VALIDATING THE USEFULNESS OF DOPPLER STUDY OF HEPATIC VEINS IN PREDICTING ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS

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CERTIFICATE

Certified that this dissertation entitled **"VALIDATING THE USEFULNESS OF DOPPLER STUDY OF HEPATIC VEINS IN PREDICTING ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS"** is a bonafide work done by **Dr. P. JAISANKAR,** Post Graduate Student of General Medicine, Madurai Medical College, Madurai - 625 020, during the academic year 2009- 2012.

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I, **DR. P. JAISANKAR**, solemnly declare that dissertation titled **"VALIDATING THE USEFULNESS OF DOPPLER STUDY OF HEPATIC VEINS IN PREDICTING ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS"** is a bonafide work done by me at Madurai Medical College and Hospital during August 2005- July 2006 under guidance and supervision of my unit chief **Dr.J.Sangumani MD** Prof of Medicine and **Dr.L.Thayumanavan MD,DM,** Prof and HOD of Medical Gastroenterology.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfilment of requirement for the award of M.D. Degree (Branch – I) in General Medicine.

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CONTENTS

INTRODUCTION

Cirrhosis represents the final common histologic pathway for a wide variety of chronic liver diseases. The term cirrhosis was first introduced by Laennec in 1826.

Cirrhosis is defined histologically as a diffuse hepatic process characterized by diffuse alteration in the hepatic architecture characterized by on-going fibrosis and regenerative nodules. The progression of liver injury to cirrhosis may occur over weeks to years.

The development of hepatic fibrosis reflects an alteration in the normally balanced processes of extracellular matrix production and degradation. Extracellular matrix, the normal scaffolding for hepatocytes, is composed of collagens (especially types I, III, and V), glycoproteins, and proteoglycans. Stellate cells, located in the peri sinusoidal space, are essential for the production of extracellular matrix. Stellate cells, which were once known as Ito cells, lipocytes, or perisinusoidal cells, may become activated into collagen-forming cells by a variety of paracrine factors. Such factors may be released by hepatocytes, Kupffer cells, and sinusoidal endothelium following liver injury.

Increased collagen deposition in the space of Disse (the space between hepatocytes and sinusoids) and the diminution of the size of endothelial fenestrae lead to the capillarization of sinusoids. Activated

stellate cells also have contractile properties. Both capillarization and constriction of sinusoids by stellate cells contribute to the development of portal hypertension.

The portal vein carries approximately 1500 mL/min of blood from the small and large bowel, the spleen, and the stomach to the liver. Obstruction of portal venous flow, as in cirrhosis, results in a rise in portal venous pressure. The response to increased venous pressure is the development of a collateral circulation diverting the obstructed blood flow to the systemic veins. These porto systemic collaterals form by the opening and dilatation of pre-existing vascular channels connecting the portal venous system and the superior and inferior vena cava.

The prevalence of oesophageal varices in patients with liver cirrhosis may range from 60% to 80%, and the reported mortality from variceal bleeding ranges from 17% to 57%. Cirrhotic patients with Portal Hypertension who develop oesophageal varices are at a very high risk of variceal bleeding and Variceal rupture is a common cause of death in cirrhosis.[3,38,39]

Normal pressure in the portal vein is 5-10 mm Hg because the vascular resistance in the hepatic sinusoids is low. An elevated portal venous pressure (>10 mm Hg) distends the veins proximal to the site of the block and increases capillary pressure in organs drained by the

obstructed veins. This will lead to the development of esophagial and fundal varices. One third of the gastrointestinal bleedings reveal pre-existent cirrhosis. In patients with cirrhosis the incidence of oesophageal varices increases by nearly 5% per year, and the rate of progression from small to large varices is approximately 5 to 10 % per year. The risk of variceal rupture is greatest in the 2 years following diagnosis.

In the 2 years following the first detection of esophageal varices , risk of variceal bleeding ranges between 20% to 30% and results in a mortality of 25% to 50% within a week of the first bleeding episode. Therefore, portal hypertensive bleeding prevention remains at the forefront of the long-term management of cirrhotic patients. As there is clear evidence that primary prevention of variceal rupture is cost effective in reducing death rate, screening for oesophageal varices (EV) is recommended.

Prophylactic treatment in patients with non-selective Beta blockers in varices that has never bled appears to decrease the incidence of bleeding by 40 to 50 % and prolong survival. So endoscopic screening for varices in patients with cirrhosis is desirable, some have suggested this should be repeated every other year. [8,9,40,41]

The American Association for the Study of Liver Disease single topic Symposium [1] 1996 stated that cirrhotic patients should be screened

for the presence of esophageal varices when portal hypertension is diagnosed. Recently, the Baveno III Consensus Conference [(2)] on portal hypertension recommended that all cirrhotic patients should be screened for the presence of esophageal varices when liver cirrhosis is diagnosed. Other authors [(3)] have suggested repeating endoscopy at 2–3 year intervals in patients without varices and at 1–2 year intervals in patients with small varices and every other year in patients with decompensated liver disease so as to evaluate the development or progression of this feature.

Endoscopic screening may take place under two circumstances: at the initial diagnosis of cirrhosis, since esophageal varices are an independent predictive factor and an early complication of cirrhosis, and during the follow-up of patients with cirrhosis without esophageal varices at risk of bleeding at first examination with or without decompensation.[(34)]

It has been estimated that it is only the large esophageal varices (LEV), which are associated with a substantially increased risk of variceal bleed. The reported incidence of LEV ranges from 9% to 49% [(4)]. In a recent review, Boyer,[(5)] using a prevalence of LEV of 20%, estimated that a 100 screening endoscopic examinations need to be performed to prevent 1 to 2 cases of variceal bleeding. It is noteworthy however that

variceal hemorrhage is not confined to patients with large esophageal varices although they are more likely to bleed from ruptured varices than patients with small esophageal varices .

Cirrhotic patients frequently undergo screening endoscopy for the presence of esophageal varices (EV). In the future, this social and medical burden will increase due to the greater number of patients with chronic liver disease and their improved survival.

Therefore, the identification of the clinical features that can accurately predict LEV and help identify patients at the greatest risk of bleeding is quite attractive. This could thus make it possible to identify the population with a high probability of LEV that requires confirmation by endoscopy, since the regular use of endoscopy is limited due to cost and discomfort, resulting in poor compliance.

The usual clinical practice is to screen all patients with established cirrhosis at the time of diagnosis by upper endoscopy for the presence of varices. Patients with large varices should be treated with non-selective beta blockers to reduce the incidence of first variceal bleeding. However, fewer than 50% of cirrhotic patients have varices at screening endoscopy and most have small sized varices, with a low risk of bleeding.

In order to reduce the increasing burden that endoscopy units will have to bear, some studies have attempted to identify characteristics that

noninvasively predict the presence of any oesophageal varices or of large oesophageal varices . These studies have shown that biochemical, clinical, and ultrasonographic parameters alone or together have good predictive power for non-invasively assessing the presence of esophageal varices . Overall, the most common result of these studies was that parameters directly or indirectly linked to portal hypertension, such as splenomegaly and decreased platelet count, were predictors of the presence of esophageal varices.

In a study by Thomopoulos et al (2003) [32] seventeen variables considered relevant to the presence of esophageal varices were tested and they came to the conclusion that Thrombocytopenia, splenomegaly and ascites are independent predictors of large esophageal varices in cirrhotic patients.The authors suggest that endoscopy could be avoided safely in cirrhotic patients with none of these predictive factors, as large varices are absent in this group of patients. However, in patients with chronic liver disease the presence of decreased platelet count may depend on several factors other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses. On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension. With this in

mind, according to Gianni et al(2003)[3], their study used the platelet count/spleen diameter ratio as a parameter linking thrombocytopenia to spleen size in order to introduce a variable that takes into consideration the decrease in platelet count, which most likely depends on hypersplenism. [30,31]

Since both platelet count and splenomegaly are influenced by so many factors other than portal pressure, it is worthwhile if we could move on, in the search of better non-invasive predictors of esophagial varices that are more sensitive and less cumbersome both for the patient and the treating physician. This will help us in identifying the suitable candidates for the initiation of prophylactic beta blockade so that a catastrophic variceal bleed can be predicted and prevented. [37]

AIMS AND OBJECTIVES

1. To validate the usefulness of Doppler study of the Hepatic veins in predicting esophageal varices in cirrhotic patients.
2. To compare the sensitivity and positive predictive value of Doppler study of hepatic veins to other suggested indices like platelet count/spleen size in non-invasively predicting the possibility of esophageal varices.
3. To assess the correlation between hepatic venous wave forms and Child Pugh score in the grading of severity of Cirrhosis.

REVIEW OF LITERATURE

Cirrhosis is a pathologically defined entity that is associated with a spectrum of clinical manifestations.[6]

Definition

A chronic disease of the liver characterized by the replacement of normal tissue with fibrous tissue and the loss of functional liver cells.

It is characterized by three cardinal features.

1. Loss of normal hepatic architecture.
2. Fibrosis.
3. Regenerative nodules.

Evolution of cirrhosis[7]

The cardinal pathological features reflect irreversible chronic injury of the hepatic parenchyma and include extensive fibrosis in association with formation of regenerative nodules. These features result from hepatocyte necrosis, collapse of supporting reticulin network with subsequent connective tissue deposition, distortion of vascular bed, and nodular regeneration of remaining liver parenchyma. The pathologic process should be viewed as a final common pathway of many types of chronic liver injury. Clinical features of cirrhosis derive from the morphological alterations and often reflect the severity of hepatic damage rather than the aetiology of the underlying liver disease. Loss of

functioning hepatocellular mass may lead to jaundice, oedema, coagulopathy, and a variety of metabolic abnormalities; fibrosis and distorted vasculature lead to portal hypertension and its sequel, including gastro oesophageal varices and splenomegaly. Ascites and hepatic encephalopathy result from both hepatocellular insufficiency and portal hypertension.

Classification of cirrhosis. [8]

The pathological patterns of cirrhosis represents a spectrum. At one end is the Micronodular cirrhosis and at the other end is the macronodular cirrhosis. Between these two extreme types are so many cases that show features of both.

1.Micronodular cirrhosis.

Nodules < 3mm in diameter. The nodules show no landmarks of lobular architecture, in the form of bile ducts or central veins.

Alcoholic cirrhosis is the prototype of micronodlar cirrhosis.

2. Macronodular cirrhosis.

Nodules are >3mm in diameter and the intervening septa in between the necrotic nodules do retain landmarks of hepatic architecture.

Cirrhosis secondary to Chronic viral hepatitis is the prototype of Macronodular cirrhosis. It is also seen in malnutrition, old age and anemia.

3. Mixed pattern

Micronodular pattern can be converted into macronodular pattern by continued regeneration and expansion of the nodules, especially seen when the patient abstains from alcohol for a long time.

Aetiology

1. Alcohol.
2. Viral hepatitis types B ± delta; C.
3. Metabolic, e.g. hemochromatosis, Wilson's disease, α1 antitrypsin deficiency, type IV glycogenosis, galactosaemia, congenital tyrosinosis and non-alcoholic steatohepatitis.
4. Prolonged cholestasis, intra-and extra-hepatic.
5. Hepatic venous outflow obstruction, e.g. venoocclusive disease, Budd-Chiari syndrome, constrictive pericarditis.
6. Disturbed immunity (autoimmune hepatitis).
7. Toxins and therapeutic agents, e.g. methotrexate, amiodarone.
8. Indian childhood cirrhosis.
9. Cryptogenic cirrhosis.

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Diagnosis of cirrhosis[6,7,8]

A) Clinical history

Fatigue and weight loss, loss of libido, anorexia and flatulent dyspepsia, abdominal pain, Jaundice, swelling of legs or abdomen, hemorrhage - nose, gums, skin, alimentary tract.

Past history: jaundice, hepatitis, drugs ingested, blood transfusion. Social: alcohol consumption.

B) Examination:

Nutrition, fever, fetor hepaticus, jaundice, pigmentation, purpura, finger clubbing, white nails, vascular spiders, palmar erythema, gynaecomastia, testicular atrophy, distribution of body hair.

Abdomen: ascites, abdominal wall veins, liver, spleen, oedema Neurological changes: mental functions, stupor, and tremor

C) Investigations :

Haematology

- Hemoglobin
- Leukocyte count
- Platelet count
- Prothrombin time

Serum biochemistry

- Bilirubin
- Transaminases Immunoglobulins
- Alkaline phosphatase
- γ - Glutamyl transpeptidase
- Albumin and globulin

If ascites present

- Serum electrolytes.
- Daily weight.
- Urea and creatinine.
- 24 hours urinary volume and sodium.
- SAAG

Serum immunological investigations

- Hepatitis B Ag, Anti HCV.
- Alpha-fetoprotein.
- Smooth muscle, mitochondrial, nuclear antibodies.

Hepatic CT scan or ultrasound :

Using ultrasound, cirrhosis is suggested by line surface nodularity and portal vein mean flow velocity. The caudate lobe is enlarged relative to the right lobe. Regeneration nodules may be shown as focal lesions.

CT scan is cost-effective for the diagnosis of cirrhosis and its complications. Liver size can be assessed and the irregular nodular surface seen. After intravenous contrast, the portal vein and hepatic veins can be identified in the liver, and a collateral circulation with splenomegaly may give confirmation to the diagnosis of portal hypertension. Ascites can be seen.

Liver biopsy :

Biopsy diagnosis of cirrhosis may be difficult. Reticulin and collagen stains are essential for the demonstration of a rim of fibrosis around the nodule.

EEG : EEG is indicated if neuropsychiatric changes are present and to detect early changes in pre-coma.

Compensated cirrhosis [7,8]

The disease may be discovered at a routine examination or biochemical screen, or at operation undertaken for some other condition. Cirrhosis may be suspected if the patient has mild pyrexia, vascular spiders, palmar erythema, or unexplained epistaxis or oedema of the

ankles. Firm enlargement of the liver and splenomegaly are helpful diagnostic signs.

Vague morning indigestion and flatulent dyspepsia may be early features in the alcoholic cirrhotic. Confirmation should be sought by biochemical tests, scanning and if necessary, by liver biopsy. Biochemical tests may be quite normal in this group. The most frequent changes are a slight increase in the serum transaminase or γ-GT level. Diagnosis is confirmed by needle liver biopsy.

Decompensated cirrhosis

The patient usually seeks medical advice because of ascites and or jaundice. General health fails with weakness, muscle wasting and weight loss.

Continuous mild fever (37.5-38°C) is often due to gram-negative bacteraemia, to continuing hepatic cell necrosis or to liver cell carcinoma. A liver flap may be present. The deeper the jaundice, the greater the liver cell dysfunction.

Pigmentation of the skin and clubbing of the fingers are occasionally seen. Purpura over the arms, shoulders and shins may be associated with a low platelet count. Spontaneous bruising and epistaxis reflect a prothrombin deficiency. The blood pressure is low. Sparse body hair, vascular spiders, palmar erythema, white nails and gonadal atrophy

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

Child Pugh classification. [7,8,9]

	A	B	C
S. Bilirubin	<2.0	2-3	>3
S. Albumin	>3.5	2.8-3.5	<2.8
Ascites	None	Slight or Controlled	Moderate or Uncontrolled
Encephalopathy	None	Minimal	Coma
ProthrombinTime (sec) Or INR	0-4 <1.7	4-6 1.7-2.3	>6 >2.3

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

Patients with compensated cirrhosis become decompensated at the rate of 10% per year. Ascites is the usual first sign. Decompensated patients have around a 20% 5-year survival.

According to Madhotra et al (2002) [10] and Zaman et al (2001) [11] the prevalence of esophageal varices in cirrhosis increases with severity of liver disease, as assessed by Child Pugh Classification.

The following points are useful prognostically:

- Liver Size. A large liver carries a better prognosis than a small one because it is likely to contain more functioning cells.
- Hemorrhage from oesophageal varices. If liver function is good, hemorrhage may be tolerated; if poor, hepatic coma and death are probable.
- Persistent hypotension (systolic BP<100 mmHg) is ominous.
- Ascites worsens the prognosis.
- If decompensation has followed hemorrhage, infection or alcoholism, the prognosis is better than if it is spontaneous, because the precipitating factor is correctable.
- Jaundice, especially if persistent, is a sign of terminal liver disease.
- Neurological complication. The significance of encephalopathy depends on the clinical circumstances. Developing in the course of progressive hepato-cellular failure, it carries a bad prognosis.
- Biochemical tests. If the serum albumin is less than 2.5g/dL the outlook is poor.

Hyponatraemia (serum sodium<120mmol/L), if unrelated to diuretic therapy, is grave.

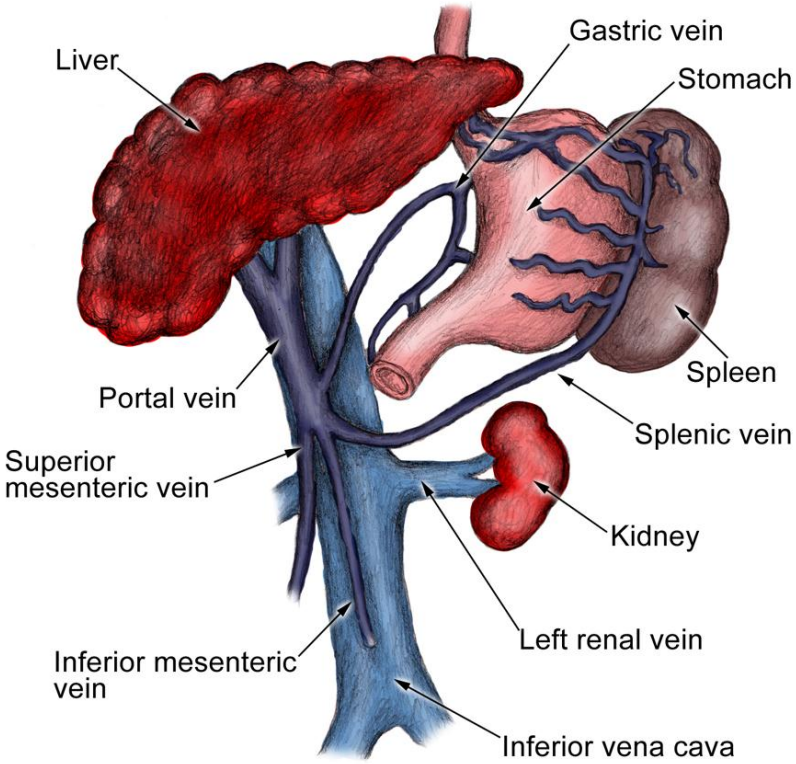
Serum transaminase and globulin levels gives no guide to prognosis.

- Alcoholic cirrhotics, if they abstain, respond better than those with 'cryptogenic' cirrhosis.
- The response to therapy. If the patient has failed to improve within 1 month of starting hospital treatment, the outlook is poor.
- Hepatic histological changes. Sections are useful in evaluating the extent of necrosis and of inflammatory infiltration. A fatty liver responds well to treatment.

PORTAL HYPERTENSION

ANATOMY OF THE PORTAL CIRCULATION.

Portal vein is formed by union of superior mesenteric vein and splenic vein just posterior to the head of pancreas and it enters the liver at the porta hepatis and it divides into two main branches, one to each lobe. Portal blood flow in man is 1000- 1200mL/min. Portal pressure is about 5-10 mm Hg. However, once the portal pressure rises to 12 mm Hg or greater, complications can arise, such as varices and ascites.



PATHOPHYSIOLOGY.

The initial factor in the pathophysiology of portal hypertension is the increase in vascular resistance to the portal blood flow. Poiseuille law, which can be applied to portal vascular resistance, states that R = 8hL/pr4, where h is the viscosity of blood, L is the length of the blood vessel, and r is the radius of the blood vessel. Because portal vascular resistance is indirectly proportional to the fourth power of the vessel radius, small decreases in the vessel radius cause large increases in portal vascular resistance and, therefore, in portal blood pressure.

Liver disease is responsible for a decrease in portal vascular radius, producing a dramatic increase in portal vascular resistance. In cirrhosis, the increase occurs at the hepatic microcirculation (sinusoidal portal hypertension). Increased hepatic vascular resistance in cirrhosis is not only a mechanical consequence of the hepatic architectural disorder, but a dynamic component also exists due to the active contraction of myofibroblasts, activated stellate cells, and vascular smooth-muscle cells of the intrahepatic veins.

The second factor that contributes to the pathogenesis of portal hypertension is the increase in blood flow in the portal veins, which is established through splanchnic arteriolar vasodilatation caused by an excessive release of endogenous vasodilators (eg, endothelial, neural, humoral). The increase in portal blood flow aggravates the increase in portal pressure and contributes to why portal hypertension exists despite the formation of an extensive network of portosystemic collaterals that may divert as much as 80% of portal blood flow. [(11)]

Formation of varices :

The hypertensive portal vein is decompressed by diverting up to 90% of the portal flow through portasystemic collaterals back to the heart resulting in enlargement of these vessels. These vessels are commonly located at the gastroesophageal junction where they lie subjacent to the

mucosa and present as gastric and esophageal varices. Varices form when the HVPG exceeds 10 mm Hg and usually do not bleed unless the hepatic venous pressure gradient (HVPG) exceeds 12 mm Hg. [12]

Mechanism of variceal haemorrhage:

Increased portal pressure contributes to increased varix size and decreased varix wall thickness, thus leading to increased variceal wall tension. Rupture occurs when the wall tension exceeds the elastic limits of the variceal wall. Varices are most superficial at the gastroesophageal junction and have the thinnest wall in that region. Variceal hemorrhage invariably occurs in this region. [12]

Variceal haemorrhage is the most common complication associated with portal hypertension. Almost 90% of patients with cirrhosis develop varices, and approximately 30% of varices bleed. The first episode of variceal haemorrhage is estimated to carry a mortality rate of 30-50%.

CLASSIFICATION AND CAUSES OF PORTAL HYPERTENSION[68]

I) Primary increased flow

1. Arterioportal venous fistula.
2 Splenic capillary hemangiomatosis.

II) Primary increased resistance

1. Prehepatic:

1.Thrombosis / cavernous transformation of the portal vein

2.Splenic vein thrombosis.

2. Intrahepatic :

1) Presinusoidal – Schistosomiasis,

Sarcoidosis,

Myeloproliferative diseases,

Congenital hepatic fibrosis,

Idiopathic portal hypertension,

Chronic arsenic hepatotoxicity,

Vinyl chloride hepatotoxicity,

Early primary biliary cirrhosis,

Early primary sclerosing cholangitis.

2) Sinusoidal / mixed – cirrhosis,

Methotrexate,

Alcoholic hepatitis,

Hypervitaminosis A,

Incomplete septal fibrosis,

Nodular regenerative hyperplasia.

3) Post sinusoidal – Veno-occlusive disease,

Hepatic vein thrombosis(Budd-Chiari syndrome).

3) Post hepatic – Inferior venacaval web,

Constrictive pericarditis,

Tricuspid insufficiency,

severe right heart failure.

CLINICAL FEATURES OF PORTAL HYPERTENSION

History:

The medical history from a patient with portal hypertension should be directed towards determining the cause of portal hypertension and, secondarily, the presence of the complications of portal hypertension. Determining the cause of portal hypertension involves the following:

* History of jaundice
* History of blood transfusions, IV drug use (hepatitis B and C)
* Pruritus
* Family history of hereditary liver disease (hemochromatosis, Wilson disease)
* History of alcohol abuse.

Determining the presence of the complications of portal hypertension involves the following:

- Hematemesis or melena (gastroesophageal variceal bleeding or bleeding from portal gastropathy)
- Mental status changes such as lethargy, increased irritability, and altered sleep patterns (presence of portosystemic encephalopathy)
- Increasing abdominal girth (ascites formation)
- Abdominal pain and fever (spontaneous bacterial peritonitis [SBP], which also presents without symptoms)
- Haematochezia (bleeding from portal colopathy)

Physical :

Signs of Porto systemic collateral formation include the following:

- Dilated veins in the anterior abdominal wall (umbilical epigastric vein shunts)
- Venous pattern on the flanks (portal-parietal peritoneal shunting)
- Caput medusa (tortuous collaterals around the umbilicus)
- Rectal haemorrhoids
- Ascites - Shifting dullness and fluid wave (if significant amount of ascitic fluid is present
- Para umbilical hernia

Signs of liver disease include the following:

- Ascites
- Jaundice
- Spider angiomas
- Gynecomastia
- Dupuytren contracture
- Muscle wasting
- Palmar erythema
- Asterixis
- Testicular atrophy
- Splenomegaly

Signs of hyperdynamic circulatory state include the following:

- Bounding pulses
- Warm, well-perfused extremities
- Arterial hypotension.

INVESTIGATIONS

Endoscopy[7,8]

The size of varix must be graded

• Grade 1 (Fl): the varices can be depressed by the endoscope

• Grade 2 (F2): the varices cannot be depressed by the endoscope

• Grade 3 (F3) the varices are confluent around the circumference of the oesophagus.

CONN'S GRADING

• Grade I - small varices detectable on valsalva only

• Grade II -1-3 mm varix- in both phases of respiration

• Grade III - 3-6 mm varices, not occluding the lumen

• Grade IV - >6mm varices, occluding the lumen

Larger the varix, the chances of bleeding is more. **Varices** usually appear white and opaque. Dilated sub epithelial veins may appear as raised **cherry red spots** and **red whale markings**. The **haemocystic spot** is approximately 4mm in diameter. It represents blood coming from deeper extrinsic veins of oesophagus straight out towards the lumen through a communicating vein into the more superficial submucosal veins. **Red colour sign** is usually associated with larger varices. All these colour changes and particularly the red colour sign predict variceal bleeding. **Portal hypertensive gastropathy** is seen largely in the fundus. It is seen as a mosaic like pattern. Variceal (azygos) blood flow can be assessed during diagnostic endoscopy by a Doppler US probe passed down the biopsy channel of the standard gastroscopy.

Imaging the portal venous system

Ultrasound:

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

Doppler ultrasound[13]

Hepatofugal Flow in the Portal Venous System: Pathophysiology, Imaging Findings, and Diagnostic Pitfalls

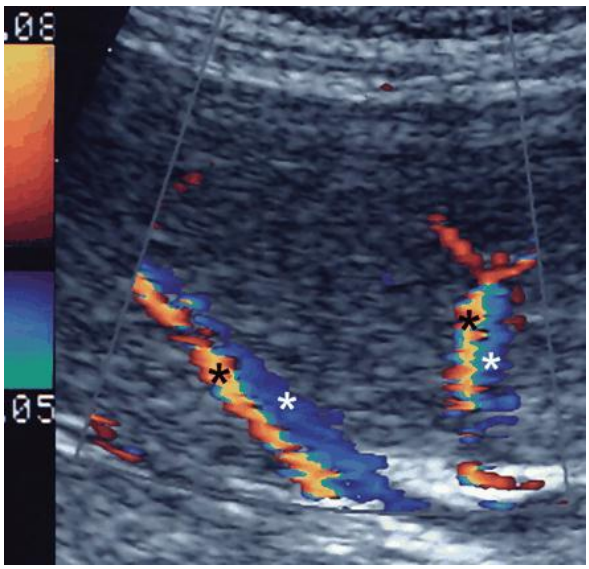
Doppler ultrasound helps in assessing the direction of flow in the main portal vein and its main tributaries and branches, and also in assessing the characteristic flow patterns described in relation to the cardiac cycle.

Normal portal venous flow is Hetatopetal (towards the liver).when the portal vascular resistance begins to increase, the flow may become reversed (Hepatofugal or away from the liver) or a mixed pattern dependent on the phases of the cardiac cycle.

At Doppler US, hepatofugal flow appears as flow directed away from the liver in the portal vein, its intrahepatic branches, or its extra hepatic tributaries. If hepatofugal flow is present in the main portal vein or an intrahepatic branch, flow is noted in the direction opposite to flow in the adjacent hepatic artery. Depending on the anatomic orientation of the involved vessel relative to the transducer, a Doppler shift above or

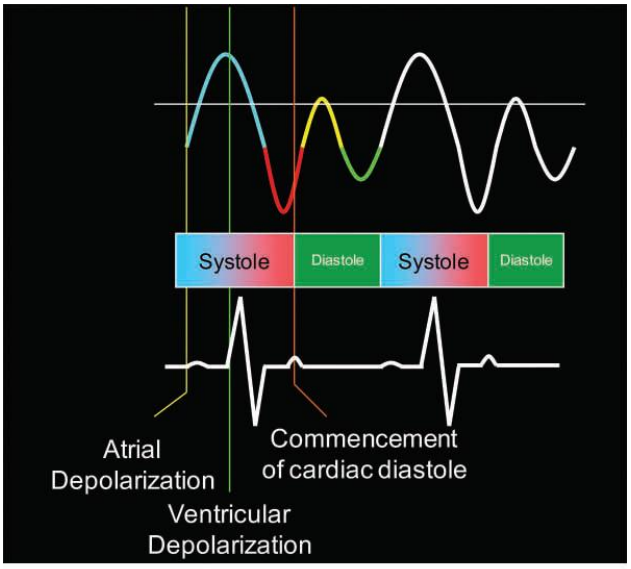
below the baseline can be produced by hepatofugal flow. A narrow portal vein and a prominent hepatic artery are common associated gray-scale US findings when flow is hepatofugal in the main portal vein. To-and-fro (bidirectional) blood flow, in which flow alternates between hepatopetal and hepatofugal during each cardiac cycle, has been observed to precede the development of frank hepatofugal flow in some patients with cirrhosis and is the correlate of stagnant flow in the portal vein noted at arteriography.

With few exceptions, hepatofugal flow in the main portal vein or an extrahepatic portal vein tributary is a specific sign of portal hypertension. One exception is hepatofugal flow in a liver transplant recipient with a large, persistent portosystemic collateral vessel that can divert a substantial amount of splanchnic venous blood; this diversion can interfere with graft function and portal vein patency but does not indicate recurrent portal hypertension. Another rare exception is hepatofugal flow caused by a congenital portosystemic collateral vessel. Hepatofugal flow in one or more solely intrahepatic portal veins can occur in patients with a focal arterio portal shunt and is therefore not specific for portal hypertension.



Opposite flow directions in the portal vein and adjacent hepatic artery in a patient with cirrhosis and portal hypertension. Transverse colour Doppler US image shows intrahepatic portal vein branches (white*) containing blue signal adjacent to hepatic artery branches (black*) containing red signal. Because blood flow is normally hepatopetal in both the portal vein and the hepatic artery, opposite colour signals in adjacent branches of these two circulations indicate hepatofugal portal vein flow.

Spectral Doppler waveform of the Hepatic Veins



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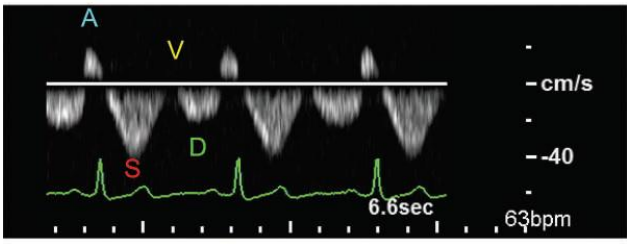


b.

The normal hepatic vein waveform, despite commonly being described as triphasic, has four components: a retrograde A wave, an antegrade S wave, a transitional V wave (which may be ante grade, retrograde, or neutral), and an antegrade D wave.

The A wave corresponds to atrial contraction. With the tricuspid valve open, blood is propelled in two directions: ante grade toward the right ventricle and retrograde toward the IVC and into the hepatic veins. At the end of atrial systole, peak retrograde velocity away from the heart

is achieved. As ventricular systole commences, the tricuspid valve closes and the retrograde velocity toward the hepatic veins begins to decrease and approach the baseline.

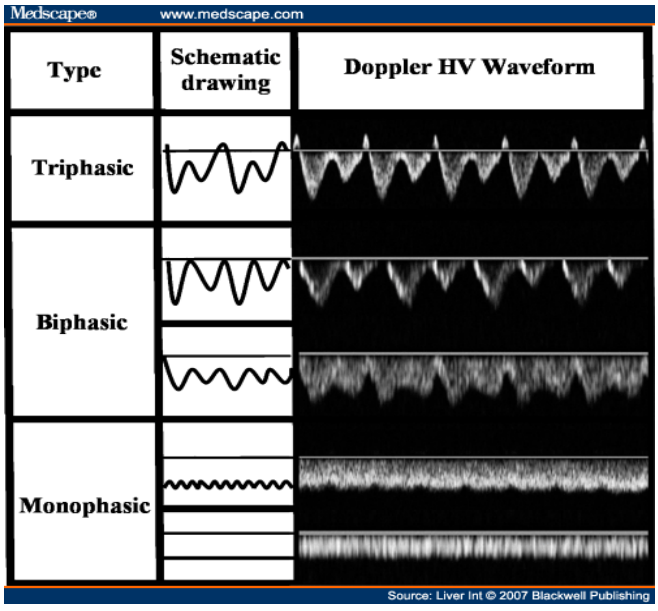
During ventricular systole, not only do the ventricular walls contract to propel blood into the right ventricular outflow tract, but there is also movement of the tricuspid valve annulus toward the cardiac apex. These actions create a relative negative pressure in the atrium, causing antegrade blood flow out of the liver and into the heart during the S wave. In the normal heart, the largest amount of antegrade blood flow is during this phase.

The V wave corresponds to atrial overfilling. As the ventricular contraction becomes less intense and the closed tricuspid valve begins to return to its original position, the atrium fills and blood flow velocity toward the heart decreases. The peak of the V wave may be below, at, or above the baseline, depending on whether there is ante grade flow throughout, transient equilibrium with no flow, or transient retrograde flow, respectively. The term triphasic does not include the V wave, perhaps because this wave represents only a transitional phase.

The D wave begins as the tricuspid valve opens. During cardiac diastole, the right atrium and ventricle fill passively, with ante grade flow of blood from the liver into the heart. In the normal patient, the velocity

of this passive flow is almost always lower in magnitude than the velocity during the S wave.

A normal variant, termed the C wave, can cause a small retrograde spike following the A wave. As atrial systole ends and ventricular systole commences, the tricuspid valve closes. The tricuspid annulus begins to move toward the cardiac apex and the retrograde velocity of flow toward the liver begins to decrease. However, before the pulmonic valve opens, the pressure in the ventricle increases with continuing contraction of the ventricle, causing a transient bulging of the tricuspid valve into the right atrium. This bulging creates a momentary retrograde pulse toward the liver, causing the C wave. When the pulmonic valve opens and blood is ejected from the right ventricle into the pulmonary outflow tract, the bulge in the tricuspid valve is relieved. Flow into the heart then resumes as usual during the S wave.



When a patient develops cirrhosis and portal hypertension as its sequel, the hepatic veins progressively fail to reflect the pressure changes in the right atrium. This will lead to the loss of normal triphasic pattern of the hepatic venous flow; which will become biphasic and later monophasic flow.

Duplex Doppler has-been used to measure portal blood flow. In cirrhosis, the portal vein velocity tends to fall and when less than 6cm/s portal hypertension is likely.

C.T scan

After contrast, portal vein patency can be established and esophageal varices may be shown as intraluminal protrusions enhancing after contrast. Gastric varices show as rounded structures, indistinguishable from the gastric wall.

In cirrhosis, the venogram varies widely. It may be completely normal or may show filling of large numbers of collateral vessels with gross distortion of the intra-hepatic pattern ('tree in winter appearance).

BLEEDING OESOPHAGEAL VARICES[15,16,17,18,19,20]

Variceal bleeding is the most serious complication of portal hypertension. Gastroesophageal varices are present in 50−60% of cirrhotic patients and about 30% of these patients will experience an episode of variceal hemorrhage within one year of the diagnosis of

varices. After the initial bleed, the risk of variceal rebleeding reported in the literature ranges from 50- 80%. About one half of all rebleeds occur within the first six weeks . Risk of rebleeding is very high in survivors of an episode of haemorrhage; in approximately 70% of patients, this will occur in the first few days following the first hemorrhage.

Predicting rupture[21]

The presence of the following factors are more often associated with bleeding risk.

1. Size of the varices - large varices were found to have bled significantly more often than small varices.
2. Colour of varices – The bleeding rate of blue coloured varices was 63%, which was significantly more than white varices.
3. Red colour sign - The three endoscopic signs studied,

   cherry red spots,

   red wale markings and

   haematocystic spots

are more often present in bleeders than in non-bleeders.

4. Location of varices - Rate of bleeding for varices extending up to locus superior was more than the varices belonging to locus medialis and locus inferior.

5. Form of varices - enlarged and tortuous varices bled more often than the straight varices.

6. Intravariceal pressure - patients with higher pressures bled more often.

Prevention of bleeding

Liver function must be improved, for instance, by abstaining from alcohol. Aspirin and NSAIDs should be avoided. Propranolol is a non-selective β-blocker, which reduces portal pressure by splanchnic vasoconstriction and, to a lesser extent, by reducing cardiac output. The drug is given in a dose, which reduces the resting pulse rate by 25% 12h after intake.

The portal pressure must be maintained at 12mm Hg or lower. Propranolol is recommended for those with large varices and with red endoscopic danger signs. Patients with an HVPG greater than 12mmHg should be treated whatever the size of the varices. Nadolol gives equivalent results. Isosorbide-5 mononitrate is equally effective in prophylaxis of the first bleed, but the probability of death is significantly greater, particularly in those more than 50 years old. The addition of nitrate to β-blocker should be reserved for those failing therapy with the β-blocker alone. Variceal sclerotherapy or ligation is not so satisfactory or cost effective as vaso-active active drugs.

Prognosis

Between 30 and 50% will die within 6 weeks of the first bleed. The prognosis is determined by the severity of the hepato-cellular disease. The ominous triad of jaundice, ascites and encephalopathy is associated with 80% mortality. The 1-year survival in good-risk (Child grade A and B) patients is about 85% and in bad - risk (Child grade C) patients about 30%. Alcoholics have a worse prognosis, as hepatocellular disease is greater. Abstinence from alcohol considerably improves the prognosis. A low portal blood velocity by Doppler predicts shorter survival.

PLATELET COUNT/SPLENIC DIAMETER RATIO

Gianni et al(2003)[3] proposed platelet count/ splenic diameter ratio as a non-invasive marker for predicting esophageal varices in patients with liver cirrhosis. Parameters directly or indirectly linked to portal hypertension, such as splenomegaly and decreased platelet count, were predictors of the presence of esophageal varices. However, in patients with chronic liver disease the presence of decreased platelet count may depend on several factors other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses. On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension. With

this in mind, the study used the platelet count/spleen diameter ratio as a parameter linking thrombocytopenia to spleen size in order to introduce a variable that takes into consideration the decrease in platelet count which most likely depends on hypersplenism caused by portal hypertension.

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

count/spleen diameter ratio. Gianni et al (2003) [3] report that the use of this ratio is of interest and is not redundant, and this hypothesis is supported by a number of both clinical and statistical reasons. Firstly, from a clinical point of view, platelet count may decrease for several reasons in patients with chronic liver disease.

Thus the use of platelet count alone as a non-invasive predictor of esophageal varices can be misleading and cannot be solely attributed to portal hypertension. Indeed, the use of the platelet count/spleen diameter ratio bypasses this possible drawback since it "normalizes" platelet count to splenic sequestration, most likely representing the aliquot of thrombocytopenia caused by portal hypertension. Secondly, from a statistical point of view, the platelet count/spleen diameter ratio was the only parameter independently associated with the presence of esophageal varices that was selected by a multi variate analysis which also included the single parameters.

The study showed that the use of the platelet count/spleen diameter ratio would have avoided performing unnecessary endoscopies in all patients with a cut off >909 without running the risk of not diagnosing esophageal varices. As far as cost benefit analysis is concerned, applying the "platelet count/spleen diameter ratio strategy" would lower the cost of oesophageal varices screening in patients with cirrhosis.

MATERIALS AND METHODS

Type of Study : Cross sectional study.

Sample : Gastroenterology, Department and Medicine Out Patient Department and In patient wards of Madurai Medical College,

Duration of study : May 2011 – November 2011

INCLUSION CRITERIA

All newly diagnosed cases of cirrhosis liver, based on physical examination, biochemical parameters, ultrasound abdomen and upper GI endoscopy.

EXCLUSION CRITERIA

- Present or previous history of portal hypertensive bleeding
- Patients with hepatocellular carcinoma
- Portal vein thrombosis
- Previous or current treatment with β blockers, diuretics or other vasoactive drugs.
- Budd Chiari Syndrome
- Patients with coexisting heart disease

METHODOLOGY

Detailed history was taken from the patients and a complete physical examination of patients was carried out. In particular attention was paid to look for signs of liver cell failure like the spider, palmar

erythema, and parotid enlargement, palmar erythema,Duptyrene contractions. History regarding cause of admission was taken. history regarding upper GI bleeding (haematemesis, melena),fever,painful ascites, jaundice was taken. history regarding encephalopathy and possible precipitating factors were taken. Duration of diagnosis and duration of treatment was noted. History regarding alcohol consumption and History regarding Hepatitis B and Hepatitis C were taken.

A careful examination of abdomen for ascites, hepato spleenomegaly, CNS examination to detect Hepatic encephalopathy including testing for constructional apraxia.24 hour urine output was noted in all patients to exclude patients with oliguria.

The following investigations were carried out:

1. Complete haemogram.
2. Urinalysis including morning spot PCR
3. LFT
4. Complete Hemogram

Hemoglobin (g/dL)	MCV (fL)
Count (cells/cmm)	MCHC (g/dL)
Differential Count	PCV
RBC (millions/cmm)	Clotting Time
Platelets (lakhs/cmm)	Bleeding Time

5. Liver Function Tests

Serum Bilirubin	Aspartate
Amino Transferase	Serum Albumin
Alanine Amino Transferase	
Prothrombin Time	Alkaline Phosphatase

6. Child Pugh Score - Graded into Class A B or C

7. Ascitic Fluid Analysis

Colour	Protein
Cell Count	Differential count
Sugar	SAAG

8. Ultrasound Abdomen with Doppler.

Liver Surface Nodularity Portal Vein Size

Architecture of the liver

Hepatic venous wave forms

Splenic vein size, Size of the liver, Spleen bipolar diameter

Presence of ascites, Collateral circulation

9. Upper Gastrointestinal Endoscopy

Presence of oesophageal and gastric varices and grading according to Conns grading for esophageal varices .

Portal Hypertensive Gastropathy

Erosions, Red Signs

PROCEDURE

Forty nine patients with cirrhosis liver, attending the medical and gastroenterology wards and outpatient departments of Madurai Medical College, Chennai, between the months of May 2011 to November 2011 were selected, based on inclusion and exclusion criteria.

All patients in the study underwent a full clinical evaluation .Clinical history and physical examination findings were recorded with particular attention to present or previous hematemesis, malena, bleeding per rectum, bleeding tendencies, alcoholism, blood transfusion, intake of hepatotoxic drugs, exposure to Sexually transmitted diseases, IV drug abuse, jaundice, anemia, edema, stigmata of chronic liver disease, dilated abdominal veins, ascites, splenomegaly and encephalopathy.

All patients underwent biochemical tests, like liver function tests, complete blood counts, renal function tests, prothrombin time, ultrasonography of the abdomen to confirm the presence of cirrhosis and to record the spleen bipolar diameter, portal vein size, ascites and presence of collaterals and ascitic fluid analysis in patients with ascites. Upper GI endoscopy was done in all patients to confirm the presence of varices and also to grade them. Data were collected in a predetermined proforma and results were analysed using Epi Info software.

Continuous variables were analyzed using t-test and categorical variables by Chi square test. Pearson Correlation was used to find correlation between two variables.

RESULTS

Table 1

Variables under study.

VARIABLE	VALUE
Age (in years)	43.8 $\pm$ 10
Sex	Male : 34(68%) Female : 15(32%)
Ascites	Nil – 21(44%); Mild- 8(16%); Moderate- 14(28%); Severe- 6(12%)
UGI bleed	Yes – 24(48%); No – 25(51%)
Varices Grade	0 - 4(8%); 1 – 11(22%); 2 – 18 (36%); 3 – 16 (34%)
Child Score	A – 7 (14%); B – 30(60%); C – 12 (26%)
Hepatic flow	Mono – 34 (70%); Biphasic – 8(12%); Triphasic – 7(14%)

The mean age = 43.84 years

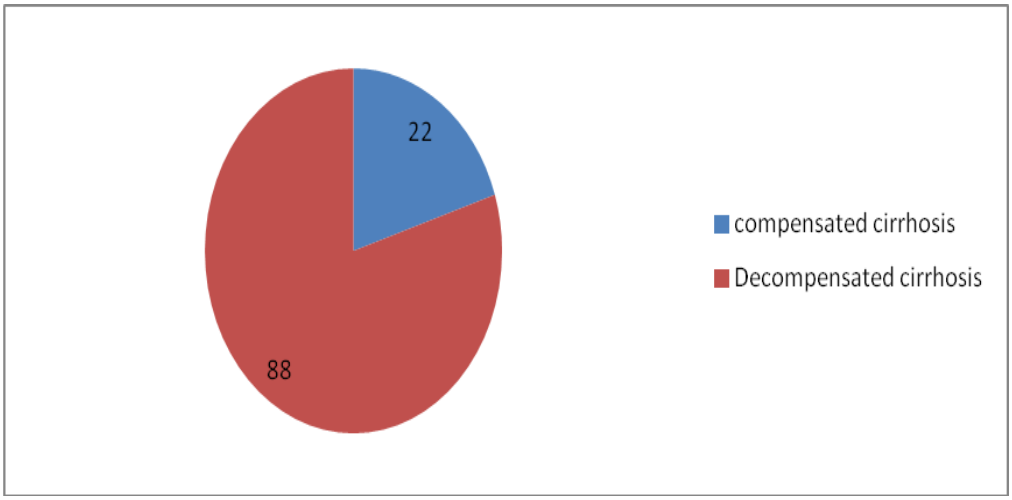
Standard deviation = 9.926

Range = 27 yrs to 60 yrs.

Males constituting = 68%.

Male female ratio = 2.125 : 1

GRAPH 1 : COMPENSATED AND DECOMPENSATED CIRRHOSIS.



GRAPH 2 : ASCITIS

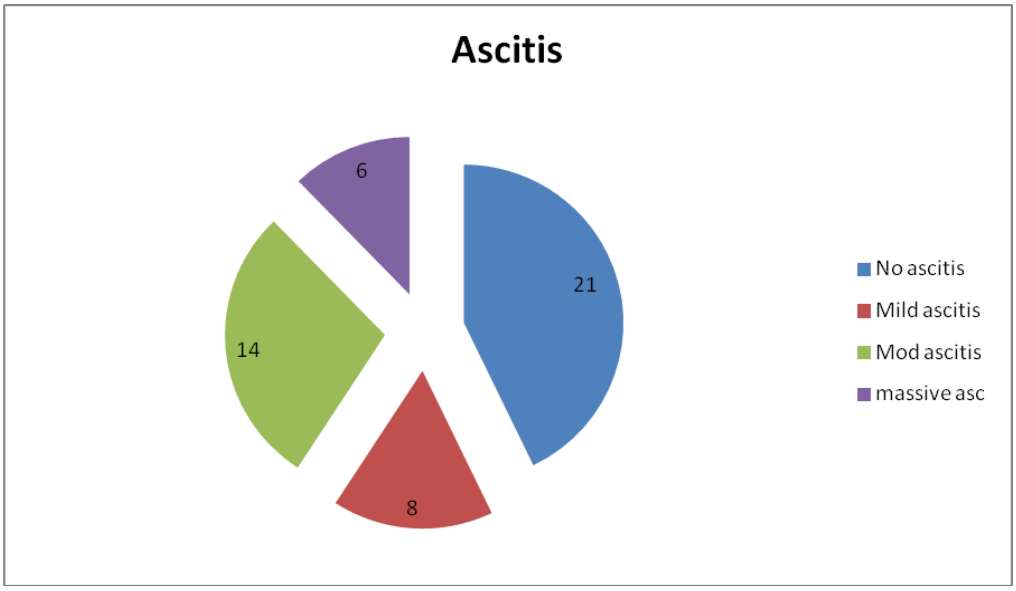


TABLE 2 : Child –Pugh score

	Number of patients	**Percentage**
A	**7**	14 %
B	30	60 %
C	12	26 %

Majority of the patients (60%) belonged to Child class B whereas 14% and 26% of patients belonged to child class A and C respectively.

The most common identifiable cause of cirrhosis was Alcoholism. Hepatitis B and C patients were excluded from the study.

The mean duration after diagnosis was 2.26 years for the sample.

Eleven (22%) out of the total 50 patients were having compensated cirrhosis while the rest 88% were decompensated.

Table - 3

Hepatic venous wave forms

	Number	Percent
Monophasic	34	70%
Biphasic	8	16%
Triphasic	7	14%

Eighty eight per cent of the patients in our study were having decompensated cirrhosis.

Thirty four (68%) of the patients showed a monophasic pattern of hepatic venous flow as against Eight patients (16%) with Biphasic flow pattern and Seven patients (14%) with monophasic flow pattern.

On breaking up further, thirty (88.2%) of the thirty four patients with monophasic flow were decompensated, as against eight (100%) with Biphasic flow and none (0%) with the normal triphasic flow pattern.

GRAPH – 3 HEPATIC FLOW AND DE COMPENSATION

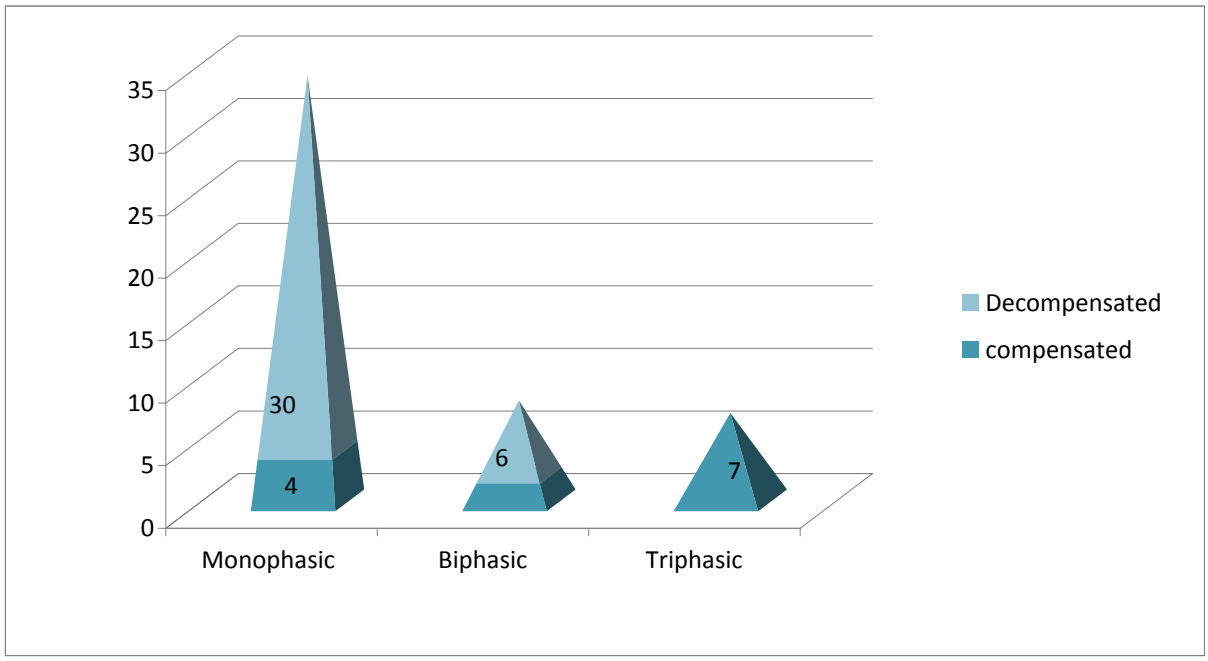


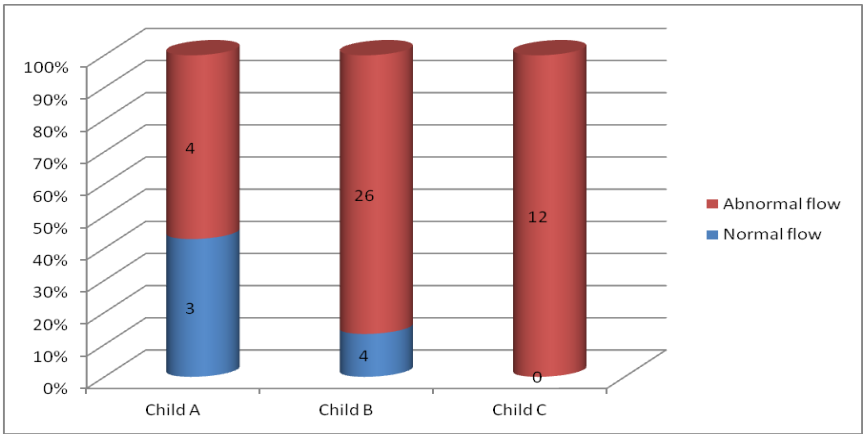
Table 4

HEPATIC FLOW AND CHILD SCORE /

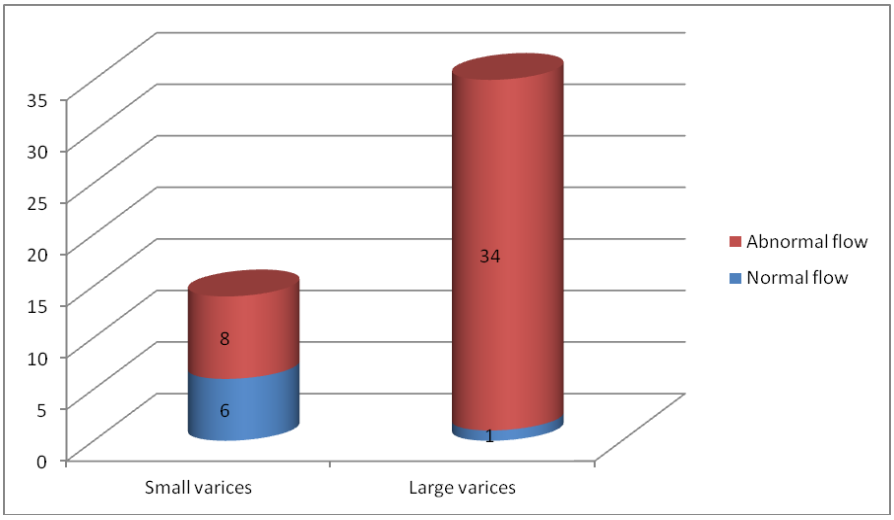
VARICES GRADE / BLEED

HEPATIC FLOW	CHILD SCORE						VARICES GRADE				UGI BLEED			
	A		B		C		SMALL (1)		LARGE (2 &3)		YES		NO	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Mono (34)	4	11.8	20	58.8	10	29.4	3	8.8	31	91.2	18	52.9	16	47.1
Biphasic(8)	-	-	6	75	2	25	5	62.5	3	37.5	5	62.5	3	37.5
Abnormal total(42)	**4**	**9.5**	**26**	**61.9**	**12**	**28.6**	**8**	**19**	**34**	**81**	**23**	**54.8**	**19**	**45.2**
Tri phasic(7) {Normal}	**3**	**42.9**	**4**	**57.5**	**-**	**-**	**6**	**14%**	**1**	**86%**	**1**	**14%**	**6**	**86%**
'p' for A & C B& C	**0.0362 Significant** 0.2448 Not significant						**0.0004 Significant**				**0.055 Not Significant**			

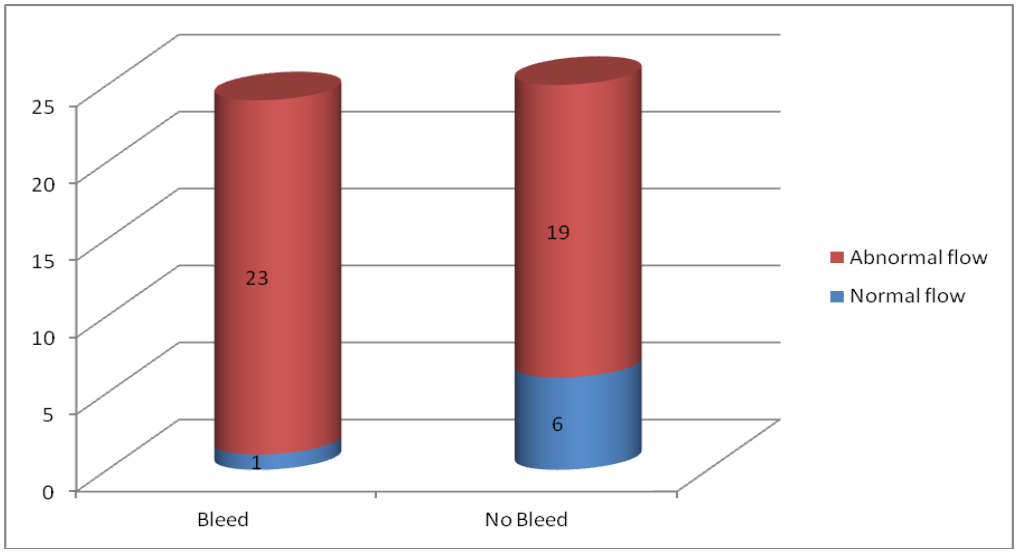
GRAPH 4 : HEPATIC FLOW AND CHILD SCORE



GRAPH 5 : HEPATIC FLOW AND VARICIAL GRADE



GRAPH 6 : HEPATIC FLOW AND UGI BLEED



Relationship between hepatic flow and Child Pugh score:

Out of the forty two patients with abnormal flow (biphasic and monophasic), four (9.5%) belonged to Child A, twenty six (61.9%) belonged to child B and twelve (28.6%) belonged to child C class of cirrhosis. The association of A and C class of cirrhosis to abnormal hepatic flow pattern was found to be significant, with a 'p' value of 0.0362.

Relationship between hepatic flow and varicial grade.

Eighty one per cent patients with an abnormal flow pattern had either grade 2 or 3 varices and one patient with normal hepatic venous flow had large varix. The association was very much significant with a 'p' value of 0.0004

Relationship between hepatic flow and varicial grade

The association between abnormal flow pattern and the presence of UG bleed was again significant with a 'p' value of 0.0077

Sensitivity : 97%

Specificity : 43 %

Positive predictive value : 81%

Negative predictive value : 86%

Relationship between hepatic flow and UG bleed:

No statistically significant association

Fisher exact 'p' value = 0.055

Sensitivity : 96%

Specificity : 24%

Positive predictive value : 55%

Negative predictive value : 86%

Table - 5

Platelet count/ splenic diameter ratio.

	Platelet count	Splenic diameter (in mm)
Range	70,000 – 1,80,000	105 - 220
Mean	1,20,060	144.6
Median	1,20,000	145
SD	23,295.84	19.79

Table - 6

Platelet count/spleen diameter ratio to grade of varices correlation

Platelet count/spleen size	Large varices +	small varices -
< 909	39	4
≥ 909	3	3

Odds ratio 9.7500

95 % CI 1.4545 to 65.3586

z statistic 2.346

P = 0.0190

Sensitivity : 93%

Specificity : 43%

Positive predictive value : 90.7 %

Negative predictive value : 50%

GRAPH 7: PLATELET COUNT/SPLEEN DIAMETER RATIO TO GRADE OF VARICES CORRELATION

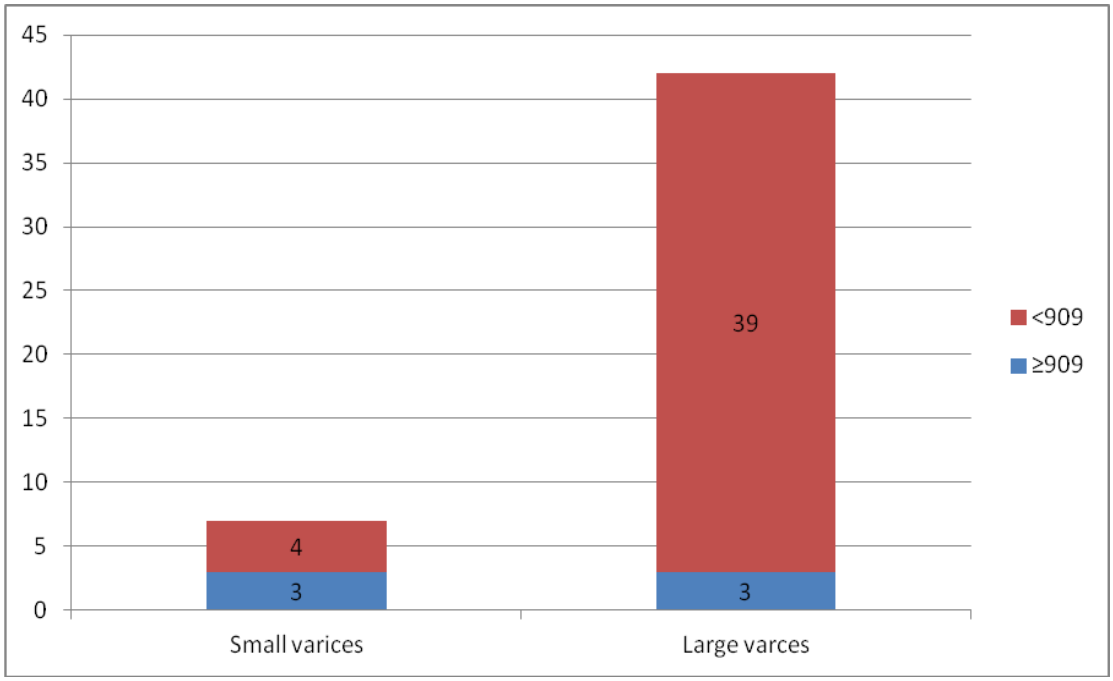


Table - 7

Hepatic waveforms Vs Platelet count/splenic diameter ratio In predicting large varices

	PC/SD ratio	Hepatic venous doppler
'p' value	0.0190	0.0001
sensitivity	93%	97%
specificity	43%	43%
Positive predictive value	90.7%	81%
Negative predictive value	50%	86%

DISCUSSION

Cirrhosis liver is an important cause of morbidity and mortality across the world. Very often, cirrhotic patients are too debilitated to undergo various invasive investigations like OGD scopy that forms an integral part of the work up and follow up of these patients.

Early reports[21,22,23,24,25] about the usefulness of non invasive predictors of esophagial varices began to appear in medical literature around the commencement of the new millennium.

Christophe Pilette et al[23] in 1999 reported a diagnostic accuracy of 72 % using 3 variables, Platelet count, Prothrombin time and spider naevi, if taken togather. They also reported that the best threshold for the diagnostic accuracy of platelet count was 160000 per dL providing a sensitivity of 80% and a specificity of 58%. Platelet count ≥260000 per dL has a negative predictive value ≥91%.

Several markers[33,35,36] have been studied, and among them platelet count is commonly reported to be a good predictor of oesophageal varices. The major drawback of platelet count is that it can depend on factors other than portal hypertension in cirrhotic patients. To avoid this bias, Giannini et al in 2003[3] developed an index based on platelet count/ spleen diameter ratio and found far better results than previous studies.

In their study, 145 patents were enrolled. 103 patients were male and 42 were female, mean age 61 years with a range of 30–86 yrs.

WW Baig et al in their study undertaken at Kasturba Medical college in Karnataka between 2004 and 2007 enrolled a total of 105 patients, of whom One hundred twenty-six men and 24 women were included in the study. The mean age was 51 years (range 20 to 80 years). A study by Jijo et al[27] at Stanley medical college, Chennai in 2009 enrolled 229 patients of whom 141 were males and the rest were females. The median age was 42 yrs with a range of 17 to 73 yrs.

A similar, but smaller study conducted at Thiruvananthapuram medical college by Thomas Joseph et al[28] included 51 patients of whom 44 were males and 7 were females.

In our study, 49 patients were enrolled of whom 34 were males and 15 were females. Mean age of patients studied here is 43.84 ±10 yrs.the male to female ratio was 2.125 : 1.

Etiological evaluation could not done in our study due to economical constrains of the Govt. institution. The majority of alcohol patients is due to the selection bias. Joshi et al have reported etiological figure in their study HBV (30%), alcohol (20%), HCV (14%). Masahiko koda et al showed HBV (33%),HCV(54.2%),alcohol (7%),primary biliary cirrhosis(4%).

Giannini in his original study in 2003, for the first time identified Platelet count/ Splenic diameter ratio as the most useful independent non invasive predictor of varices. They reported an odds ratio 0.527 and a 'p' value of <0.0001. Sixty one per cent of their patients with varices had a platelet count/spleen diameter ratio <909 and 100% of patients with a platelet count/spleen diameter ratio >909 were free from varices. In the study by WW Baig et al, [26] the sensitivity and specificity for the platelet count to spleen diameter ratio cut-off of 909 were 80% and 89%, respectively and the positive and negative predictive values were 95.4% and 95.1%, respectively.

In our study, the sensitivity was 93% and specificity was 43% when a cut of ≤ 909 was used as proposed by Giannini.

Doppler assessment of Hepatic vein and using the loss of the normal triphasic hepatic venous wave forms as a marker for the presence of varices was attempted by Thomas Joseph et al[28] from Thiruvanathapuram medical college hospital. In the 51 patients analysed by the, 4 had a triphasic pattern, 26 had a biphasic pattern and 21 had monophasic wave forms. Among the 49 patients we analysed, flow was triphasic in 7, biphasic in 8 and monophasic in 34 patients. The sensitivity of the study in predicting large esophagial varices (grade 2 and 3) was 97% and the specificity was 43 %. The positive predictive value was 81

% and the negative predictive value was 86%. The study group from Trivandrum reported a sensitivity of 95.2%, a specificity of only 10%, positive predictive value of only 43% and a negative predictive value of 75%.

The delineation of varices into small and large rather than the presence and absence of varices is important because, the current AASLD guidelines[29] suggest that the varices be graded as just small(<5mm) and large (>5mm) only patients with large varices will need prophylactic treatment with beta agonists and those with small varices just needs to be followed up. Our study has revealed a sensitivity of 97% for the loss of normal hepatic venous triphasic waveform in predicting large esophagial varices. This will further push the acceptance of non invasive methods in predicting and following up esophagial varices.

SUMMARY AND CONCLUSIONS

1. Loss of normal hepatic venous triphasic wave form is a very sensitive non invasive marker for predicting the presence of large esophagial varices with reasonably high positive and negative predictive value.
2. Platelet count/splenic diameter ratio, if taken with a cut off of ≤909, can predict the presence of large esophagial varices with reasonably good accuracy.
3. Comparing hepatic venous flow pattern to platelet count splenic diameter ratio,the formor is more strongly associated with the presence of large varices and scores over the latter in terms of negative predictive value.
4. Both are comparable in terms of sensitivity, specificity and positive predictive value.
5. Hepatic venous flow pattern did not have a statistically significant correlation with the incidence of UGI bleed.

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LIMITATIONS OF THE STUDY

1. Small population studied.

2. Etiology of cirrhosis not taken into account.

3. Hepatic venous Doppler and platelet count/ splenic diameter ratio in the normal population not assessed.

4. No patients had grade 4 varices.

PROFORMA

S. No: IP No: Address:

Name: Age: Sex:

Unit/Ward:

CLINICAL FEATURES		PAST HISTORY			
Hemetemesis		Alcoholism		Cardiac disease	
Malena		Hepatitis		T2DM/HTN	
Bleeding PR		Drugs			
Bleeding tendencies		COMPLETE HEMOGRAM		BIOCHEMISTRY	
Anaemia		Hb (g/dL)		Blood urea	
Jaundice		TC (cells/cmm)		Creatinine	
Pedal Oedema		DC		Serum Bilirubin	
Stigmata of CLD		RBC(millions/cmm)		Total	
Dilated veins		Platelet(Lakhs/cmm)		Direct	
Hepatomegaly		MCV(fL)		Indirect	
Splenomegaly		MCHC(g/dL)		Serum Protein	
Ascites		PCV		Albumin	
Encephalopathy		PT/INR		Globulin	
		Peripheral smear		AST	
		Platelet count		ALT	
				ALP	

PRESENTING COMPLAINTS

USG ABDOMEN	

Cirrhosis	
Spleen bipolar	
Diameter (mm)	
Portal Vein size (cm)	
Splenic Vein (cm)	
Ascites	
Collaterals	

USG ABDOMEN

Liver architecture:

Spleen :

Portal vein:

Hepatic venous doppler :

CHILD PUGH SCORE

OGD scopy :

Remarks

ABBREVIATIONS

EV	–	Esophagial Varices
OGD	–	Oesophago Gastro Duodenoscopy
LEV	–	Large Esophagial Varices
SAAG	–	Serum Ascitis Albumin Gradient
HBV	–	Hepatitis B
HCV	–	Hepatitis C
CT	–	Computerised Tomography
EEG	–	Electro Encephalogram
γ-GT	–	Gamma Glutamyl Transferase.
INR	–	International Normalised Ratio
HVPG	–	Hepatic Venous Pressure Gradient
IVC	–	Inferior Vena Cava
NSAID	–	Non Steroidal Anti Inflammatory Drugs
ROC	–	Receiver operating characteristic curve
LFT	–	Liver Function Tests
SD	–	Standard Deviation.
ALP	–	Alkaline Phosphatase
ALT	–	Alanine Amino Transferase
AST	–	Aspartate Amino Transferase.

	MASTER CHART																		
no	NAME	AGE	SEX	ASCITES	UGI BLEED	ENCEPHA LOPATHY	HEPATIC FLOW	Varices grade	PLATELET COUNT/SPLEEN SIZE	INFECTION	years of diagnosis	years of alcohol	hepatitis B	heapatitis C	Urea	creatinine	Platelet count	CHILD SCORE	SPLEEN SIZE
1	Amsa	60	M	severe	nil	1	Mono	2	714.29	nil	0	0	nil	nil	24	0.6	100000	C	140
2	Bhoopathi	40	M	moderate	yes	MHE	Biphasic	0	827.59	nil	5	0	nil	nil	42	0.5	96000	B	116
3	Sripushpam	36	F	nil	yes	0	biphasic	2	1125.00	nil	2	nil	nil	nil	26	0.8	180000	B	160
4	selvaraj	38	M	moderate	yes	2	mono	2	750.00	nil	3	13	nil	nil	16	1.3	120000	C	160
5	pandi	48	M	mild	nil	0	mono	3	766.67	nil	8	23	nil	nil	28	1.5	115000	B	150
6	petchiammal	60	F	nil	nil	0	mono	2	642.86	nil	4	0	nil	nil	26	1.8	90000	A	140
7	eluvi	58	F	nil	nil	0	mono	1	733.33	nil	4	0	nil	nil	20	1.3	110000	B	150
8	raja	40	M	moderate	yes	MHE	Mono	0	833.33	nil	2	22	nil	nil	21	1.2	150000	C	180
9	rajeswari	36	F	nil	nil	0	triphasic	2	1031.25	nil	7	nil	nil	nil	16	0.9	165000	B	160
10	lakkusami	56	M	mild	yes	0	biphasic	1	833.33	nil	0	5	nil	nil	24	1.5	125000	B	150
11	kanimuthu	35	M	mild	yes	0	Mono	1	857.14	nil	0	8	nil	nil	27	1.4	120000	C	140
12	mariappan	53	M	nil	nil	0	Mono	3	866.67	nil	4	9	nil	nil	29	1.8	130000	B	150
13	muthupillai	60	M	moderate	yes	MHE	Mono	3	727.27	nil	2	26	nil	nil	31	1.2	80000	B	110
14	raghupathi	35	M	mild	nil	0	Mono	3	823.53	nil	4	4	nil	nil	26	1.2	140000	B	170
15	kannadasan	42	M	moderate	nil	MHE	Mono	1	800.00	nil	3	16	nil	nil	30	1.6	120000	B	150
16	glory	40	F	mild	yes	0	triphasic	2	915.49	nil	4	0	nil	nil	28	1.8	130000	B	142
17	balamurugan	40	M	mild	nil	0	Mono	1	775.86	nil	4	18	nil	nil	21	1.8	90000	A	116
18	chandrakumar	36	M	mild	nil	0	triphasic	1	923.08	nil	0	11	nil	nil	29	1.9	120000	B	130

19	palanisamy	50	M	nil	yes	0	Mono	2	866.67	nil	4	18	nil	nil	22	1.2	130000	B	150
20	subbalakshmy	52	F	nil	nil	0	Mono	0	847.46	nil	3	0	nil	nil	26	1.6	100000	A	118
21	pitchai	58	M	severe	yes	MHE	Biphasic	2	1153.85	nil	0	23	nil	nil	24	1.9	150000	C	130
22	latha	36	F	nil	nil	0	triphasic	1	875.00	nil	0	0	nil	nil	23	1.3	140000	A	160
23	subramani	54	M	nil	nil	0	Mono	0	1000.00	nil	3	26	nil	nil	26	1.2	160000	B	160
24	MUNIYANDI	35	m	nil	nil	MHE	mono	2	718.75	nil	1	8	nil	nil	22	1.4	115000	B	160
25	ibrahim	46	M	moderate	nil	0	Mono	3	846.15	nil	2	9	nil	nil	28	1.4	110000	A	130
26	nagaraj	45	M	nil	nil	2	Mono	3	810.81	nil	3	18	nil	nil	30	1.8	120000	C	148
27	murugan	37	M	moderate	nil	MHE	Mono	1	1080.00	nil	0	2	nil	nil	19	1.6	135000	B	125
28	selvaraj	40	M	moderate	yes	1	Mono	3	857.14	nil	4	13	nil	nil	18	1.7	120000	C	140
29	basha	54	M	severe	yes	1	Biphasic	3	538.46	nil	6	20	nil	nil	26	1.2	70000	C	130
30	sulthani	55	F	nil	yes	3	Mono	3	505.88	nil	0	0	nil	nil	24	1	86000	B	170
31	chinnakannan	38	M	moderate	yes	0	Mono	3	700.00	nil	2	9	nil	nil	22	1.4	112000	B	160
32	peyammal	30	F	moderate	yes	0	Mono	2	862.07	nil	1	0	nil	nil	28	1.6	125000	C	145
33	pandiyammal	38	F	nil	yes	0	Mono	2	866.67	nil	3	0	nil	nil	24	1.8	130000	B	150
34	parameswaran	27	M	nil	nil	0	triphasic	3	568.18	nil	0	0	nil	nil	22	1.4	125000	A	220
35	ganesan	28	M	nil	nil	0	Biphasic	2	1000.00	nil	0	6	nil	nil	21	1.6	140000	B	140
36	uma	29	F	moderate	yes	2	Mono	2	681.48	nil	2	0	nil	nil	20	1.8	92000	C	135
37	nithya	35	F	nil	yes	0	Biphasic	2	896.55	nil	3	0	nil	nil	26	1.9	130000	B	145
38	petchiammal	55	F	nil	yes	0	Mono	2	884.62	nil	4	0	nil	nil	26	1.4	115000	A	130
39	murugesh	45	M	nil	nil	0	Biphasic	3	782.61	nil	4	11	nil	nil	22	1.6	90000	B	115
40	kannan	39	M	severe	yes	2	Mono	2	857.14	nil	6	9	nil	nil	27	1.6	120000	C	140
41	muthupandi	49	M	nil	yes	0	Mono	3	900.00	nil	2	16	nil	nil	24	1.6	135000	B	150
42	muthammal	58	F	moderate	yes	MHE	Mono	1	967.74	nil	0	0	nil	nil	28	1.8	150000	B	155
43	subramanian	40	M	severe	yes	3	Mono	2	761.90	nil	3	16	nil	nil	22	1.4	80000	C	105

44	lalitha	35	F	nil	nil	0	triphasic	2	903.23	nil	2	0	nil	nil	22	1.4	140000	B	155
45	lakshman	57	M	nil	nil	0	triphasic	1	896.55	nil	5	18	nil	nil	29	1.9	130000	B	145
46	muthuraj	37	M	severe	yes	3	Mono	1	892.86	nil	2	6	nil	nil	26	1.2	125000	C	140
47	eswaran	59	M	mild	nil	0	Mono	3	774.19	nil	2	26	nil	nil	27	1.2	120000	B	155
48	sathyamoorthy	54	M	moderate	nil	MHE	Mono	3	700.00	nil	3	23	nil	nil	22	1.6	98000	B	140
49	selvapandi	35	M	moderate	nil	MHE	Mono	3	906.25	nil	0	10	nil	nil	21	1.8	145000	B	160