson WP, Caughey JL, Whipple AO, Rousselot LM. Splenic vein pressure incongestive splenomegaly (Banti's syndrome). J Clin Invest 1937;16(4):571-572.
42. Warren JV, Brannon ES. A method of obtaining blood samples directlyfrom hepatic vein in man. ProcSocExpBiol Med 1944;55:144-146.
43. Arthur BH. The portocaval shunt in the surgical treatment of portal hypertension. AnnSurg 1948;128(4):825-841.
44. Coman IM. Christian Andreas Doppler: the man and his legacy. Eur J Echocardiography 2005;6(1):7–10.
45. Dempsey PJ. The history of breast ultrasound. J Ultrasound Med 2004;23(7):887–894.

46. Philips C, Arora A, Shetty R, Kasana V. A Comprehensive Review of Portosystemic Collaterals in Cirrhosis: Historical Aspects, Anatomy, and Classifications. International Journal of Hepatology. 2016;2016:1-15.
47. Kaproth-Joslin K, Nicola R, Dogra V. The History of US: From Bats and Boats to the Bedside and Beyond:RSNA Centennial Article. RadioGraphics. 2015;35(3):960-970.
48. Moult PJ, Waite DW, Dick R. Posterior mediastinal venous masses in patients with portal hypertension. Gut. 1975;16(1):57-61.
49. Ayuso C, Luburich P, Vilana R, Bru C, Bruix J. Calcifications in the portal venous system: comparison of plain films, sonography, and CT. AJR. American journal of roentgenology. 1992;159(2):321-3.
50. Kawasaki T, Kambayashi JI, Sakon M, Shiba E, Yokota M, Doki Y, et al. Portal vein calcification: a clinical review of the last 50 years and report of a case associated with dysplasminogenemia. Surgery today. 1993;23(2):176-81.
51. Yen TS, Liu CA, Chiu NC, Chiou YY, Chou YH, Chang CY. Relationship between severity of venous calcifications and symptoms of phlebosclerotic colitis. World Journal of Gastroenterology: WJG. 2015 Jul 14;21(26):8148.
52. Wang CE, Sun CJ, Huang S, Wang YH, Xie LL. Extensive calcifications in portal venous system in a patient with hepatocarcinoma. World Journal of Gastroenterology: WJG. 2014;20(43):16377.
53. Ginai AZ, Van Buuren HR, Hop WC, Schalm SW. Oesophageal varices:how reliable is a barium swallow?.The British journal of radiology. 1993;66(784):322-6.
54. Chang D, Levine MS, Ginsberg GG, Rubesin SE, Laufer I. Portal hypertensive gastropathy: radiographic findings in eight patients. American Journal of Roentgenology. 2000;175(6):1609-12.
55. Choudhuri G, Dhiman RK, Agarwal DK. Endosonographic evaluation of the venous anatomy around the gastro-esophageal junction in patients with portal hypertension. Hepato-gastroenterology. 1996;43(11):1250-5.

56. Konishi Y[1], Nakamura T, Kida H, Seno H, Okazaki K, Chiba T.Catheter US probe EUS evaluation of gastric cardia and perigastric vascular structures to predict esophageal variceal recurrence. Gastrointest Endosc. 2002;55(2):197-203.
57. Lee YT, Chan FK, Ching JY, Lai CW, Leung VK, Chung SC, Sung JJ. Diagnosis of gastroesophageal varices and portal collateral venous abnormalities by endosonography in cirrhotic patients. Endoscopy. 2002;34(05):391-8.
58. Sato T, Yamazaki K, Toyota J, Karino Y, Ohmura T, Akaike J. Endoscopic ultrasonographic evaluation of hemodynamics related to variceal relapse in esophageal variceal patients. Hepatology Research. 2009;39(2):126-33.
59. Hammoud GM, Ibdah JA. Utility of endoscopic ultrasound in patients with portal hypertension. World Journal of Gastroenterology. 2014;20(39):14230.
60. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol 2013; 7: 141-155.
61. Berzigotti A, Piscaglia F; EFSUMB Education and Professional Standards Committee. Ultrasound in portal hypertension – part 2 – and EFSUMB recommendations for the performance and reporting of ultrasound examinations in portal hypertension. Ultraschall Med.33(1), 8–32; quiz 30 (2012).
62. Goyal AK, Pokharna DS, Sharma SK. Ultrasonic measurements of portal vasculature in diagnosis of portal hypertension. A controversial subject reviewed. Journal of ultrasound in medicine. 1990;9(1):45-8.
63. Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, D'Amico G, Pasta L, Craxì A, Saitta A, Raimondo G. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection?. Hepatology. 2001;33(2):333-8.
64. Perisic M, Ilic-Mostic T, Stojkovic M, Culafic D, Sarenac R. Doppler hemodynamic study in portal hypertension and hepatic encephalopathy. Hepato-gastroenterology. 2005;52(61):156-60.
65. Rokni YH, Khalilian MR. Sonographic assessment of respiratory variations in diameter of portal and splenic veins in cirrhotic patients and healthy controls. 2005;2:95-98.

66. Wu CC. Ultrasonographic evaluation of portal hypertension and liver cirrhosis. Journal of Medical Ultrasound. 2008;16(3):188-93.
67. Cokkinos DD, Dourakis SP. Ultrasonographic assessment of cirrhosis and portal hypertension. Current Medical Imaging Reviews. 2009;5(1):62-70.
68. Anand A, Sonawane B, Gupta S, Tembhekar N, Titare P, Rathod P. Portal hypertension evaluation by Doppler ultrasound. Portal. 2014;69:1.
69. Ahamed MS, Kabir S, Mohiuddin AS, Chowdhury PK. Diagnosis of portal hypertension by transabdominal ultrasound. Bangladesh Medical Journal Khulna.2014;47(1-2):21-4.
70. Bolondi L, Mazziotti A, Arienti V. Ultrasonographic study of portal venous system in portal hypertension and after portosystemic shunt operations. Surg 1984;95:261.
71. Zoli M, Dondi C, Marchesini G, Cordiani MR, Melli A, Pisi E. Splanchnic vein measurements in patients with liver cirrhosis : A case control study. J Ultrasound Med 1985;4:641.
72. Kurol M, Forsberg L. Ultrasonographic investigation of respiratory influence on diameters of portal vessels in normal subjects. ActaRadiolDiagn (Stockh) 1986;27:675.
73. Lafortune M, Marleau D, Breton G. Portal venous system measurements in portal hypertension. Radiol 1984;151:27.
74. Kostin B. Duplex Doppler in portal hypertension. Semin – Ultrasound and CT, MR 1992;13:22-33.
75. Leeven V. Doppler ultrasound : Clinical applications. Radiol 1990;174:309-319.
76. Bellamy EA, Bossi MC, Cosgrove DO. Ultrasound demonstration of changes in the normal portal venous system following a meal. Br J Radiol 1984;57:147.
77. Rabin N, Adam EJ. Ultrasound demonstration of variations in normal portal vein diameter with posture. Br J Radiol 1985;58:313.
78. Aly A. Elbarbarya, Mohamed M. Elbedewyb, Amr M. Elbadrya. Hemodynamic analysis of portal hypertension in patientswith liver cirrhosis. Tanta Medical Journal 2014; 42(4):130–137.

79. Bolondi L, Gandolfi L, Arienti V, Caletti GC, Corcioni E, Gasbarrini G, Labo G. Ultrasonography in the diagnosis of portal hypertension: diminished response of portal vessels to respiration. Radiology. 1982;142(1):167-72.
80. Geleto G, Getnet W, Tewelde T. Mean normal portal vein diameter using sonography among clients coming to radiology Department of Jimma University Hospital, Southwest Ethiopia. Ethiopian journal of health sciences. 2016;26(3):237-42.
81. Aube C, Winkfield B, Oberti F, et al. New Doppler ultrasound signs improve the non-invasive diagnosis of cirrhosis or severe liver fibrosis. Eur J Gastroenterol Hepatol 2004;16:743–51.
82. Lechowicz R, Elwertowski M. Standards of the Polish Ultrasound Society. Ultrasound examination of the portal system and hepatic vessels. Journal of ultrasonography. 2015;15(61):208-226.
83. Koslin B. Duplex Doppler examination of portal venous system. J Clin ultrasound 1987;15:675-686.
84. Chakenahalli N, Lingaiah RN, Varun SM. Role of Ultrasound Doppler in Evaluation of Portal Hypertension. International Journal of Anatomy, Radiology and Surgery. 2018;7(1).
85. Geleto G, Getnet W, Tewelde T. Mean normal portal vein diameter using sonography among clients coming to radiology Department of Jimma University Hospital, Southwest Ethiopia. Ethiopian journal of health sciences. 2016;26(3):237-42.
86. Patriquin H, Lafortune M, Burns PN, Dauzat M. Duplex Doppler examination in portal hypertension: technique and anatomy. American Journal of Roentgenology. 1987;149(1):71-6.
87. Gaiani S, Bolondi L, Li Bassi S, Zironi G, Siringo S, Barbara L. Gastroenterology. 1991; 100(1):160-7.
88. Von Herbay A, Frieling T, Häussinger D. Color Doppler sonographic evaluation of spontaneous portosystemic shunts and inversion of portal venous flow in patients with cirrhosis. Journal of clinical ultrasound. 2000;28(7):332-9.

89. Takayasu K, Takashi M, Musha H. Spontaneous reversal of portal blood flow demonstrated by percutaneous transhepaticcatheterization : Report of two cases. Gastroenterol 1982;82:753.
90. Mittal P, Gupta R, Mittal G, Kalia V. Association between portal vein color Doppler findings and the severity of disease in cirrhotic patients with portal hypertension. Iranian Journal of Radiology. 2011;8(4):211.
91. Ahirwal A S, Agrawal B R, Sharma C S. Role Of Colour Doppler In Portal And Hepatic Vessels Liver Disease With Histopathological Correlation. National Journal of Medical and Dental Research, 2015: Volume-4, Issue-1, Page 36-40.
92. Kuo CH, Changchien CS, Tai DI, Chen JJ. Portal vein velocity by duplex Doppler ultrasound as an indication of the clinical severity of portal hypertension. Changgeng yi xue za zhi. 1995;18(3):217-23.
93. Gerstenmaier JF, Gibson RN. Ultrasound in chronic liver disease. Insights into imaging. 2014;5(4):441-55.
94. Mildenberger, R. Lotz, K.-F. Kreitner. Duplex sonography of the normal portal vein. Dtsch med Wochenschr 1987; 112(50): 1936-1939.
95. Riahinezhad M, Rezaei M, Saneian H, Famouri F, Farghadani M. Doppler assessment of children with liver cirrhosis and portal hypertension in comparison with a healthy control group: An analytical cross-sectional study. Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences. 2018;23.
96. Elbarbary AA, Elbedewy MM, Elbadry AM. Hemodynamic analysis of portal hypertension in patients with liver cirrhosis. Tanta Medical Journal. 2014;42(4):130.
97. Mukhopadyay I, Saha A. Quantitative assessment of portal vein by colour Doppler imaging in patients with various liver diseases in West Bengal and reflection of pathophysiological haemodynamics and evaluation of prognosis. Int. J. Recent Scient. Res. 2015;6:5234-6.
98. Berzigotti A, Piscaglia F. Ultrasound in portal hypertension – part 1. Ultraschall Med. 32(6), 548–68; quiz 569, 2011.

99. Patriquin H, Lafortune M, Burns PN, Dauzat M. Duplex Doppler examination in portal hypertension : Technique and Anatomy. AJR 1987;149:71.

100. Mildenberger P. Duplex sonography of the normal portal vein. Dutch Med Woehenschr 1987;112:1936-1939.

101. Burns P, Taylor K, Blein A. Doppler flowmetry and portal hypertension. Gastroenterology 1987;92:824.

102. Stine JG, Wang J, Shah PM, Argo CK, Intagliata N, Uflacker A, Caldwell SH, Northup PG. Decreased portal vein velocity is predictive of the development of portal vein thrombosis: A matched case-control study. Liver International. 2018;38(1):94-101.

103. Achar S, Dutta HK, Gogoi RK. Extrahepatic Portal Vein Obstruction in Children: Role of Preoperative Imaging.J Indian Assoc Pediatr Surg.2017;22(3):144-149.

104. Iranpour P, Lall C, Houshyar R, Helmy M, Yang A, Choi JI, Ward G, Goodwin SC. Altered Doppler flow patterns in cirrhosis patients: an overview. Ultrasonography. 2016;35(1):3.

105. Kauzlaric D, Petrovic M, Barmeir E. Sonography of cavernoma transformation of portal vein. Am J Roentgenol 1984;142:383-384.

106. Gansbeke VD, Avni EF, Engeholm DC, Struyven J. Sonographic features of portal vein thrombosis. Am J Roentgenol 1985;144:749-752.

107. Al-Nakshabandi NA. The role of ultrasonography in portal hypertension. Saudi J Gastroenterol. 2006;12:111–117.

108. Doehner GA, Ruzicka FF, Rousselot LM, Hoffman G. The portal venous system Onits pathological roentgen anatomy. Radiol 1956;66:206.

109. Shastri M, Kulkarni S, Patell R, Jasdanwala S. Portal Vein Doppler: A Tool for Non-Invasive Prediction of Esophageal Varices in Cirrhosis. Journal of Clinical and Diagnostic Research : JCDR. 2014;8(7):MC12-MC15.

110. Schwaighofer B, Fruhwald F, Hay U. VarizendiagnostickbeiLeberzirrhose :Duplexultraschall versus gastroskopie. FortschfRontgenstr 1987;146:38.

111. Saddekni S, Hutchinson DE, Cooperberg PL. The sonographically patent umbilical vein in portal hypertension. Radiology 1982;145:441.

112. Ditchfield MR, Gibson RN, Donald JD, Gibson PR. Duplex Doppler Ultrasound sign of portal hypertension. Relative diagnostic value of examination of paraumbilical vein, portal vein and spleen. Australasian Radiology 2007. 2008;36(2):102-105.

113. Bhattarai S, Gyawali M, Dewan KR, Shrestha G, Patowary BS, Sharma P. Study of Portal Vein Diameter and Spleen Size by Ultrasonography and Their Association with Gastro-esophageal Varices. Nepalese Journal of Radiology.2014;4(2):6-14.

114. Cosgrove D, Blomley M. Liver tumors: evaluation with contrastenhanced ultrasound. Abdom imaging 2004; 29(4): 446-54.

115. Allan RI, AMS HS. Ultrasound assessment of portal hypertension. Educational supplement. Issue. 2006;1:22-7.

116. Mandal L, Mandal SK, Bandyopadhyay D, Datta S. Correlation of portal vein diameter and splenic size with gastro-oesophageal varices in cirrhosis of liver. J Ind Aca Clin Med. 2011;12(4):266-70.

117. Berzigotti A, Zappoli P, Magalotti D, et al. Spleen enlargement on follow-up evaluation: A noninvasive predictor of complications of portal hypertension in cirrhosis. Clin Gastroenterol Hepatol 2008; 6(10): 1129-34.

118. F. Piscaglia, G. Donati, L. Cecilioni, N. Celli, B.Stagni, P. Pini, et al.Influence of the spleen on portal haemodynamics: a non-invasive study with Doppler ultrasound in chronic liver disease and haematological disorders. Scand J Gastroenterol, 2002; .37:1220-1227.

119. Wilson SR, Withers CE. In: Rumack CM, Wilson SR, Charboneau JW, Johnson JAM. Diagnostic ultrasound, third edition. St. Louis, Elsevier Mosby 2005; 77-145.

120. Kim G, Cho YZ, Baik SK, Kim MY, Hong WK, Kwon SO. The accuracy of ultrasonography for the evaluation of portal hypertension in patients with cirrhosis: a systematic review. Korean journal of radiology. 2015;16(2):314-24.

121. Antil N, Sureka B, Mittal MK, Malik A, Gupta B, Thukral BB. Hepatic Venous Waveform, Splenoportal and Damping Index in Liver Cirrhosis: Correlation with Child Pugh's Score and Oesophageal Varices. Journal of clinical and diagnostic research: JCDR. 2016;10(2):TC01.
122. Sudhamshu KC, Matsutani S, Maruyama H, et al. Doppler study of hepatic vein in cirrhotic patients: Correlation with liver dysfunction and hepatic hemodynamics. World J Gastroenterol 2006; 12(36): 5853-8.
123. Vizzutti F, Arena U, Romanelli RG, Rega L, Foschi M, Colagrande S, Petrarca A, Moscarella S, Belli G, Zignego AL, Marra F. Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. Hepatology. 2007 1;45(5):1290-7.
124. Lemoine M, Katsahian S, Ziol M, Nahon P, Ganne-Carrie N, Kazemi F, et al. Liver stiffness measurement as a predictive tool of clinically significant portal hypertension in patients with compensated hepatitis C virus or alcohol-related cirrhosis. Alimentary pharmacology & therapeutics. 2008;28(9):1102-10.
125. Robic MA, Procopet B, Métivier S, Péron JM, Selves J, Vinel JP, Bureau C. Liver stiffness accurately predicts portal hypertension related complications in patients with chronic liver disease: a prospective study. Journal of hepatology. 2011;55(5):1017-24.
126. Zardi EM, Di Matteo FM, Pacella CM, Sanyal AJ. Invasive and non-invasive techniques for detecting portal hypertension and predicting variceal bleeding in cirrhosis: a review. Ann Med 2014; 46: 8-17.
127. Cho EJ, Kim MY, Lee JH, Lee IY, Lim YL, Choi DH, Kim YJ, Yoon JH, Baik SK. Diagnostic and Prognostic Values of Noninvasive Predictors of Portal Hypertension in Patients with Alcoholic Cirrhosis. PLoS One 2015; 10: e0133935.
128. Piscaglia F, Marinelli S, Bota S, Serra C, Venerandi L, Leoni S, Salvatore V. The role of ultrasound elastographic techniques in chronic liver disease: current status and future perspectives. Eur J Radiol 2014; 83: 450-455.

129. Piscaglia F, Salvatore V, Mulazzani L, Cantisani V, Schiavone C. Ultrasound Shear Wave Elastography for Liver Disease. A Critical Appraisal of the Many Actors on the Stage. Ultraschall Med 2016; 37: 1-5.
130. Berzigotti A. Non-invasive evaluation of portal hypertension using ultrasound elastography. Journal of hepatology. 2017;67(2):399-411.
131. Sharma P, Mishra SR, Kumar M, Sharma BC, Sarin SK. Liver and spleen stiffness in patients with extrahepatic portal vein obstruction. Radiology.2012;263(3):893-9.
132. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Takabatake H, Matsueda K, Yamamoto H. Portal hypertension in patients with liver cirrhosis: diagnostic accuracy of spleen stiffness. Radiology. 2015;279(2):609-19.
133. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Toshikuni N, Takabatake H, Shimomura H, Doi A, Sakakibara I, Matsueda K. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. Gastroenterology. 2013;144(1):92-101.
134. Colecchia A, Colli A, Casazza G, Mandolesi D, Schiumerini R, Reggiani LB, Marasco G, Taddia M, Lisotti A, Mazzella G, Di Biase AR, Golfieri R, Pinzani M, Festi D. Spleen stiffness measurement can predict clinical complications in compensated HCV-related cirrhosis: a prospective study. J Hepatol 2014; 60: 1158-1164.
135. Procopet B, Berzigotti A, Abraldes JG, Turon F, Hernandez-Gea V, García-Pagán JC, Bosch J. Real-time shear-wave elastography: applicability, reliability and accuracy for clinically significant portal hypertension. J Hepatol 2015; 62: 1068-1075.
136. Balakrishnan M, Souza F, Muñoz C, Augustin S, Loo N, Deng Y, Ciarleglio M, Garcia-Tsao G. Liver and spleen stiffness measurements by point shear wave elastography via acoustic radiation force impulse: intraobserver and interobserver variability and predictors of variability in a US population. Journal of Ultrasound in Medicine. 2016;35(11):2373-80.

137. Ma X, Wang L, Wu H, Feng Y, Han X, Bu H, Zhu Q. Spleen stiffness is superior to liver stiffness for predicting esophageal varices in chronic liver disease: a meta-analysis. PLoS One. 2016 9;11(11):e0165786.

138. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Takabatake H, et al. Prediction of oesophageal variceal bleeding by measuring spleen stiffness in patients with liver cirrhosis. Gut. 2016;65(2):354-5.

139. Adam A, Dixon AK. Ultrasound general principles. In : Cosgrove DO, MeireHB,Adeinlim, Eckersley RJ, edts., Grainger and allisons diagnostic radiology a text book of medical imaging, Chapter 3, 5th edn., Vol. 1. Churchill Livingstone Elsevier 2008:p.55-78.

140. Thomas S. Curry, James E. Dowdey, Robert C., Murry JR. Ultrasound, Chapter – 20, In: Christensen's Physics of Diagnostic Radiology. 4th Edn. Lea and Febiger, UK; 1990:323–325.

141. Foster FS. Transducer material and probe construction of ultrasound. Ultrasound Med Biol. 2000;26 (1):2–25.

142. Park SE, Shrout TR. Characteristics of relaxer based piezoelectric single crystal for ultrasound transducer IEEE transactions ultrasonic, ferroelectrics frequency control. 1998;45:1071–1076.

143. Zwiebel WJ, Pellerito JS. Physics and instrumentation in Doppler and B-mode ultrasonography. In :Zagzebski JA, edt., Introduction to vascular ultrasonography, Chapter2, 5th edn. Elsevier Saunders Publication 2009:19-60.

144. McNaughton DA, Abu-Yousef MM. Doppler US of the liver made simple. Radiographics. 2011;31(1):161-88.

145. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. Diagnostic and interventional imaging. 2013;94(5):487-95.

ETHICAL COMMITTEE CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 61/2016
Date. 03/10/2016
BLDE U's Shri B.M. Patil Medical College

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-10-2016 *at* 3.00pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Role of colour Doppler ultrasonography in the Evaluation of portal venous Hypertension"

Name of P.G. student Dr. Shivu Jayadev
Dept of Radiodiagnosis

Name of Guide/Co-investigator Dr Ramesh. C. Pattanshetti
Professor of Radiodiagnosis

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

CASE PROFORMA

NAME: AGE: Yrs SEX: M / F

IP/OP NO: DATE:

CHIEF COMPLAINTS:

- Pain abdomen
- Abdominal distension
- Haematemesis
- h/o jaundice,
- h/o alcoholism,
- Symptoms of hepatic encephalopathy(altered sensorium/lethargy/coma)
- h/o HTN/ DM/ TB/ Blood Transfusion

GENERAL PHYSICAL EXAMINATION:

Pallor	Cyanosis
Icterus	Clubbing
Edema	

VITALS: PR- BP- mm/Hg

RS/CVS :

PER ABDOMINAL EXAMINATION FINDINGS:

Inspection: abd. dist/ engorged veins/ spider naevi/ caput medusa

Palpation: fluid thrill/ hepatomegaly/ splenomegaly

Percussion: tympanic/ dull/ shifting dullness

Auscultation:

CLINICAL DIAGNOSIS:

LAB PARAMETERS:

LFT	TEST VALUES	UNITS
S. Biluribin (Total)		mg/dL
S. Biluribin (Conjugated)		mg/dL
S. Biluribin (Unconjugated)		mg/dL
S. Protein		g/dL
S. Albumin		g/dL
S. A/G Ratio		
SGOT		Units/L
SGPT		Units/L
Alkaline Phosphatase (ALP)		Units/L

HBsAg : HCV : HIV :

RADIOLOGICAL (ULTRASONOGRAPHIC) FINDINGS:

1) Liver span, echotexture & margin:
2) Spleen span:
3) Ascites:
4) Portal vein:
    a. Diameter (Quiet respiration):
    b. Diameter (Deep inspiration):
    c. Respiratory variation:
    d. Lumen: clear/ thrombus/ cavernoma
    e. Portal flow velocity:
    f. Portal flow direction: hepatopetal/ hepatofugal/ bidirectional/ no flow

5) Splenic vein:

6) Superior mesenteric vein:

7) Hepatic veins flow:

8) Damping Index:

9) Presence of collaterals or varices:

Splenorenal	Anterior abdominal wall
Paraumbilical vein	Perigastric
Coronary vein	GE junction
GB wall varices	Portal cavernoma

10) Spleen stiffness (ARFI): Median shear wave velocity (Vs)=

11) USG Diagnosis :

INFORMED CONSENT FORM

B.L.D.E.DEEMED TO BE UNIVERSITY's SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA

TITLE OF THE PROJECT : ROLE OF COLOUR DOPPLER ULTRASONOGRAPHY IN THE EVALUATION OF PORTAL VENOUS HYPERTENSION

GUIDE : DR. RAMESH C PATTANSHETTI MDRD
PROFESSOR

P.G. STUDENT : DR.SHIVU JAYADEV

PURPOSE OF RESEARCH:

I have been informed that this is being done to describe the role of ultrasound in evaluation of portal hypertension. I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

PROCEDURE:

I have been explained that, I will be subjected to ultrasound scan of abdomen to describe spectrum of colour Doppler sonographic findings and spleen stiffness in portal hypertension.

RISKS AND DISCOMFORTS:

I understand that necessary measures will be taken to reduce these complications as and when they arise.

BENEFITS:

I understand that my participation in this study will describe the role of ultrasound in the evaluation of portal hypertension.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code

number. The code key connecting name to numbers will be kept in a separate secure location. If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time Dr. Shivu Jayadev is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I/my ward understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. Shivu Jayadev will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: DR. Ramesh C Pattanshetti (Guide) Dr Shivu Jayadev (Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Shivu Jayadev has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

Name of Participant: _____

Signature/Thumb print of Participant Date

_____

(Witness to above signature) Date

KEY TO MASTERCHART

PV : PORTAL VEIN

Q : QUIET RESPIRATION

SMV : SUPERIOR MESENTERIC VEIN

SPLV : SPLENIC VEIN

HV : HEPATIC VEIN

CIR : CIRRHOSIS

HCC : HEPATOCELLULAR CARCINOMA

PVO : PORTAL VEIN OCCLUSION

N : NORMAL

THR : THROMBOSIS

CAV : CAVERNOMA

PETAL : HEPATOPETAL

FUGAL : HEPATOFUGAL

BD : BIDIRECTIONAL

NF : NO FLOW

MP : MONOPHASIC

BP : BIPHASIC

TP : TRIPHASIC

P : PRESENT

A : ABSENT

SR : SPLENORENAL

CV : CORONARY VEIN

GEJ : GASTROESOPHAGEAL JUNCTION

ABD : ANTERIOR ABDOMINAL WALL

PU : PARAUMBILICAL

GBV : GALL BLADDER VARICES

PG : PERIGASTRIC

MASTER CHART

Sl. no	NAME	OPD/IPD No.	AGE (yrs)	SEX	ETIOLOGY	PV Diameter (mm)		PV lumen	PV Flow direction	PV Flow velocity (cm/s)	SMV			SPLV			HV		Spleen span (cm)	Ascites	Collaterals/varices	Spleen Stiffness (Median Vs (m/s))	SEVERITY OF PHTN
						Q	% variation				Diameter (mm)	Lumen	Flow	Diameter (mm)	Lumen	Flow	Flow Waveform	Damping Index					
1	Danamma	36470	45	F	CIR	16	17	N	Petal	12	10	N	Petal	11	N	Petal	MP	0.86	14	P	SR,CV,GEJ	3.9	Severe
2	Hanamanth	37665	43	M	CIR	15	17	N	Petal	12	10	N	Petal	11	N	Petal	MP	0.89	14	P	SR,CV,GEJ	3.4	Severe
3	Annappa	39452	56	M	CIR	19	8	N	BD	9	12	N	Fugal	13	N	fugal	BP	0.64	18	P	SR, ABD	3.17	Severe
4	Hanamanth	40069	40	M	CIR	14	18	N	Petal	8	8	N	Petal	10	N	Petal	MP	0.83	15	P	PU,ABD	3.26	Severe
5	Ramesh	40231	62	M	CIR	13	8	N	Petal	12	10	N	Petal	11	N	Petal	BP	0.68	17	P	SR	3.12	Severe
6	Basappa v k	41911	70	M	HCC	10	2	THR	NF	0	6	N	NF	8	N	Petal	TP	0.48	12	P	-	2.85	Mild
7	Siddalingappa	11152	38	M	CIR	14	18	N	Petal	13	8	N	Petal	10	N	Petal	MP	0.85	15	P	PU,GBV,ABD	3.81	Severe
8	Pundalikappa	1583	53	M	CIR	16	9	N	Petal	8	12	N	Petal	11	N	Petal	BP	0.62	13	P	SR	3.0	Severe
9	Babugouda	1674	40	M	CIR	14	18	N	Petal	13	9	N	Petal	10	N	Petal	BP	0.61	15	P	PU,ABD	3.28	Severe
10	Shekhar	2559	41	M	CIR	15	18	N	Fugal	12	9	N	Petal	10	N	Petal	BP	0.64	16	P	SR,ABD	3.21	Severe
11	Basamma	36634	62	F	PVO	11	1	THR	NF	0	8	N	Petal	9	N	Petal	TP	0.51	12	P	PU,ABD	2.84	Mild
12	Mallu Y Agasar	5315	32	M	CIR	10	23	N	Petal	15	6	N	Petal	7	N	Petal	TP	0.36	11	A	-	2.54	Mild
13	Siddanagouda M P	6801	36	M	CIR	12	27	N	Petal	20	7	N	Petal	9	N	Petal	TP	0.48	12	A	-	2.82	Mild
14	Renuka	10023	46	F	CIR	13	14	N	Petal	10	11	N	Petal	12	N	Petal	MP	0.89	17	P	SR,PG	3.23	Severe
15	Hanamanth V K	11013	37	M	CIR	13	22	N	Petal	14	8	N	Petal	9	N	Petal	BP	0.61	13	P	PU,GBV	3.06	Severe
16	Kasturi	125897	45	F	PVO	9	0	THR	NF	0	7	N	Petal	7	N	Petal	TP	0.55	15	P	GEJ,ABD	3.22	Mild
17	Ashok Lamani	12725	35	M	CIR	12	25	N	Petal	15	7	N	Petal	8	N	Petal	TP	0.41	14	P	SR	2.98	Mild
18	Halappa B K	15388	63	M	CIR	14	8	N	Petal	11	10	N	Petal	10	N	Petal	BP	0.65	17	P	SR	3.16	Severe
19	Babu R P	17335	53	M	CIR	14	11	N	Petal	8	10	N	Petal	11	N	Petal	BP	0.67	18	P	SR,PG	3.57	Severe
20	Mallikarjun A L	20966	45	M	CIR	13	15	N	Petal	10	11	N	Petal	12	N	Petal	BP	0.65	14	P	SR	2.71	Severe
21	Prakash	226237	34	M	CIR	12	25	N	Petal	20	7	N	Petal	8	N	Petal	TP	0.51	13	A	-	2.65	Mild
22	Mahesh	22641	32	M	CIR	11	24	N	Petal	22	6	N	Petal	6	N	Petal	TP	0.42	11	A		2.55	Mild
23	Madiwalappa	22815	35	M	CIR	12	26	N	Petal	18	7	N	Petal	8	N	Petal	TP	0.53	10	A	-	3.28	Mild
24	Dongisab A B	24740	75	M	HCC	9	4	THR	NF	0	9	N	NF	8	THR	NF	MP	0.81	14	P	SR	3.24	Severe
25	Pushparaj S G	26636	35	M	CIR	11	25	N	Petal	14	7	N	Petal	9	N	Petal	TP	0.39	13	P	-	2.88	Mild
26	Kamalabai G K	26941	38	F	PVO	11	2	THR	NF	0	10	N	Petal	7	THR	Petal	TP	0.52	15	P	SR	3.16	Mild
27	Suresh P B	27265	44	M	CIR	15	17	N	Petal	7	9	N	Petal	11	N	Petal	MP	0.87	14	P	SR,CV,GEJ	4.1	Severe
28	Ramesh	27773	48	M	CIR	17	12	N	Fugal	9	11	N	Petal	13	N	Petal	MP	0.86	17	P	SR,PG,ABD	3.31	Severe
29	Dyaneshwar	28215	48	M	CIR	15	13	N	Petal	11	12	N	Petal	13	N	Petal	MP	0.87	17	P	SR,PG.PU	3.56	Severe
30	Nagaraj V B	29486	46	M	CIR	13	14	N	Petal	10	10	N	Petal	12	N	Petal	BP	0.66	16	P	SR,PG	3.22	Severe
31	Kavita S C	29386	42	F	Others	0	0	CAV	Petal	8	9	N	Petal	9	N	Petal	BP	0.68	14	P	CAV	3.16	Severe
32	Savita N	195972	40	F	PVO	8	0	THR	NF	0	7	N	Petal	8	N	Petal	TP	0.49	12	P	-	2.94	Mild

33	Hanamantraya B K	19129	40	M	CIR	15	18	N	Petal	13	9	N	Petal	10	N	Petal	MP	0.83	15	P	SR,PU	3.24	Severe
34	Ramesh	27773	45	M	CIR	13	15	N	Petal	6	10	N	Petal	12	N	Petal	BP	0.66	16	P	SR	3.18	Severe
35	Shivappa N P	27965	65	M	CIR	15	7	N	Petal	5	11	N	Petal	11	N	Petal	BP	0.66	17	P	SR	3.17	Severe
36	Mallappa G P	29776	48	M	CIR	17	12	N	Petal	11	12	N	Petal	13	N	Petal	BP	0.66	17	P	SR,PG	3.22	Severe
37	Vijayakumar V H	30264	49	M	CIR	16	10	N	Petal	9	12	N	Petal	13	N	Petal	BP	0.62	14	P	SR	3.11	Severe
38	Balu M C	30573	34	M	CIR	10	27	N	Petal	22	7	N	Petal	7	N	Petal	TP	0.44	11	A	-	2.66	Mild
39	Shivashankar C P	30620	68	M	HCC	9	3	THR	NF	0	8	N	NF	8	N	Petal	TP	0.53	13	P	-	3.18	Mild
40	Rajesh S N	30658	40	M	CIR	15	18	N	Petal	13	9	N	Petal	10	N	Petal	MP	0.85	16	P	SR,PU,ABD	3.24	Severe
41	Sharanappa S N	30678	47	M	CIR	15	14	N	Petal	11	11	N	Petal	13	N	Petal	BP	0.63	17	P	SR,ABD	3.44	Severe
42	Avinash	346871	45	M	CIR	15	17	N	Petal	12	9	N	Petal	11	N	Petal	MP	0.88	14	P	CV,GEJ	3.37	Severe
43	Iranna B	35392	38	M	CIR	14	18	N	Petal	14	8	N	Petal	9	N	Petal	BP	0.68	14	P	PU,GBV,ABD	3.48	Severe
44	Parashuram B T	40323	70	M	HCC	11	5	THR	NF	0	9	N	NF	6	THR	NF	MP	0.92	15	P	SR	3.18	Severe
45	Santosh D K	40852	33	M	CIR	11	22	N	Petal	16	6	N	Petal	7	N	Petal	TP	0.49	11	A	-	2.78	Mild
46	Mahantesh K B	41005	45	M	CIR	13	17	N	Petal	10	10	N	Petal	12	N	Petal	BP	0.61	15	P	SR,ABD	3.16	Severe
47	Shrishail	8925	49	M	CIR	13	10	N	Petal	9	11	N	Petal	13	N	Petal	BP	0.61	15	P	SR	3.18	Severe
48	Hunakabai	3753	51	F	PVO	9	0	THR	NF	0	6	N	Petal	7	N	Petal	TP	0.51	11	P	-	2.72	Mild
49	Gamanabai	10122	55	F	Others	0	0	CAV	Petal	11	10	N	Petal	9	N	Petal	BP	0.67	13	P	CAV	2.98	Severe
50	Dulappa B M	11762	37	M	CIR	13	23	N	Petal	14	8	N	Petal	9	N	Petal	TP	0.55	14	P	-	2.79	Mild
51	Yankappa S D	12061	38	M	CIR	14	18	N	Petal	13	8	N	Petal	10	N	Petal	BP	0.62	15	P	PU,ABD	3.22	Severe
52	Babu Y M	16547	51	M	CIR	16	11	N	Petal	8	11	N	Petal	11	N	Petal	BP	0.68	18	P	SR,PG	3.76	Severe
53	Basavaraj S P	16810	35	M	CIR	11	30	N	Petal	19	7	N	Petal	8	N	Petal	TP	0.45	14	A	-	2.64	Mild
54	Ashabai M N	16599	38	F	Others	0	0	CAV	Petal	9	11	N	Petal	7	N	Petal	BP	0.64	13	P	CAV	2.78	Severe
55	Kashinath	22200	66	M	CIR	16	7	N	Fugal	5	10	N	Petal	10	N	Petal	MP	0.91	14	P	SR	3.18	Severe
56	Deepak	25070	42	M	CIR	15	18	N	Petal	12	9	N	Petal	8	N	Petal	BP	0.65	16	P	SR,PU	3.47	Severe
57	Satish M	25942	46	M	CIR	15	14	N	Fugal	10	12	N	Fugal	12	N	Fugal	MP	0.84	17	P	SR,ABD	3.23	Severe
58	G S Choudhari	28185	45	M	CIR	16	17	N	Petal	10	10	N	Petal	12	N	Petal	BP	0.62	15	P	SR,CV	3.8	Severe
59	Vijay K	32005	55	M	CIR	18	8	N	BD	10	12	N	BD	14	N	BD	BP	0.64	19	P	SR,ABD	3.68	Severe
60	Malkappa H	34019	44	M	PVO	10	6	THR	NF	0	9	THR	Petal	8	N	Petal	TP	0.55	16	P	-	2.96	Mild
61	Siddappa D	36952	48	M	CIR	17	12	N	Petal	9	12	N	Petal	13	N	Petal	BP	0.62	14	P	PG	2.74	Severe
62	Annappa S S	42539	32	M	CIR	11	24	N	Petal	20	6	N	Petal	6	N	Petal	TP	0.38	13	P	-	2.86	Mild
63	Shivakumar B B	42302	42	M	CIR	15	17	N	Petal	12	9	N	Petal	9	N	Petal	MP	0.87	14	P	SR,CV,GEJ	3.38	Severe
64	Lalsab K M	44499	55	M	CIR	17	9	N	Petal	10	11	N	Petal	10	N	Petal	BP	0.63	13	P	SR,PU	2.96	Severe
65	Lakkappa Y C	44507	50	M	CIR	16	10	N	Petal	8	11	N	Petal	12	N	Petal	BP	0.68	13	P	PG	3.22	Severe