STUDY OF RIGHT LOBE OF LIVER DIAMETER TO ALBUMIN RATIO AS A NON-INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

M.D. DEGREE EXAMINATION

BRANCH I - GENERAL MEDICINE

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CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled ***"STUDY OF RIGHT LOBE OF LIVER DIAMETER TO ALBUMIN RATIO AS A NON-INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS"*** submitted by ***Dr. P.SINRASU***, to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of **Doctor Of Medicine (M.D) Branch-I - General Medicine,** is a bonafide research work carried out by him under my direct supervision & guidance.

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DECLARATION

I, ***Dr. P.SINRASU,*** solemnly declare that, this dissertation entitled, ***"STUDY OF RIGHT LOBE OF LIVER DIAMETER TO ALBUMIN RATIO AS A NON-INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS"*** is a bonafide record of work done by me at the Department of General Medicine, Govt. Rajaji Hospital, Madurai, under the guidance of ***Dr.C.Dharmaraj,. M.D., Department of General Medicine, Madurai Medical College, Madurai***.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of **M.D Degree General Medicine Branch-I;** examination to be held in **April 2019.**

Place: Madurai

Date: ***Dr. P.SINRASU***

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TABLE OF CONTENTS

INTRODUCTION

One of the most dreaded complications of liver cirrhosis is oesophageal varices which is a result of portal hypertension. It carries a very high risk of mortality (20 to 35%).

The risk of developing oesophageal varices in cirrhotic patients over their life time amounts to about 5 to 15 percent per year and the rate of progression from small to large varices amounts to 8 percent per year. Therefore early identification and grading of varices remains the foremost step for risk assessment and thereby prevention of mortality.

Upper gastrointestinal endoscopy remains the gold standard test for identification of varices. Patients who do not have varices with compensated cirrhosis should receive an endoscopic examination every 2–3 years. Those with small varices should receive an examination every 1–2 years. But it has the following disadsvantages:

- invasive procedure that is unpleasant for patients
- poses heavy burden on endoscopy units
- detrimental effects of increase in risk of infections and bleeding
- costly procedure.

Predicting the presence of oesophageal varices by non-invasive means increases compliance and this would restrict the performance of endoscopy on those patients with a high probability of having varices.

Thus there is a need for some reliable non invasisive predictors for oesophageal varices which are cost effective , quick, simple and reproducible not adding burden to the patients.

Many studies have been foccussed on such non -invasive predictors like platelet count , spleen size, portal vein diameter etc., and many models have been proposed. The sensitivity and specificity of these models are highly variable and this study focuses on a superior method of variceal prediction based on right lobe liver diameter albumin ratio.

The right lobe liver diameter is a very easy parameter that can be measured simply as a part of ultrasound abdomen and serum albumin levels are measured as routine biochemical investigation. Thus this method requires parameters which can be easily detected without any additional efforts and thereby carries increased compliance.

AIMS &OBJECTIVES

- To study the value of biochemical and ultra sonographic parameters in prediction of presence and size of oesophageal varices.

- Right lobe of liver to albumin ratio can be used as a screening tool to suspect the presence of oesophageal varices.

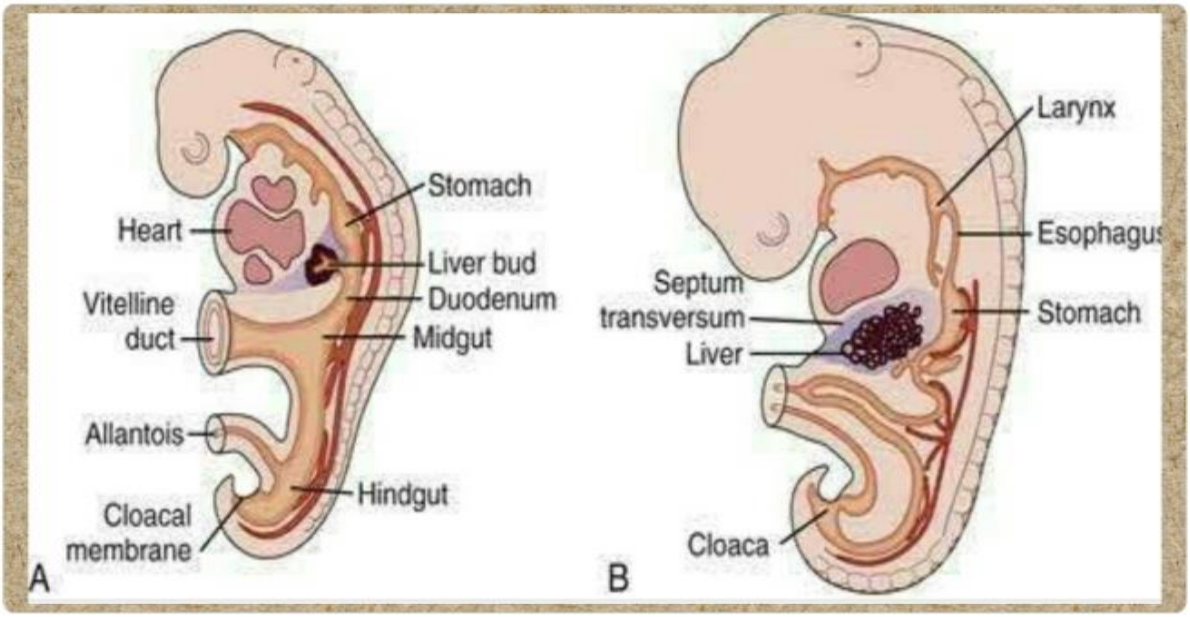
REVIEW OF LITERATURE

LIVER

An accessory digestive gland that also serves many other vital functions .It is covered by Glisson's capsule. It weighs about 1.2 to 1.5 kg

DEVELOPMENT

At third week of gestation from foregut endodermal bud which divides into two-cranial and caudal. The cranial bud develops into liver and the hilar biliary tract. The caudal develops into gallbladder, cystic duct and ventral pancreas.

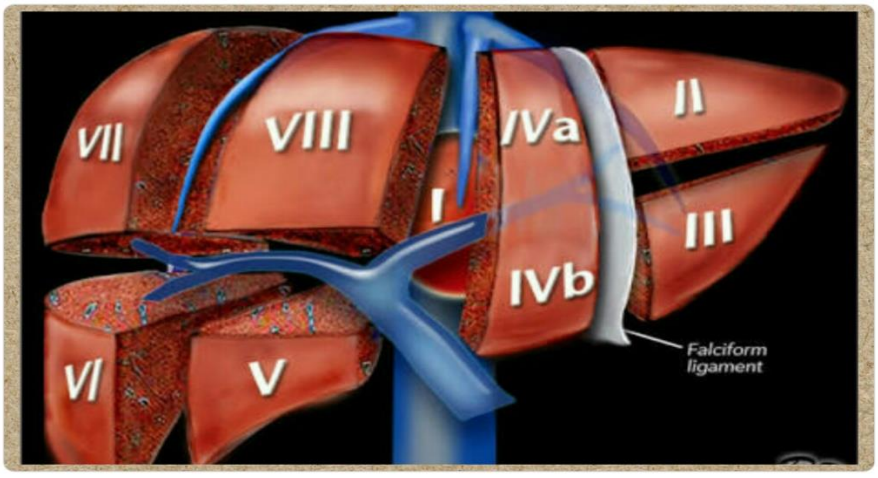


ANATOMY

Based on external appearance divided by falciform ligament into right and left lobes. But they are not of equal size. True right and left lobes are divided by cantlie line – passing through the bed of gall bladder and the notch of inferior vena cava. But these are not true functional lobes.

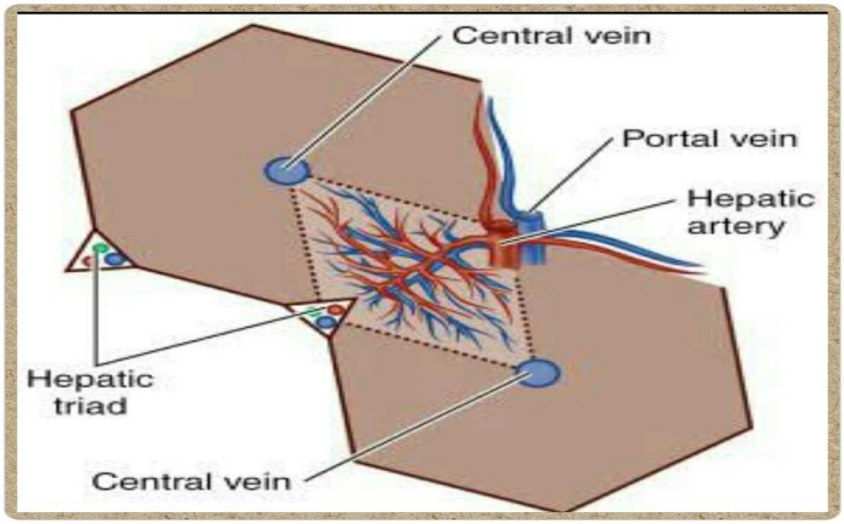
COUINAUD SYSTEM

This widely accepted system follows the distribution of portal and hepatic veins.



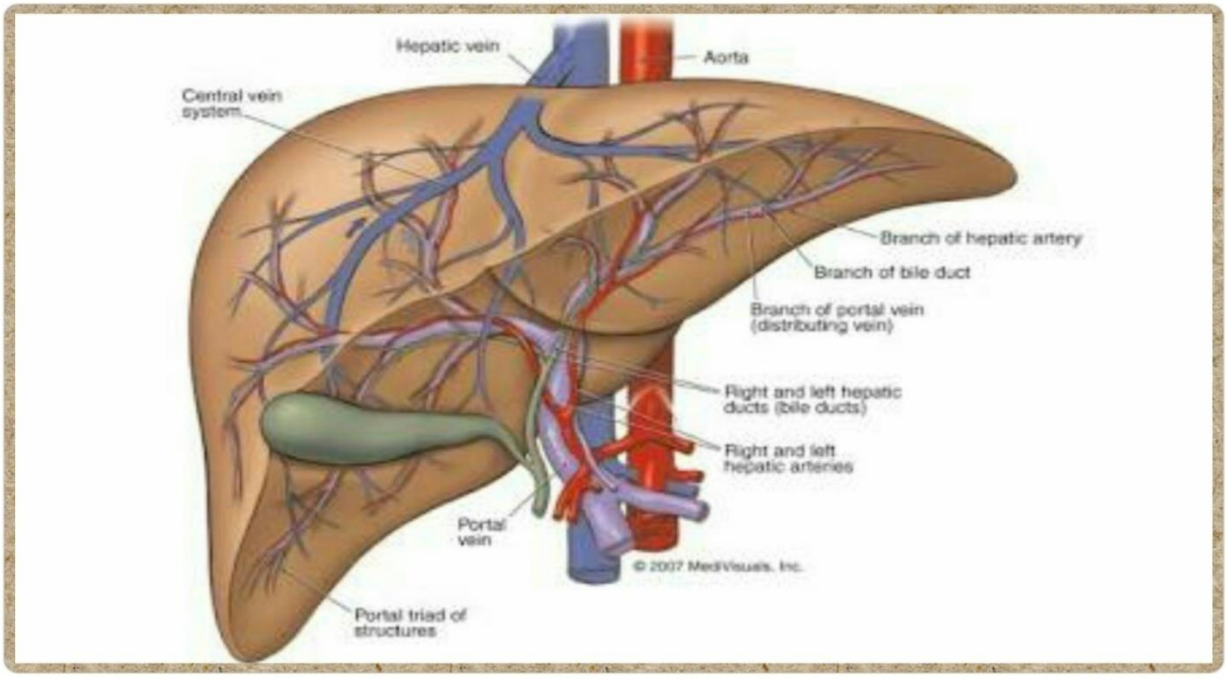
HEPATIC ACINUS

It is the functional unit of liver, described by Kiernan. Hepatocytes lie in 3 zones. The vulnerability of hepatocytes to different perfusion and toxins contribute to the patchy nature of liver injury.



BLOODSUPPLY

Dual blood supply – portal vein 70% (formed by spleenic vein and superior mysentric vein) and hepatic artery 30%(from celiac trunk).



VENOUS DRAINAGE

Hepatic sinusoids – interlobular veins – sublobular veins – hepatic veins- inferior vena cava.

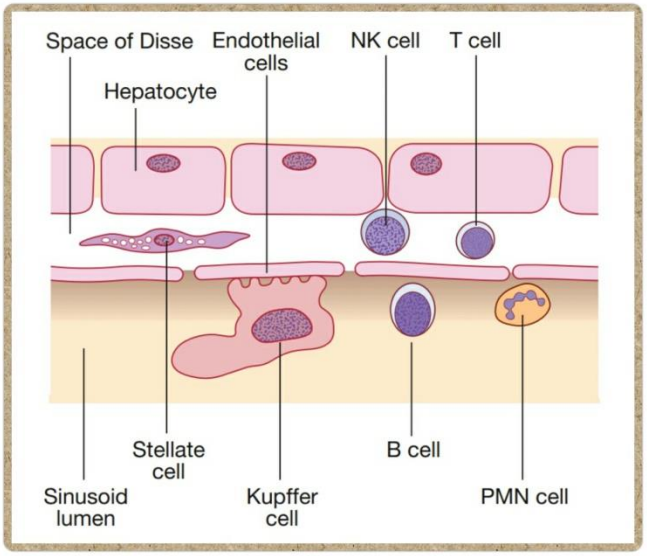
NERVE SUPPLY

Hepatic nerve plexus(both sympathetic T7 to T10 and parasympathetic).

LYMPHATICS

Terminate in caval, hepatic, coeliac and few in mediastinal nodes.

HISTOLOGY



The zone 3 adjacent to terminal hepatic veins suffers most of the insults – viral , toxic or anoxic. In cirrhosis, the bridging necrosis may extend from zone 1 to zone 3. The space of Disse, contains the Stellate cells that are responsible

for the proliferation of fibroblasts during disease processs ultimately leading to cirrhosis.

PORTOSYSTEMIC ANASTAMOSES

Form important route of collateral circulation in portal obstruction due to portal hypertension. Various sites include :

- Lower end of oesophagus (oesophageal varices)
- Lower end of rectum (haemorrhoids)
- Around umbilicus (caput medusa)
- Bare area of liver.

FUNCTIONS OF LIVER

- Nutrient metabolism (carbohydrates, proteins and lipids).
- Storage of iron, copper, vitamins A, D , B12.
- Synthesis of proteins like albumin, coagulation factors, complement factors, haptoglobin, ceruloplasmin, transferrin, protease inhibitors like alpha 1 antitrypsin
- Excretion of bile salts, bilirubin, drugs, cholesterol and phospholipids.
- Immune functions by kupffer cells. (constitute the largest single mass of tissue resident macrophages in the body accounting for the phagocytic

activity eliminating bacteria, viruses, antigen antibody complexes and endotoxins)

- Detoxification of variety of toxins.

REGENERATIVE PROPERY OF LIVER

Liver has immense potential of regeneration . Only about 20% of residual mass is enough for regeneration. Regeneration is induced by various signalling pathways including cytokines, growth factors, hormones and nuclear receptors. Regeneration is brought about mainly by hepatocytes. Cell proliferation is aided by angiogenesis. But as the disease process still continues the irreversible changes progress and lead on to fibrosis resulting in cirrhotic liver.

CIRRHOSIS

It is defined as diffuse hepatic fibrosis and nodular formation altering the liver architecture. Chronic liver diseases usually alter the liver parenchyma resulting in liver cirrhosis. Usually after the hepatic injury there is tremendous increase in the extracellular matrix of liver especially type 1 and 3 collagen rather than type4. There is loss of endothelial cell fenestrations thereby metabolic exchange between blood and livercells is affected leading to accumulation of type 1 collagen leading to fibrogenesis. The principal cell

involved in this entire process is the stellate cell present in the space of Disse. It is activated by kupffer cells and hepatocytes in chronic liver diseases and it proliferates increasing the production of type 1 collagen leading to fibrosis.

Cirrhosis is a histological diagnosis classified as micro nodular and macro nodular cirrhosis. Cirrhosis results in decreased liver function and increased resistance to flow of portal venous blood. Cirrhosis is generally irreversible in the late stages and liver transplantation is the only treatment option left in the advanced stage. Certain conditions causing cirrhosis responds to treatment of the underlying cause even resulting in reversal of the process in the early stages .This is seen especially in cirrhosis caused by hepatitis C, alcohol and obesity.

Cirrhosis is the end stage of chronic injury leading to inflammation and destruction and regeneration of the hepatocytes, inflicted by various conditions

ETIOLOGY

The most common etiologies for development of cirrhosis is alcohol followed by viral hepatitis in developing countries like India.

In developed countries the scenario changes due to the sedentary lifestyle thus the commonest etiology remains Nonalcoholic fatty liver disease (NASH-Non Alcoholic Steato Hepatitis) followed by viral cirrhosis (hepatitis C).

Cirrhosis is not a single step process. The main etiological agent with additional cofactors contribute to the pathological process and the rate of fibrotic changes increase with the persistence of the etiological agent.

Cofactors include genetic factors, age, sex, alcohol, iron intake, duration of disease, immunological factors. The various causes may also co interact. For example, the rate of cirrhotic changes is faster in a patient with viral hepatitis who drinks. Older the age, the fibrotic progression is rapid.

Thus all changes revolve around a principal factor which interacts with various cofactors contributing to the cirrhosis. And also these changes have high individual variability based on patient's susceptibility .

Any condition leading to persistant or recurrent hepatocye death or prolonged biliary damage and obstruction or blockage of venous return from liver –all these above mentioned conditions trigger the cirrhotic changes defying the body's hepato protective mechanisms.

VARIOUS CAUSES

- Toxic
    - Alcohol
    - Arsenic
- Viral

- HBV
- HCV
- HDV

- Autoimmune
  - Autoimmune hepatitis
  - PSC
  - PBC
- Metabolic
  - α1-Antitrypsin deficiency
  - Wilson's
  - Galactosemia
  - Glycogen storage disease
  - Hemochromatosis
  - NASH - Nonalcoholic fatty liver disease and steatohepatitis
- Biliary
  - Atresia
  - Stone
  - Tumor

- Vascular
    - Budd-Chiari syndrome
    - Cardiac fibrosis
- Genetic
    - CF
    - Lysosomal acid lipase deficiency
- Iatrogenic
    - Biliary injury
    - Drugs: high-dose vitamin A, methotrexate

Cryptogenic cirrhosis is a diagnosis of exclusion. It is an end stage chronic liver disease in which the underlying etiology remains unknown even after extensive clinical, pathological and serological evaluations. The diagnosis should be finalised only after thorough assessment and evaluation for other causes.

Cirrhosis is an irreversible process. The changes can be reversible only if the etiological agent is removed at very early stages. Cirrhosis progresses from a compensated state to a decompensated state.

CLINICAL MANIFESTATIONS

Patient may be presenting with different scenarios. May be asymptomatic and incidentally be identified during checkup for unrelated causes or present with abnormal liver tests but clinically normal or may present with the complications at the very first visit .

Clinically , cirrhosis may be

- Compensated or
- Decompensated

When complicated by one or more features like –ascites, jaundice, hepatic encephalopathy, bleeding varices cirrhosis is said to be decompensated. First sign of decompensation is usually marked by ascites.

In compensated cirrhosis all these features and any complication secondary to portal hypertension is absent. This clinical distinction isvital because it delineates prognosis and management and most importantly a key role in deciding morbidity and mortality.

Ten year survival rate is 50% for patients with compensated cirrhosis whereas decompensated patients have a survival rate of about 50% in 18 months. When the inciting cause or the precipitating cause is removed, a

decompensated patient may become compensated thus, the prognosis improves to a tremendous extent.

FOUR CLINICAL STAGES OF CIRRHOSIS

1. Absence of ascites and varices
2. Varices without bleeding and absence of ascites
3. Ascites with or without variceal bleeding
4. Variceal bleeding with or without ascites.

Stages 1 and 2-compensted cirrhosis: 3 and 4- decompensated cirrhosis.

COMPENSATED CIRRHOSIS:

The cirrhotic process of the liver is not severe enough to alter the function significantly at this stage. So the patients may be either asymptomatic or may be picked incidentally due to alteration in biochemical parameters or imaging studies. Patients may present with fatigue, flatulence ,dyspepsia, abdominal pain, anorexia, weight loss. Palmar erythema, pedal edema, spider naevi on general examnation may provide clues suggestive of cirrhosis. On abdominal examination an epigastric mass which is the enlarged left lobe of the liver and mild splenomegaly may be the findings. In this group, biochemical tests are usually within normal limits. Mildly elevated transaminase may be some times the only finding. Confirmation can be attributed only by liver

imaging or liver biopsy (the gold standard test). Decompensation in compensated cirrhosis may be precipitated by factors like bacterial infection, trauma, or medications or surgery .

DECOMPENSATED CIRRHOSIS:

When the patients present with ascites, jaundice, altered sensorium, bleeding manifestations the cirrhosis is said to be decompensated.

SYMPTOMS

Patient may complain jaundice, pedal edema, abdominal distension, melena, hematemesis suggestive of upper GI bleed , pruritus, altered sensorium which may present either as altered sleep pattern or florid confusion and coma suggestive of hepatic encephalopathy.

Menstrual irregularities are common due to anovulation in women .Hypogonadism in the form of impotence, loss of sexual drive, testicular atrophy and infertility may be the presenting complaints in men.

GENERAL EXAMINATION

Decreasing blood pressure - with progression of cirrhosis, mean arterial pressure often decreases. Hypertensive patients may become normotensive.

Patient has an ill look with cirrhotic facies. Patients may be febrile (37.5 - 38 C) which is due to bacteremia due to gram negative organisms. It may also

be due to ongoing hepatocyte necrosis, development of hepatocellular carcinoma.

From head to foot one or more signs of liver cell failure can be identified as follows:

- Head :Aloepecia, madarosis
- Face: bilateral parotid enlargement
- Eyes :
    - Jaundice (because of functional impairment due to hepatocyte destruction thathas exceeded the process of regeneration. Depth of jaundice correlates with degree of decompensation.
    - Bitot spot
    - Subconjunctivalhemorrhage, kf ring
- Oral cavity : Fetor hepaticus - the breath of the cirrhosis patients that has a sweet pungent nature because of presence of mercaptans.
- Loss of axillary hair
- Skin findings:
    - the presence of bronze pigmentation of the skin throws light on the etiology as it occurs in hemochromatosis.

- Hands:
    - Palmar erythema (warm and red palms especially over the thenar eminence, hypothenar eminence and the pulp of the finger)
    - Dupytrens contracture: thickened palmar fascia resulting from unorganized proliferation of the fibroblasts.
    - Clubbing : pan digitally especially with development of hepato pulmonary syndrome or in cystic fibrosis .Hypertrophic osteoarthropathy has also been observed
    - Terry nails:Leukonychia (related to hypoalbuminemia)
    - Asterixis / flapping tremors.
- Chest wall
    - Presence of spider naevi (arterial spiders/ vascular spiders / spider telangiectasia/ spider angioma). Seen along distribution of drainage areas of superior vena cava. New spiders may appear as liver function worsens, frequently associated with alcoholic cirrhosis . It is a normal finding in pregnancy .Multiple spiders and clubbing should arise the suspicion of hepato pulmonary syndrome

- Painless gyenacomastia in males seen along with other features of feminization like change in the male pattern of pubic hair, loss of axillary hair and chest hair because the androstenedione that is synthesized by the adrenals gets aromatized in to estrone and finally in to estradiol in the adipose tissue.
- Breast atrophy in females.

Hyperoestrogenic state is the mechanism behind both arterial spiders and palmar erythema . Due to liver failure, estrogen cannot be inactivated in the liver. Serum free testosterone is reduced even though serum estradiol level is normal .The high estradiol/free testosterone ratio may be attributed to these findings.

- Abdominal findings
  - Ascites — excessive collection of peritoneal fluid .In massive ascites fluid thrill may be present and in moderate ascites shifting dullness is present.
  - Liver -On palpation, liver size is normally reduced; consistency is firm and nodular. Palpable liver in cirrhosis should arise suspicion of transformation into hepatocellular carcinoma, primary biliary cirrhosis, cardiac cirrhosis, alpha 1 antitrypsin

deficiency, Indian childhood cirrhosis, hemochromatosis, Budd Chiari syndrome. The shape, consistency, tenderness should be better appreciated on palpation as the estimation of liver size correlates less accurately with imaging studies.

- Splenomegaly - Splenomegaly in cirrhosis results from portal hypertension due to congestion. But correlation between splenic size and portal pressure is poor .
- Umbilical hernia
- Caput medusa –The appearance resembles the head (caput) of the mythical Gorgon Medusa and so named caput medusae. Due to portal hypertension the porto systemic anastamoses open up. The mechanism being- the portal venous blood that gets carried through the peri umbilical veins in to the umbilical vein which becomes patent in cirrhosis .Then the blood drains into the upper and lower abdominal veins that end up in systemic circulation resulting in the engorgement and prominence of the veins around umbilicus. Thereby the portal blood gets shunted to systemic circulation.
- Dilated abdominal veins: they also develop in SVC obstruction and IVC obstruction and should be differentiated

from dilated veins due to cirrhosis. To know the cause of obstruction assessment of direction of flow is vital. In cirrhosis the flow of the blood is away from the umbilicus. In IVC obstruction the flow is below upwards. The test may be misleading some times since these veins in both conditions may lack valves, the flow may be bidirectional. The dilated veins due to IVC obstruction are more commonly seen in the back and loin.

- Genitourinary findings
    - Testicular atrophy
    - Scrotal edema
    - Loss of pubic hair
- Bilateral pitting pedal edema

ENDOCRINE CHANGES

- Hyperglycemia (in 80% patients)
- Hypothalamo pituitary dysfunction
- Hypogonadism
- Altered metabolism of hormones
- Muscle cramps due to increased RAS activity

Drug metabolism is also affected therefore drugs are to be prescribed with extreme degree of caution.

ABDOMINAL PAIN IN ALCOHOLIC CIRRHOTIC PATIENTS

Peptic ulcers occur in about 11% of cirrhosis patients. Duodenal ulcers are more common because colonization by helicobacter pylori is higher in cirrhosis when compared to normal population.

Alcoholics are more prone for chronic pancreatitis. Hence these two conditions must be ruled out in the view of abdominal pain in alcoholic cirrhosis.

INVESTIGATIONS

Liver function test

- Bilirubin - the bilirubin levels are usually normal in compensated stage of cirrhosis . Increasing levels of bilirubin marked decompensation . It is one of the prognostic indicators used in Child Pugh score.
- Aminotransferases -In cirrhosis patients the enzymes can be moderately elevated or within normal values .In chronic hepatitis, initially ALT is increased more than AST. Then as hepatitis progresses to cirrhosis ,AST becomes more elevated than ALT. The ratio of AST to ALT is reversed from <1 to greater than 1 .

- Alkaline phosphatase — It is elevated 2 to 3 times in cirrhosis. Primary biliary cirrhosis or sclerosing cholangitis should be considered as the etiology if elevated more than that.
- Gamma- glutamyltransferase– GGT is present in the microsomes and is induced due to alcohol intake. GGT and alkaline phosphatase are usually proportionately elevated Disproportionately high levels of GGT will be seen in alcoholic liver disease.
- Serum electrolytes – In ascites, hyponatremia occurs. If severe indicates the worsening of cirrhosis.
- Albumin — Albumin is synthesized exclusively in the liver about 15 g/day. With worsening cirrhosis albumin levels also fall. It is also one of the prognostic indicators for survival in child scoring system.

  It is the most important plasma protein which accounts for 75% of the plasma colloid oncotic pressure and is synthesized by hepatocytes. In an average adult about 300 to 500 g of albumin distributed in body fluids. The liver can double the rate of synthesis in the setting of rapid albumin loss or a dilutional decrease in the serum albumin concentration.

The half-life of albumin is 14 to 21 days. This long half-life of albumin in serum accounts for its unreliability as a marker of hepatic synthetic function in acute liver injury. Changes in nutritional status, osmotic pressure, systemic inflammation, and hormone levels regulate albumin synthesis. The differential diagnosis of serum hypoalbuminemia, in addition to hepatocellular dysfunction, includes malnutrition, excessive loss from protein-losing enteropathy or nephrotic syndrome, chronic systemic inflammatory conditions, and hormonal imbalances.

Serum albumin levels less than 3 g/dL in a patient with features of hepatitis should arise suspicion of chronic process.

Thus serum albumin is an excellent marker of hepatic synthetic function in patients with chronic liver disease and cirrhosis

Albumin globulin ratio- A/G reversal is seen in cirrhosis. In cirrhosis, the globulin levels are high because of shunting of bacterial antigens in the portal venous blood which are normally filtered by the liver in to systemic circulation. This leads to production of immunoglobulins. But marked elevations of IgG points towards the presence of autoimmune hepatitis.

- Prothrombin time — a measure of the extrinsic coagulation pathway, is a marker for the synthetic function of the liver because most of the coagulation factors are synthesized in liver. Thereby coagulopathy worsens as cirrhosis progresses.

- Hematologic abnormalities -

Thrombocytopenia, anemia and leucopenia manifest.

- Among them the earliest abnormality to occur is thrombocytopenia and it is a potential marker for the development of portal hypertension. Platelet count does not fall below 50,000. Bleeding can get aggravated in the presence of coagulopathy.
- Pancytopenia – it can even be the presenting feature in asymptomatic compensated cirrhosis due to sequestration of the cells in the enlarged spleen.
- Anemia- Mainly because of upper GI bleed in cirrhosis. It can also be present as a result of direct suppression of bone marrow by alcohol, sequestration and hemolysis, folate deficiency.
- Viral markers - HBsAg, HCV, HIV

IMAGING STUDIES:

NON INVASIVE

- Ultrasonography — Anon-invasive investigation to diagnose cirrhosis. Various parameters like the liver size, the nodularity, the portal vein diameter, presence of ascites and splenomegaly can be assessed. Also the presence HCC, portal vein thrombosis can be made out.
- Doppler studies can also be done. This checks the direction of blood flow in the portal vein thereby aiding in the diagnosis of portal hypertension.
- CT- useful only when investigating liver malignancy or secondaries or pancreatic pathology. Not the first choice in the diagnosis of cirrhosis.
- MRI- it is very useful in hemochromatosis to reveal iron overload.
- MRA - determines portal vein flow and dynamics.

INVASIVE TECHNIQUES

Liver biopsy:

It is the gold standard investigation for diagnosing cirrhosis . Nowadays liver biopsy is not frequently used to diagnose cirrhosis.

Performing liver biopsy may be required in special circumstances such as for demonstrating the underlying metabolic cause of cirrhosis such as NASH, Wilson disease, hemochromatosis and alpha 1 antitrypsin deficiency.

Upper GI endoscopy

Gold standard for variceal detection

PROGNOSIS

Child-Turcotte-Pugh Score (CTP):

It is a simple scoring system, for predicting the prognosis from the major complications of the cirrhosis patients which is widely in use in clinical practice. Though practically difficult, this score has reasonable accuracy.

This is used in the stratification of patients in to risk groups before taking them up for porto systemic shunt surgeries and to prioritize the patients to be taken up for liver transplantation (Child Pugh class B). Now this system has been replaced by MELD score for selection of patients for liver transplantation.

"Child-Turcofte-Pugh Classification for Severity of Cirrhosis"			
	"Points*		
	1	2	3
Encephalopathy	None	Grade 1-2 (or precipitant induced)	Grade 3-4 (or chronic)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	<2	2 - 3	>3
Albumin (gfdL)	>3.5	2.8 – 3.5	<2.8
INR	<1.7	1.7 – 2.3	>2.3
Class A- 5 to 6 points (least severe liver disease)			
Class B -7 to 9 points (moderately severe liver disease)			
Class C -10 to 15 points (most severe liver disease)"			

Model for End-stage Liver Disease (MELD) score is derived methodologically in order to prognosticate the patients with cirrhosis and portal hypertension .It is calculated based on three noninvasively obtained variables: serum bilirubin, serum creatinine

"MELD Score
MELD = 3.78 x Iog serum bilirubin (mg/dL) + 11.20 X 109e INR + 9.57 x loge serum creatinine (mg/dL) + 6.43 (constant for liver disease etiology)
NOTES • If the patient has been dialyzed twice within the Iast 7days,then the value for serum creatinine used should be 4.0 • Any vaIue less than one is given a value of 1 (ie. if bilirubin is 0.8,a value of 1.0 is used) to prevent the occurrence of scores below 0 and INR"

Patient with a score > 10 is to be considered for liver transplantation. Based on this the patients with cirrhosis are given priority for liver transplantation. The advantage is that it is completely objective for assessment

of severity of the disease and there is no inter observer variation. Grading is more precise as it has wider range of values.

COMPLICATIONS OF CIRRHOSIS

Complications occur as a result of either the decreased synthetic, excretory, metabolic functions of the liver with the progression of cirrhosis attributed to the development of portal hypertension

Various complications include,

- Portal hypertension
- Upper GI bleed (Gastroesophageal varices)
- Ascites
- Splenomegaly, hypersplenism
- Spontaneous bacterial peritonitis
- Coagulopathy
- Hepatic encephalopathy
- Hepato renal syndrome
- Hepato pulmonary syndrome
- Porto pulmonary hypertension
- Bone disease(osteopenia, osteoporosis, osteomalacia)
- Haematological abnormalities (anaemia, neutropenia, thrombocytopenia)

- Malnutrition
- Infections
- Portal gastropathy
- Cirrhotic cardiomyopathy

PORTAL HYPERTENSION:

The normal hepatic venous pressure gradient (HVPG) is 5 to 6 mm Hg Portal hypertension is defined as “the elevation of the hepatic venous pressure gradient (HVPG) to >5 mmHg”.

CAUSES

- pre-hepatic
- intra-hepatic causes
- post hepatic.

Pre-hepatic causes are those that results in development of sinistral hypertension or left sided portal hypertension. It includes portal vein thrombosis and splenic vein thrombosis. Also Portal vein thrombosis can occur secondary to pancreatitis, abdominal trauma and infection or hematological causes such as essential thrombocytosis, polycvthemia vera, Protein C and S deficiency

Intra-hepatic causes may be pre sinusoidal, sinusoidal or post sinusoidal. Pre – sinusoidal causes include schistosomiasis and congenital portal fibrosis . Cirrhosis causes sinusoidal form of portal hypertension. Post sinusoidal causes includes veno-occlusive disease

Post hepatic causes affect the hepatic veins and venous drainage in to the heart. Budd Chiari syndrome veno occlusive disease, constrictive pericarditis, chronic right sided congestion, restrictive cardiomyopathy are some conditions causing post sinusoidal portal hypertension.

PATHOGENESIS

Portal hypertension results due to two simultaneous processes :

- Increased resistance to the flow of the portal blood due to the altered liver architecture due to fibrosis and regenerating nodules
- Increased blood flow secondary to splanchnic vasodilatation.

The development of portal hypertension may be revealed by the presence of thrombocytopenia, appearance of an enlarged spleen, encephalopathy, development of ascites and esophageal varices with or without bleeding in patients with liver cirrhosis

60% of cirrhotics develop significant portal hypertension leading to complications. The primary complications of portal hypertension include ascites, bleeding varices and hypersplenism.

GASTRO OESOPHAGEAL VARICES

Among those affected one third of the patients with cirrhosis have gastric and oesophageal varices. So mandatory screening of all patients with established cirrhosis for the presence of varices using upper GI endoscopy is necessary.

Several factors like the varices size, severity of cirrhosis, tense ascites, and increased wedged hepatic vein pressure together govern the development of varices

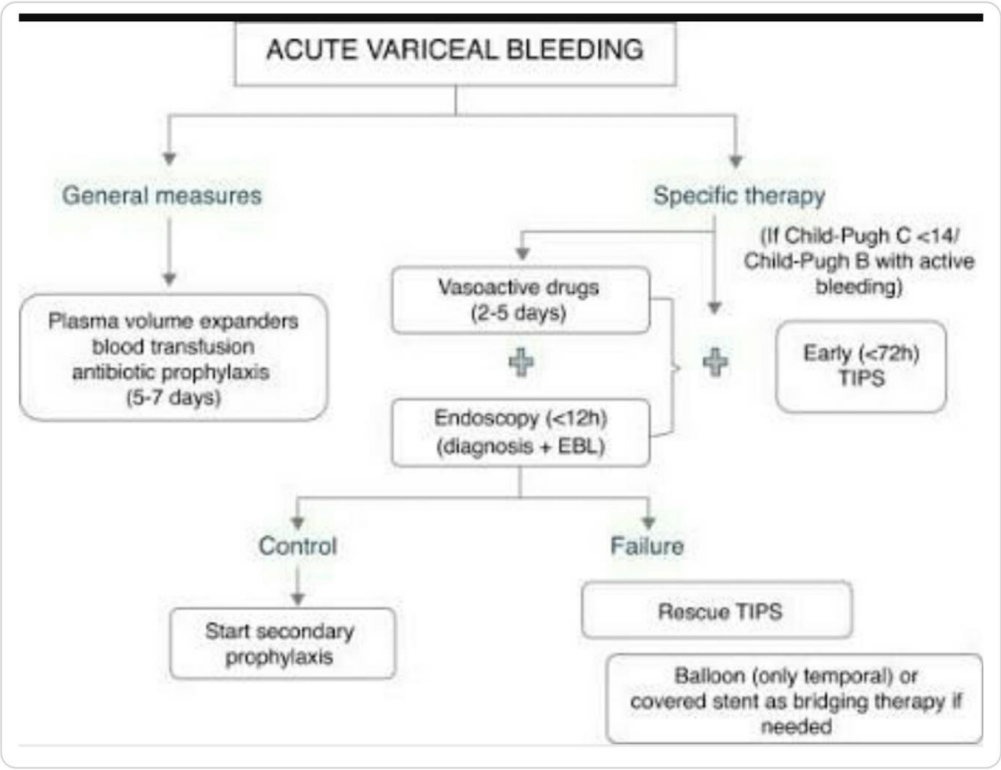
Diagnosis is made by upper gastro oesophageal endoscopy which is an invasive procedure.

ENDOSCOPIC GRADING OF ESOPHAGEAL VARICES

GRADE	***FINDING***
0	Abscence of varices. Repeat endoscopy in 2-3 years.
1	Microcapillaries present. Repeat endoscopy in 1-2 years.
2	1-2 small varices, no hemmorhage
3	Medium sized varices
4	Large sized varices

CT or MRI abdomen can be performed in doubtful cases or interventional radiological procedure to determine the free and wed hepatic vein pressure and the gradient between the two can be found out .The normal value is 5 mm Hg and if more than 12 mm Hg it signifies increased risk of bleeding.

Acute therapy is given to arrest the bleed and then followed by prophylaxis against repeated bleeding. Administration of intravenous fluids and blood products and use of octreotide at a rate of 50-100 mic/hour immediately to arrest bleeding. Then is endoscopic variceal band ligation done to obliterate the varices. In case of failure, TIPS can be tried. For prophylaxis non selective beta-blockers can be used.



ASCITES:

It is defines as excessive accumulation of peritoneal fluid. In cirrhosis it may be de novo or may be due to spontaneous bacterial peritonitis or development of malignancy.

PATHOGENESIS

Mechanisms that contribute to the occurrence of ascites in cirrhosis with portal hypertension include:

Increase in the intrahepatic resistance causes increase in portal pressure . This is accompanied by vasodilatation in splanchnic arterial system due to release of vasodilatory substances such as nitric oxide which results in increased portal inflow. All these ultimately leads to increase in the production of splanchnic lymph.

The intravascular volume depletion occuring due to splanchnic vasodilatation results in under filling in other vascular beds leading to increased activity of the renin angiotensin system .Finally there is increase in release of aldosterone leading to sodium and water retention and thus peripheral edema and ascites. This is also aided by the decreased oncotic pressure due to hypoalbuminemia.

Ascites may lead to hepatic hydrothorax also due to the diaphragmatic pores . Most common being right sided pleual effusion.

Ascitic fluid tapping is to be done and ascitic fluid analysis must be interpreted includingproteins, cell count and sugar levels. In cirrhotic patients, the ascitic protein content is very low, less than 1.1 g/dl which is an indirect indicator for increased risk of spontaneous bacterial peritonitis.Ascitic fluid polymorphonuclear cell count, of more than 250 cells/mic L indicates the presence of infection RBCs in ascetic fluid indicates the presence of malignancy, omentalvarices or traumatic tap. SAAG ratio ('serum to ascites albumin gradient') is a recent parameter for assessment of the nature of ascitic fluid. If SAAG ratio < 1.1 g/dl infection or malignancy has to be ruled out. If it is>1.1 g/dl it denotes that ascites is due to portal hypertension.

Management in case of mild ascites is attained by salt restriction < 2 g /day and life style modifications.

Moderate ascites is managed by pharmacological means by diuretics. From a starting dose of 40 mg frusemide and 100 mg spirinolactone dose can be escalated up to 400-600 mg spirinolactone and furosemide upto 160 mg. Ascites is said to be refractory if it is still present with these dosage of diuretics and a strict salt restricted diet. Alpha antagonists like clonidine, midodrine can

be tried. Resistant ascites has a bad prognosis with survival rates not more than 50% at the end of two years.

For repeated large volume refractory ascites therapeutic tapping, intravenous albumin infusion and TIPS are the choice.

SPLEENOMEGALY

Moderate spleenomegaly develops in cirrhosis due to congestion from increased portal pressure. Sometimes thrombocytopenia due to hyperspleenism may be the first presentation of portal hypertension even before ascites may develop.

SPONTANEOUS BACTERIAL PERITONITIS:

Occurs spontaneously due to infection of the ascitic fluid without an intraabdominal source. SBP is usually monobacterial, if polymicrobial - perforation of viscus is to be considered. Mechanism behind SBP is not very clear .The probable mechanism may be bacterial translocation from the intestines in to the mesenteric lymph nodes followed by bacteremia and seeding of ascites.

The commonest organism cultured is Escherichia coli. Other gram positive bacteria causing SBP include, Streptococcus viridians, enterococcus and staphylococcus aureus. Symptoms include fever, sudden increase in ascites,

abdominal pain and altered sensorium. Treatment is with second generation cephalosporins (1 g iv bd). High risk patients are those with prior history of SBP, very low proteins in ascitic fluid and in patients with upper GI bleeding. They are provided with once weekly as prophylaxis**.**

ABNORMALITIES OF COAGULATION:

Coagulopathy results due to the decreased production of clotting factors and impaired clearance of anticoagulants. Thrombocytopenia as a result of hypersplenism due to portal hypertension also contributes to bleeding manifestation.. Platelet function is also abnormal (thrombasthenia) is also evident apart from reduction in its number.

HEPATIC ENCEPHALOPATHY:

More common in patients with cirrhosis. It is defined as a complex syndrome of neuropsychiatric manifestations with disturbances in conscious level and personality changes which fluctuate from day to day occurring either in chronic liver disease or fulminant hepatic failure. Also called as porto systemic encephalopathy.

PATHOGENESIS

Due to the deficient detoxifying ability of cirrhosed liver, there occurs accumulation of gut-derived neurotoxins in the systemic circulation These

neurotoxins mainly include ammonia, levels of which when elevated in CLD patients attribute to the symptoms in hepatic encephalopathy. Other compounds like mercaptans, GABA are also elevated that contribute to encephalopathy.

Factors precipitating hepatic encephalopathy include constipation, SBP, hypokalemia, dehydration, UGI bleed, increased dietary protein load , overt use of diuretics and inadventparacentesis. Avoidance of these precipitating factors is the foremost step to be done in management process.

Earliest symptom is the alteration of sleep pattern.other features include behavioural alterations, loss of consciousness, slurring of speech , rarely convulsions.

Earliest sign that can be elicited is constructional apraxia. Others include flapping tremors(also called -Asterixis .It is elicited by having the patients extend their arms and bending their wrists backward. In this maneuver, patients who are encephalopathic may have a “liver flap”-i.e. a sudden jerky forward movement of the wrist every 5 to 10 seconds), hyperreflexia, bilateral plantar extensor.

The EEG shows slowing of alpha waves initially later delta waves appear.

The first step in management is to avoid the precipitating factors.

Ryles tube aspiration to check any ongoing GI bleed and patients to be appropriately hydrated. Correction of electrolyte abnormalities. Vegetable proteins are preferred over animal proteins. Bowel wash to be given.

Lactulose 15 to 20 ml an osmotic cathertic a non-absorbable disaccharide, converts ammonia into ammonium by enhancing acidic medium and prevents the diffusion of ammonia produced in the gut in to portal system. It also alters the gut flora in such a way that they favourable. .Their use became limited due to side effect such as ototoxicity and peripheral neuropathy. The gut antibiotic of choice now is Rifaximin at a dosage of 550 mg twice daily. Zinc supplement can also be tried.

HEPATORENAL SYNDROME:

There is marked reduction in glomerular filtration rate and renal plasma flow (RPF), without any other contributing cause to renal failure. This is very typical of hepato renal syndrome.

HRS is attributed to the reversible functional renal impairment which develops in patients with end stage liver cirrhosis or those with acute fulminant liver failure without any anatomical alteration.

PATHOGENESIS

It occurs in the end stage of liver cirrhosis. The peculiarity is that, the function of the renal tubules is normal. There is no proteinuria or abnormal histology in the kidneys.

HRS is attributed to severe vasoconstriction in the renal vascular bed. There is paradoxical peripheral arterial vasodilation. The development of HRS is the end result of the interaction between multiple mechanisms.

- Splanchnic vasodilation associated with hyper dynamic circulation with consequent renal vasoconstriction.
- There is activation of renal sympathetic nervous system.
- Cardiac dysfunction that may result in decreased renal gfr.
- Different vasoactive mediators and cytokines act over renal circulation.
- All ultimately leads to peripheral arterial vasodilation.

TYPES

Two types of HRS exists

- Type 1 HRS

It is defined as the “rapidly progressive which is of acute onset oliguric renal failure unresponsive to volume expansion with the doubling of serum creatinine value to more than 2.5 mg/dl within 2 weeks duration”.

Diagnosis of type 1 HRS should be made only when it fulfils the criteria defining acute kidney injury. There should be an abrupt increase in serum creatinine more than or equal to 0.3 mg/dl or an increase of more than 1.5 times from the baseline. This ensures there is no unnecessary delaying of treatment as baseline creatinine is a predictor of HRS reversal with vasoconstrictors.

- Type 2 HRS

It manifests clinically as refractory ascites. It has a slower progression and the cut off of serum creatinine is 1.5 mg/dl.

In type 1 HRS, a precipitating factor is identified frequently but there are no such factors involved in development of type 2 HRS. In type 2 HRS there is gradual progression of the mechanisms responsible for development of HRS whereas in type 1 HRS, worsening of the kidney function is sudden due to inability of the compensatory mechanisms to maintain the perfusion in the renal arteries

There is increased production of certain vasodilating factors such as nitric oxide, in patients with cirrhosis and portal hypertension and to a lesser extent in systemic circulation .This leads to both splanchnic and systemic vasodilatation. Thus there is splanchnic blood pooling as there is also increased resistance to the flow of the portal blood through the fibrosed liver.

As a result of all above mechanisms, the effective circulating intravascular volume decreases. Stimulation of carotid baroreceptors thereby increasing the activity of sympathetic nervous system (SNS). Also there is decrease in the effective volume of renal blood flow stimulating the renin angiotensin aldosterone system (RAAS). There is decreased peripheral vascular resistance and renal vasoconstriction resulting in a hyper dynamic circulation.

As the cirrhosis progresses, this process becomes a vicious cycle. There by further increase in splanchnic vasodilatation, worsening the renal vasoconstriction.

Effect of stimulation of the Renal SNS:

Reflexes such as hepato renal reflex determines the renal vasoconstriction in response to increased pressure in hepatic sinusoids. Renal sympathetic system mediates this process.

The following are the problems with assay , that makes it difficult as a diagnostic tool:

- It needs further standardization.
- The levels are highly variable as they may be altered in infection and by drugs such as steroids ,ACE inhibitors and calcineurin inhibitors.
- Also assay is a costlier technique.

Use of Cystatin C is still not validated though it is a marker for fibrosis progression in liver cirrhosis because this could represent a possible bias during the process of interpretation of the results.

Renal Doppler Ultrasonography:

The major pathology behind all these is renal vasoconstriction. Assesment of this renal vasoconstriction is possible by using Doppler ultrasound of the renal arteries through an index called renal resistive index (RI). There have been numerous studies conducted to elicit the use of renal resistive index in cirrhosis patients thereby identifying early renal dysfunction. It is determined using the formula

'Renal Resistive Index'

"RI" = "Peak systolic frequency shift - Lowest diastolic frequency shift"

"Peak systolic frequency shift"

A high RI value (>0.7) has been documented in cirrhotic patients even in whom RFT is norm al. Thus RI is increased in cirrhosis when compared to the normal population.

Future development of HRS in patients with cirrhosis can be predicted to some extent by early detection of renal vasoconstriction through Doppler

ultrasound. “HRS develops in 26% of patients with elevated resistive indices compared with 1% of those with normal indices ($P < 0.001$) and the probability that patients with high RI would subsequently develop HRS is 55%.”

A gradient decreasing from the hilum towards the outer cortex is exhibited normally by RI. In cirrhotic patients with diuretic responsive ascites this gradient is well maintained. Whereas as the severity increases and in cirrhotic patients with refractory ascites this gradient is lost. Renal cortex vasoconstriction is suspected when RI at the level of the cortex measured in interlobular arteries is high. This happens earlier even before serum creatinine raises . In cirrhotic patients an increased RI in spite of normal values of serum creatinine should raise the suspicion that they are at a greater risk for development of renal dysfunction and also elevation of serum creatinine.

Liver transplantation decreases the RI. Thus renal RI assessment using Doppler ultrasound can be used as an early marker for renal impairment in cirrhosis patients. The disadvantage is that “raised RI does not differentiate whether the cause of renal dysfunction is due to vasoconstriction alone or if it is associated with intrinsic kidney damage.”

HEPATO PULMONARY SYNDROME

It is defined as “Clinical disorder associated with advanced liver disease, pulmonary vascular dilatation and a defect in oxygenation in the absence of detectable primary cardiopulmonary disease”

Among the patients with decompensated cirrhosis almost about 1/3rd have reduced arterial oxygen saturation. They may even be cyanosed. “Po2 is < 80mmHg (10.6 kPa) and the alveolar – arterial oxygen gradient is > 15 mmHg (2 kPa) breathing room air”.

It is characterised by:

- Orthodeoxia (fall in the arterial Po2 in the upright position.
- Platypnoea (shortness of breath relieved by lying down).

There is intrapulmonary shunting due to marked dilatation of precapillary and capillary vessels leading to the diffusion limitation of capillary oxygenation and ventilation – perfusion mismatch.

The probable vasoactive substances that could induce pulmonary vasodilatation in cirrhosis include NO, endothelin - 1 and tumour necrosis factor α. HPS leads to poorer quality of life and the mortality rate is twice that of cirrhotic patients without HPS

DIAGNOSIS

Diagnosis is by demonstration of pulmonary vasodilatation and an increased alveolar – arterial oxygen gradient on breathing room air. The demonstration of abnormal passage of microbubbles through the pulmonary circulation into the left side of the lung can be made by contrast - enhanced echocardiograph .

Other less sensitive techniques include Technetium 99m (99m Tc) macroaggregated albumin lung scanning . Pulmonary angiography shows large pulmonary arteriovenous shunts. Exclusion of intracardiac shunts is done bythe transoesophageal contrast echocardiography.

No effective pharmacological therapy has been found. In some patients, Transjugular intrahepatic portosystemic shunt (TIPS) has improved arterial oxygen saturation . But the results are unpredictable.

Currently, the only effective treatment is liver transplantation. Indication for liver transplant is progressive and severe hypoxaemia. However hypoxemia following transplantation may take weeks or months to resolve. When pulmonary arteriovenous shunts are large reversal is not always possible. So coil embolotherapy , should precede transplant.

PORTOPULMONARY HYPERTENSION

It is defined as, “portal hypertension and a mean pulmonary artery pressure above 25 mmHg and pulmonary vascular resistance above 240 dynes/s/cm 5 , in the absence of other diseases associated with pulmonary hypertension” and can occur with hepatic or prehepatic portal hypertension.

About 5% of transplant candidates have portopulmonary hypertension. Patients mostly complain of non - specific chest discomfort or dyspnoea on exertion. A right ventricular heave or a loud second heart sound is the usual finding. The pulmonary arteries show dilatation and thickening of the wall and, rarely, thrombi. There is plexogenic pulmonary arteriopathy. Significant pulmonary hypertension (mean pulmonary artery pressure > 35 mmHg) can result in perioperative deaths from acute right ventricular failure. Thus it is a relative contraindication to liver transplant. So all liver transplant candidates should be screened using echocardiography.Treatment is with prolonged oral sildenafil . Response is good with a reduction in pulmonary vascular resistance and pulmonary artery. Bosentan is an alternative treatment but the limitation is that it is not recommended for patients with moderate to severe hepatic impairment.

BONE DISEASE IN CIRRHOSIS:

Vitamin D malabsorption due to cholestasis is responsible for osteomalacia. Ultimately this leads to increase in the rate of bone resorptionwhich exceeds that of new bone formation in patients with cirrhosis, resulting in bone loss.

For the determination of osteoporosis and osteopenia , Dual x-ray absorptiometry (DEXA) is a useful. Bisphosphonates are the treatment of choice as they are effective at inhibiting resorption of bone and highly efficacious in the treatment of osteoporosis.

INFECTIONS

In cirrhotic patients, bacteraemia, pneumonia and urinary tract infections are common. This is because of the bacteriologically sterile nature of human liver and the portal venous blood rarely contains any organisms.

But in the cirrhotic patients, the intestinal bacteria could reach the general circulation either by passing through a faulty hepatic filter or through porto systemic collaterals. About 10 to 20% patients with ascites are prone to spontaneous bacterial peritonitis

Spontaneous bacterial empyema in a pre - existing hydrothorax can also occur. Bacterial meningitis should be considered in the cirrhotics with febrile

coma. In cirrhotic patients with unexplained pyrexia or deterioration, sepsis should always be suspected. Other infections common are pneumonia, lymphangitis, endocarditis.

CIRRHOTIC CARDIOMYOPATHY

Cardiac abnormalities in cirrhosis are mainly due to the toxic effect of alcohol on the heart. But cirrhosis per se can cause cardiac dysfunction.

The presence of one or more of the following defines cirrhotic cardiomyopathy

- systolic and/or diastolic dysfunction
- baseline increased cardiac output but blunted ventricular response to stimuli
- electrophysiological abnormalities including prolonged Q – T interval on electrocardiography and chronotropic incompetence .
- absence of overt left ventricular failure at rest

Overt cardiac failure may be precipitated by major stresses such as TIPS, liver transplantation or sepsis may .

PATHOGENESIS

- the cardiomyocyte β - adrenergic signalling pathway

- changes in the lipid composition causing decreased fluidity of the cardiomyocyte plasma membrane and the negative effects of substances such as nitric oxide, carbon monoxide and endo cannabinoids on heart muscle.

The treatment of cirrhotic cardiomyopathy includes diuretics, long - term aldosterone antagonists and beta - blockers. Avoid vasodilators and digitalis.. Cardiac function is improved by liver transplantation.

MATERIALS AND METHODS

SETTING :

The study was conducted on 100 patients admitted in Government Rajaji Hospital & Madurai Medical College during the study period from March 2018 to August 2018.

INCLUSION CRITERIA

All patients aged 18 years and above diagnosed to have cirrhosis of liver admitted in Medicine Department and Medical Gastroenterology department.

EXCLUSION CRITERIA

- Previous history of portal hypertensive bleeding, hepatocellular carcinoma, portal vein thrombosis.
- Previous or current treatment with β blockers, diuretics or other vasoactive drugs.
- Budd Chiari Syndrome and other causes of non-cirrhotic portal hypertension.

ANTICIPATED OUTCOME:

Increased right lobe of liver diameter to serum albumin ratio correlates with the severity of varices in cirrhosis patients.

DATA COLLECTION

- After confirmation of diagnosis and explaining the purpose & procedure of study, written informed consent in Tamil will be obtained. The selected patients will be evaluated as per pro forma.
- Serum urea and serum creatinine will be taken at the time of admission. Ultrasonography and renal doppler for measuring renal resistive index will be taken prior to coronary angiography. Serum urea and serum creatinine will be taken 24 hours and 48 hours post procedure

DESIGN OF STUDY: Prospective analytical study.

PERIOD OF STUDY: March 2018 to August 2018

COLLABORATING DEPARTMENTS:

Department of Biochemistry

Department of Radiology

Department of Medical gateroentrology

ETHICAL CLEARANCE: Approved

CONSENT: Individual written and informed

ANALYSIS: STATISTICAL METHODS:

The data collected during the study was formulated into a master chart in Microsoft office excel and statistical analysis was done with help of computer using statistical software package SPSS V.17 for windows. Using this software, frequencies, range, mean, standard deviation and 'p'were calculated through student 't' test, one way ANOVA, pearson correlation and chi square test .

P value of < 0.05 was taken as significant.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: NIL

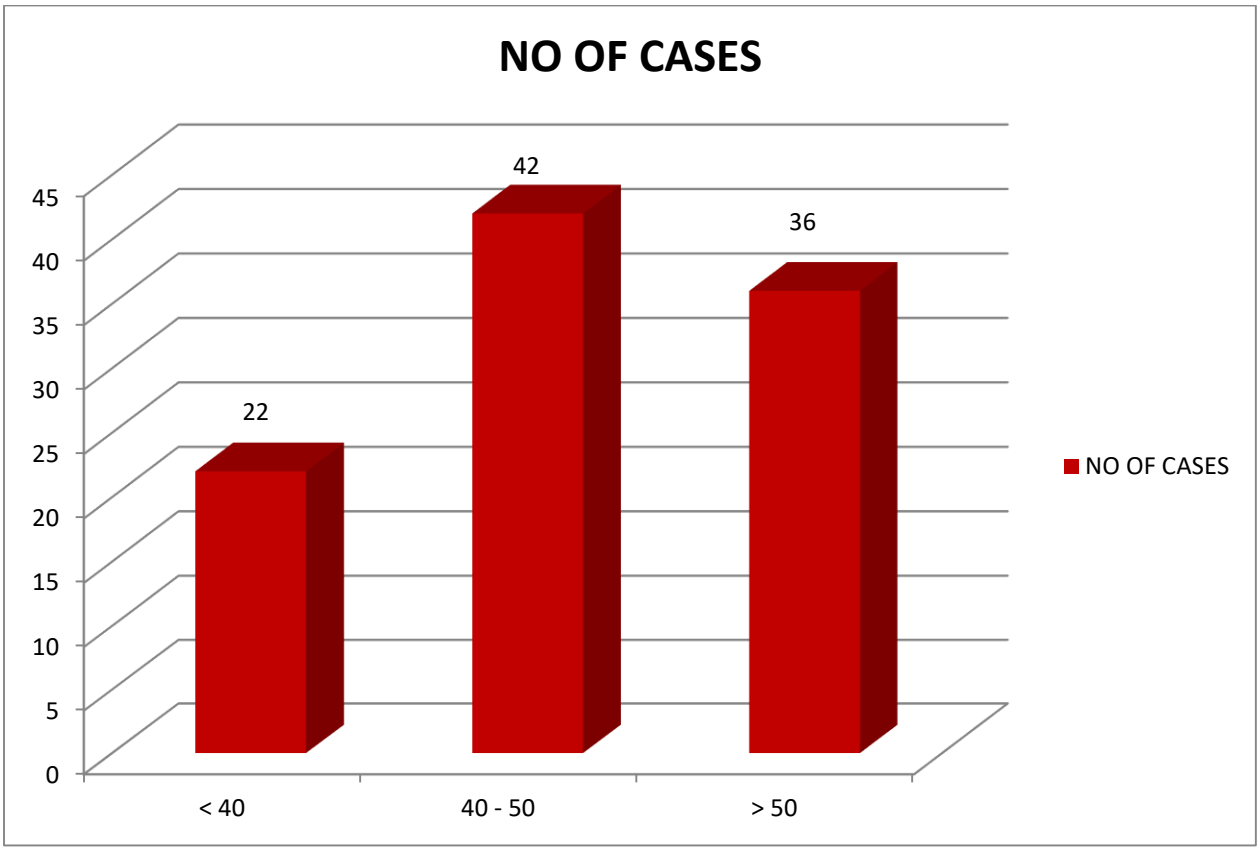
PARTICIPANTS: Patients of age>18yrs, admitted as in-patients at Govt.Rajaji hospital, Madurai who are diagnosed as cirrohosis.

OBSERVATION AND RESULTS

TABLE 1: AGEWISE DISTRIBUTION

AGE	*NUMBER OF CASES*
< 40	22
40 – 50	42
> 50	36
Total	100

CHART 1: AGEWISE DISTRIBUTION

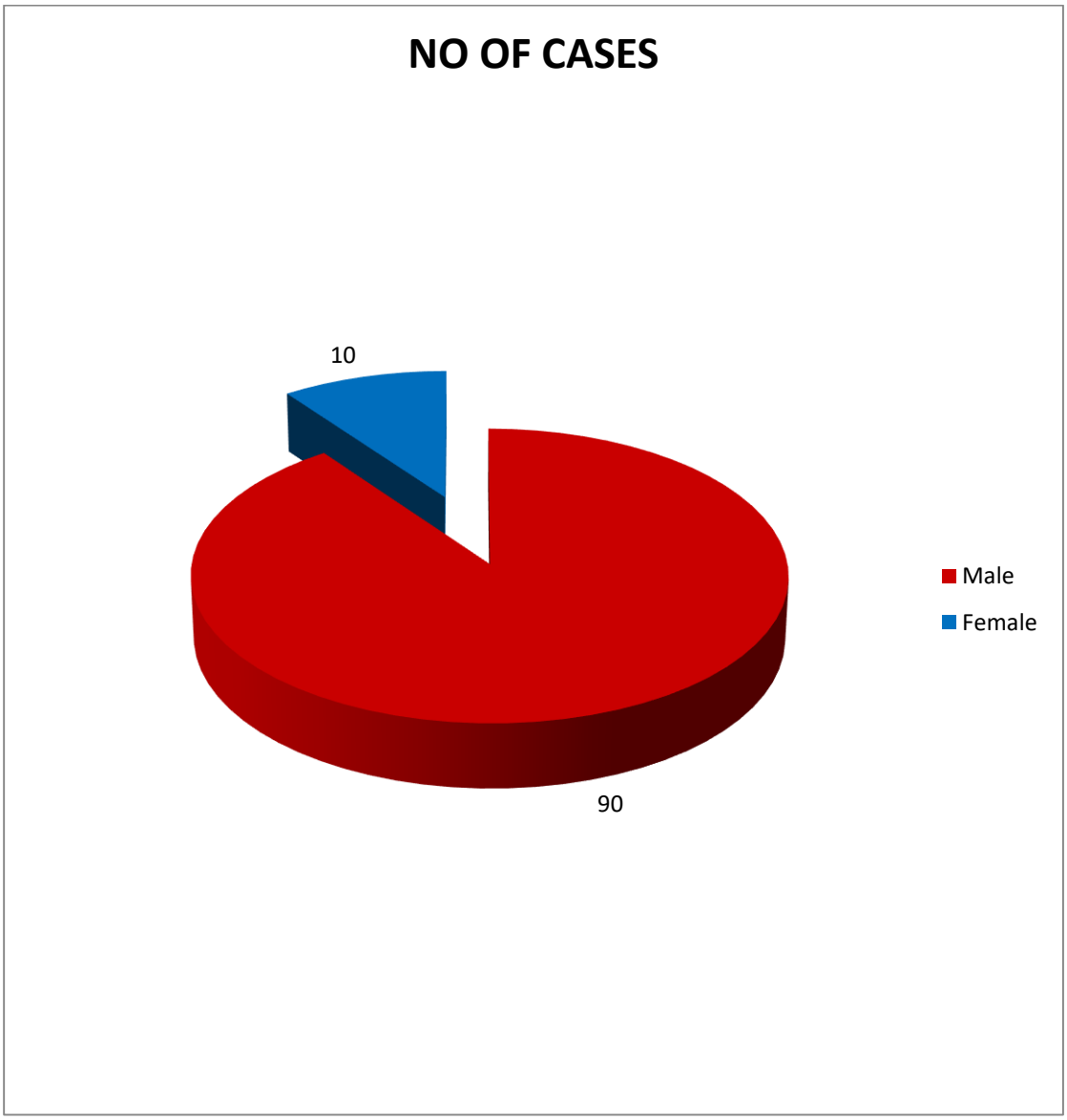


Among 100, about 42% belong to the age group of 40 to 50.

TABLE 2: GENDER WISE DISTRIBUTION

SEX	***NO OF CASES***
Male	90
Female	10
Total	100

CHART 2: GENDER WISE DISTRIBUTION

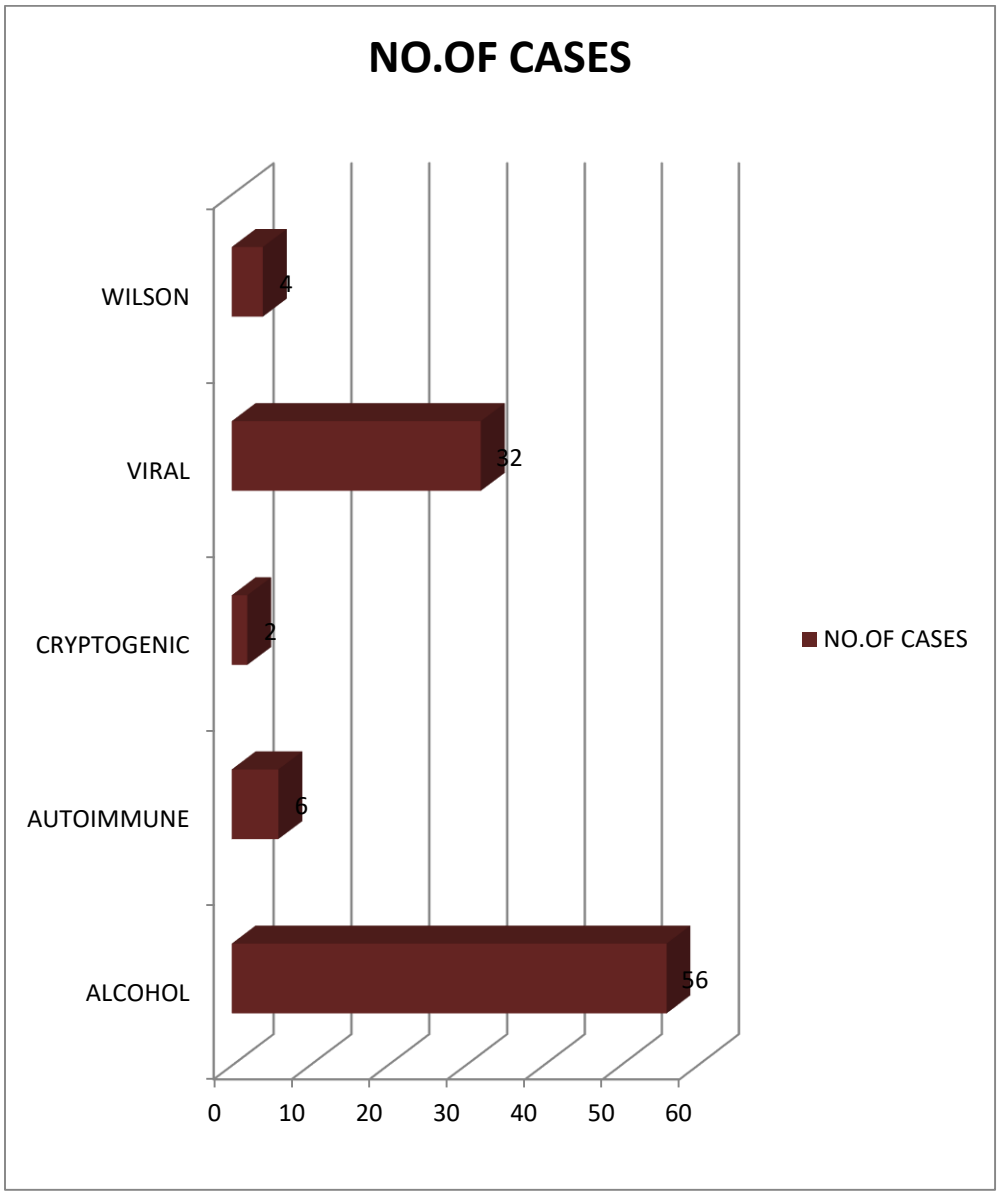


Among 100, there were 90 male and 10 females.

TABLE 3: DISTRIBUTION WITH RESPECT TO ETIOLOGY

ETIOLOGY	NO.OF CASES
ALCOHOL	56
AUTOIMMUNE	6
CRYPTOGENIC	2
VIRAL	32
WILSON	4
Total	100

CHART 3: DISTRIBUTION WITH RESPECT TO ETIOLOGY

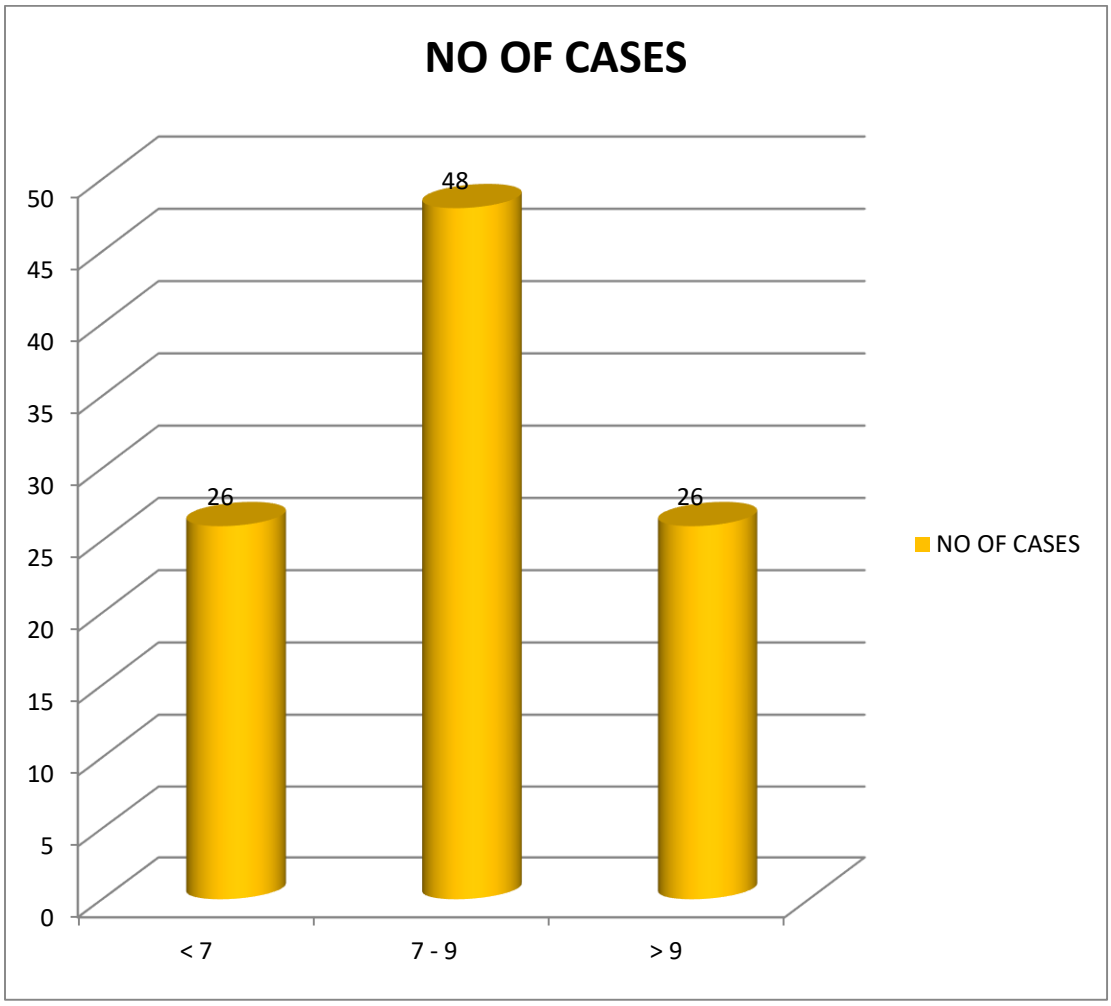


Alcoholism is the most common etiology contributing about 56% which is followed by viral 32%

TABLE 4: SERUM BILIRUBIN VALUES

SR.BILIRUBIN	NO OF CASES
< 7	26
7 - 9	48
> 9	26
Total	100

CHART 4: SERUM BILIRUBIN VALUES

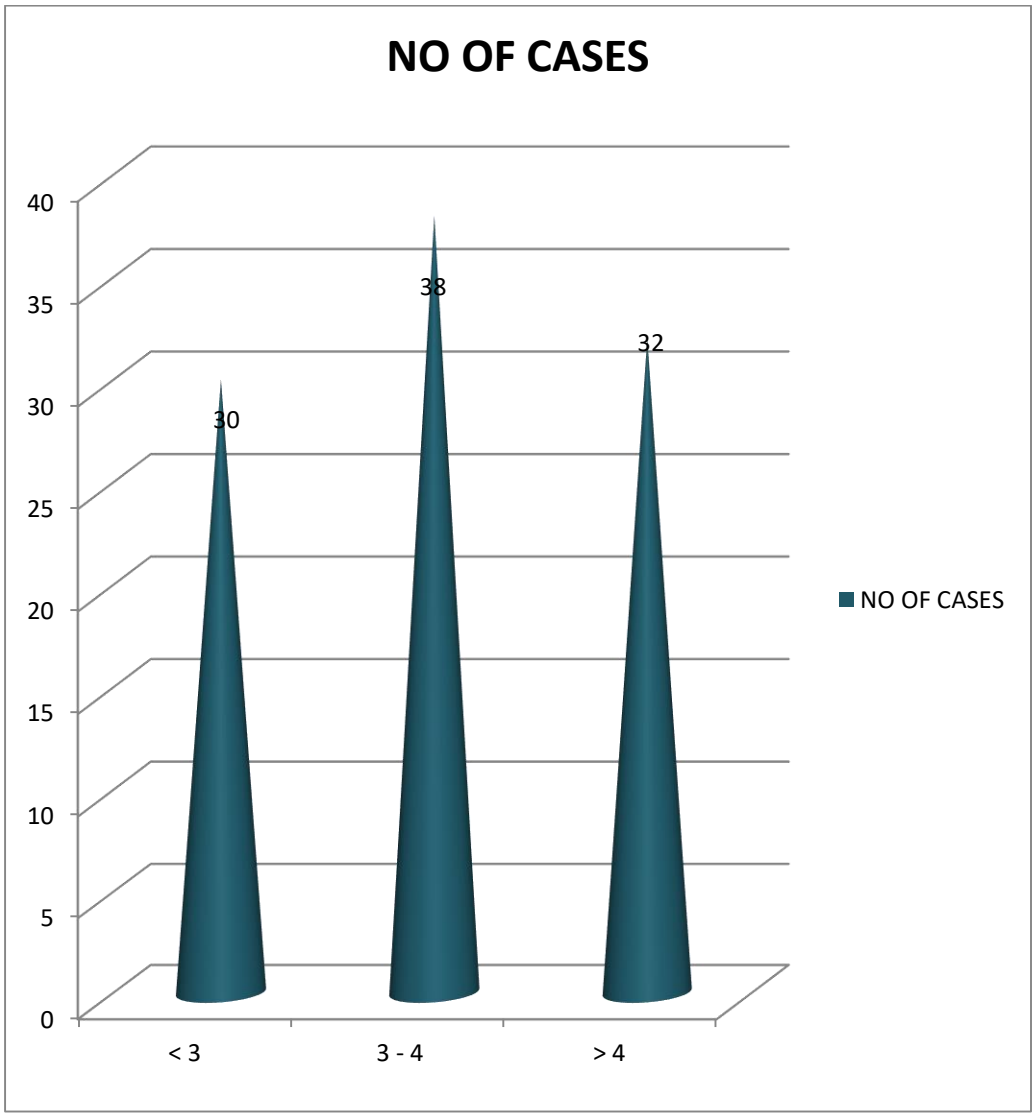


The serum bilirubin values of most patients about 48% lie between 7-9 mg/dl.

TABLE 5: SERUM ALBUMIN VALUES

ALBUMIN	NO OF CASES
< 3	30
3 - 4	38
> 4	32
Total	100

CHART 5: SERUM ALBUMIN VALUES

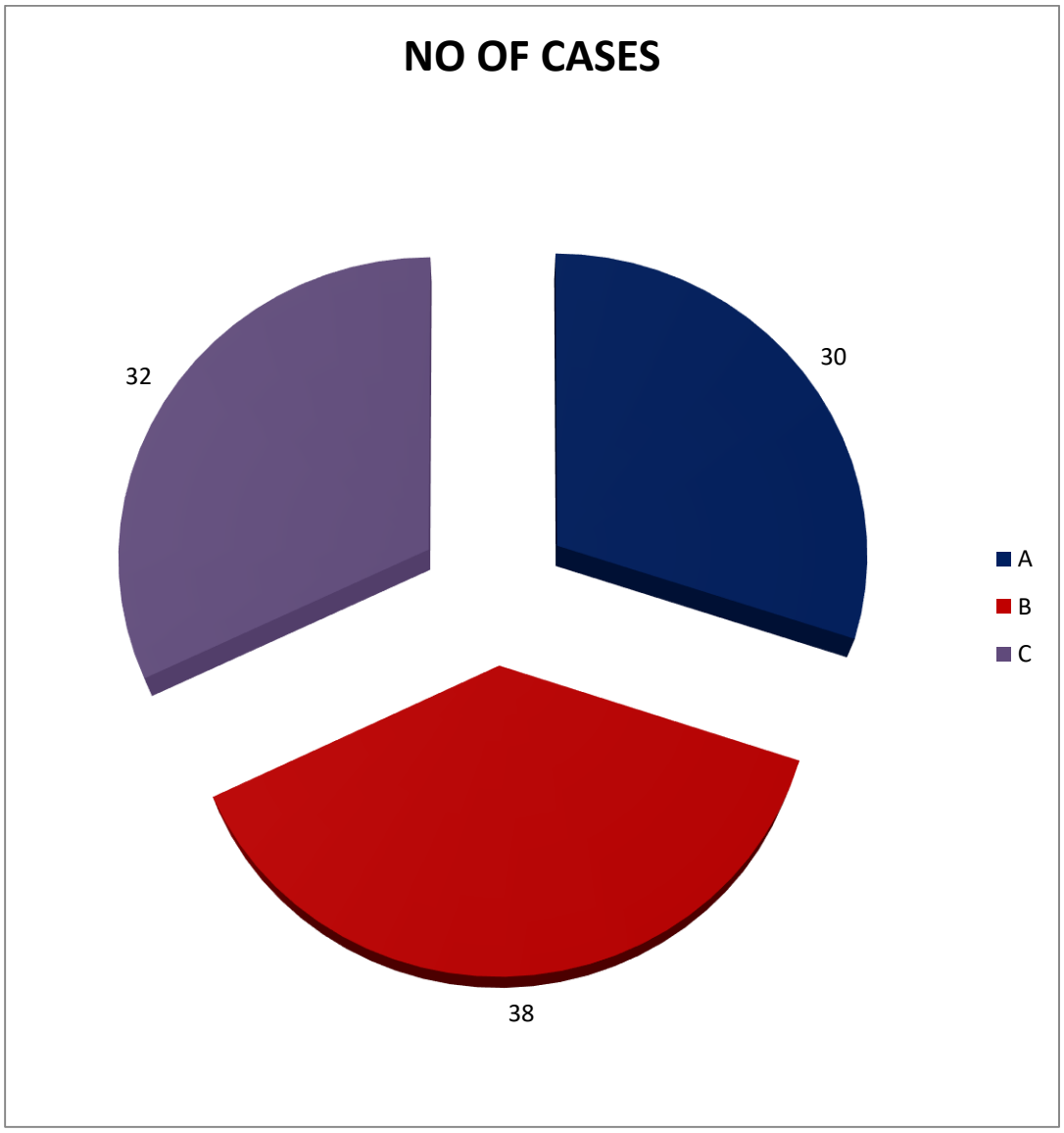


Serum albumin levels of most of the patients about 38% fall between 3-4 g/dl.

TABLE 6: DISTRIBUTION BASED ON CHILD PUGH

CHILD PUGH	NO OF CASES
A	30
B	38
C	32
Total	100

CHART 6: DISTRIBUTION BASED ON CHILD PUGH

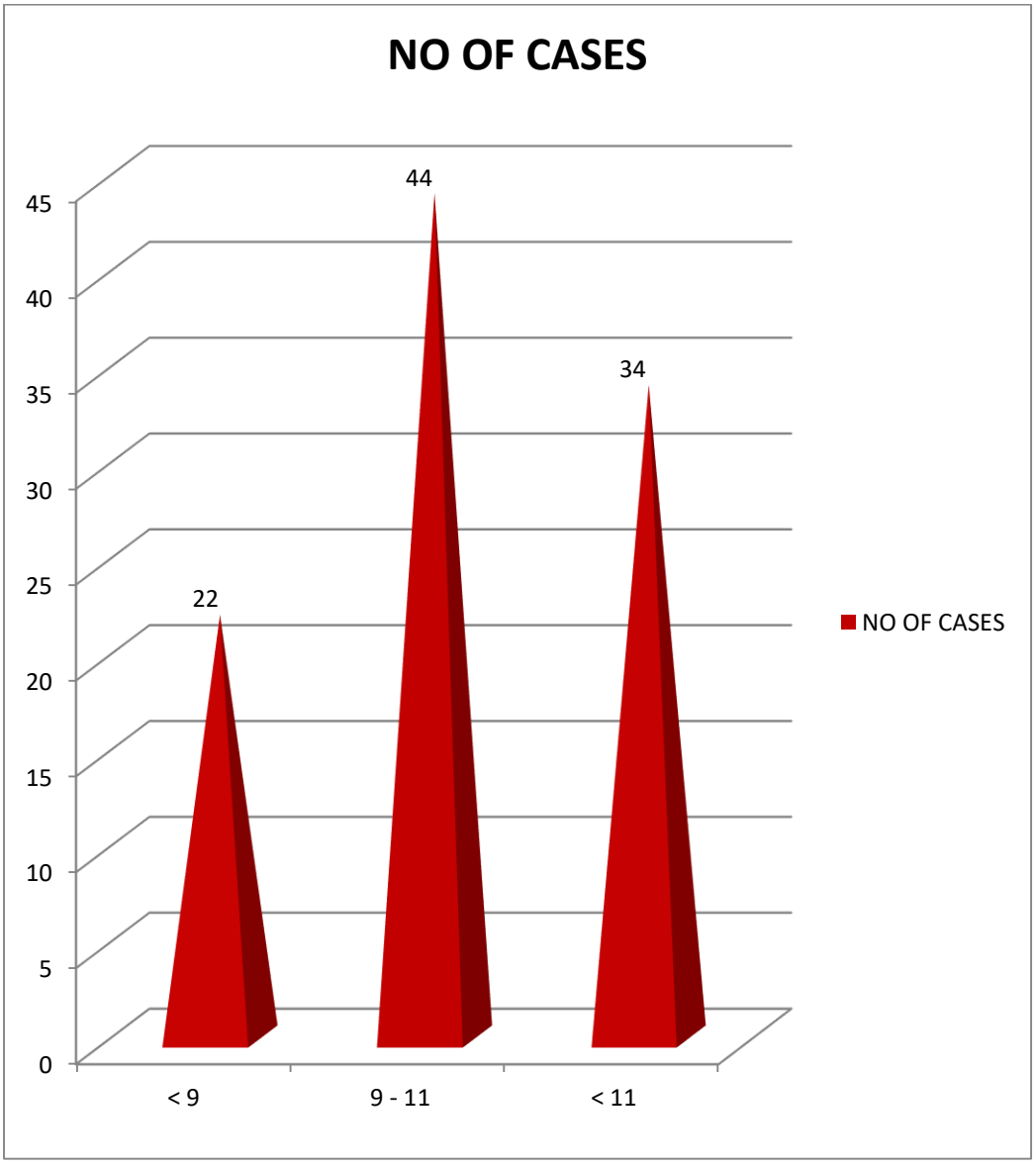


About 38% fall under category B of Child Pugh classification

TABLE 7: DISTRIBUTION BASED ON RIGHT LOBE LIVER DIAMETER

RIGHT LOBE OF LIVER	NO OF CASES
< 9	22
9 - 11	44
< 11	34
Total	100

CHART 7: DISTRIBUTION BASED ON RIGHT LOBE LIVER DIAMETER

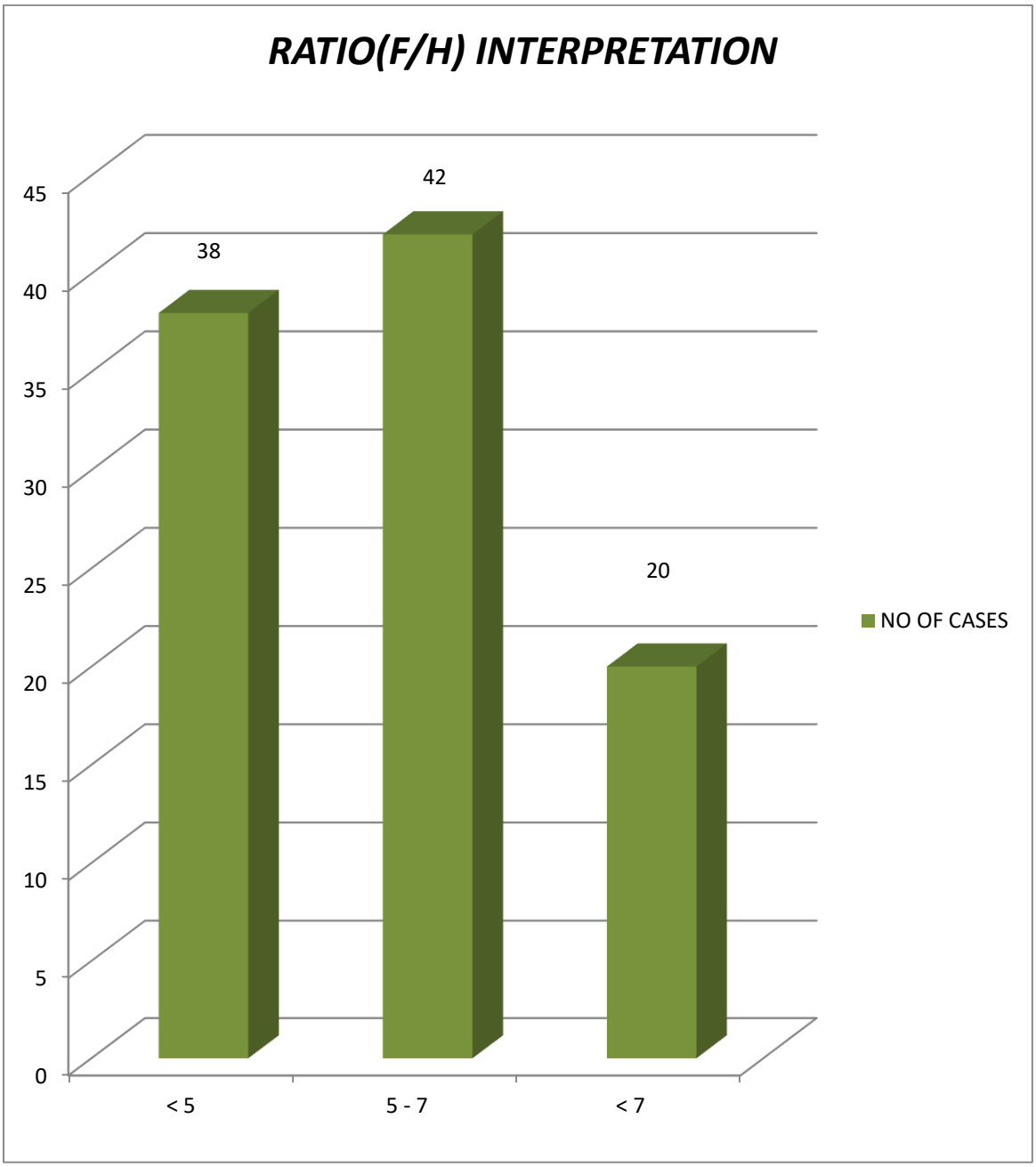


The right lobe liver diameter of about 44% of patients fall between 9-11cm.

TABLE 8: RATIO (F/H) INTERPRETATION

RATIO(F/H)	NO OF CASES
< 5	38
5 - 7	42
< 7	20
Total	100

CHART 8: RATIO(F/H) INTERPRETATION

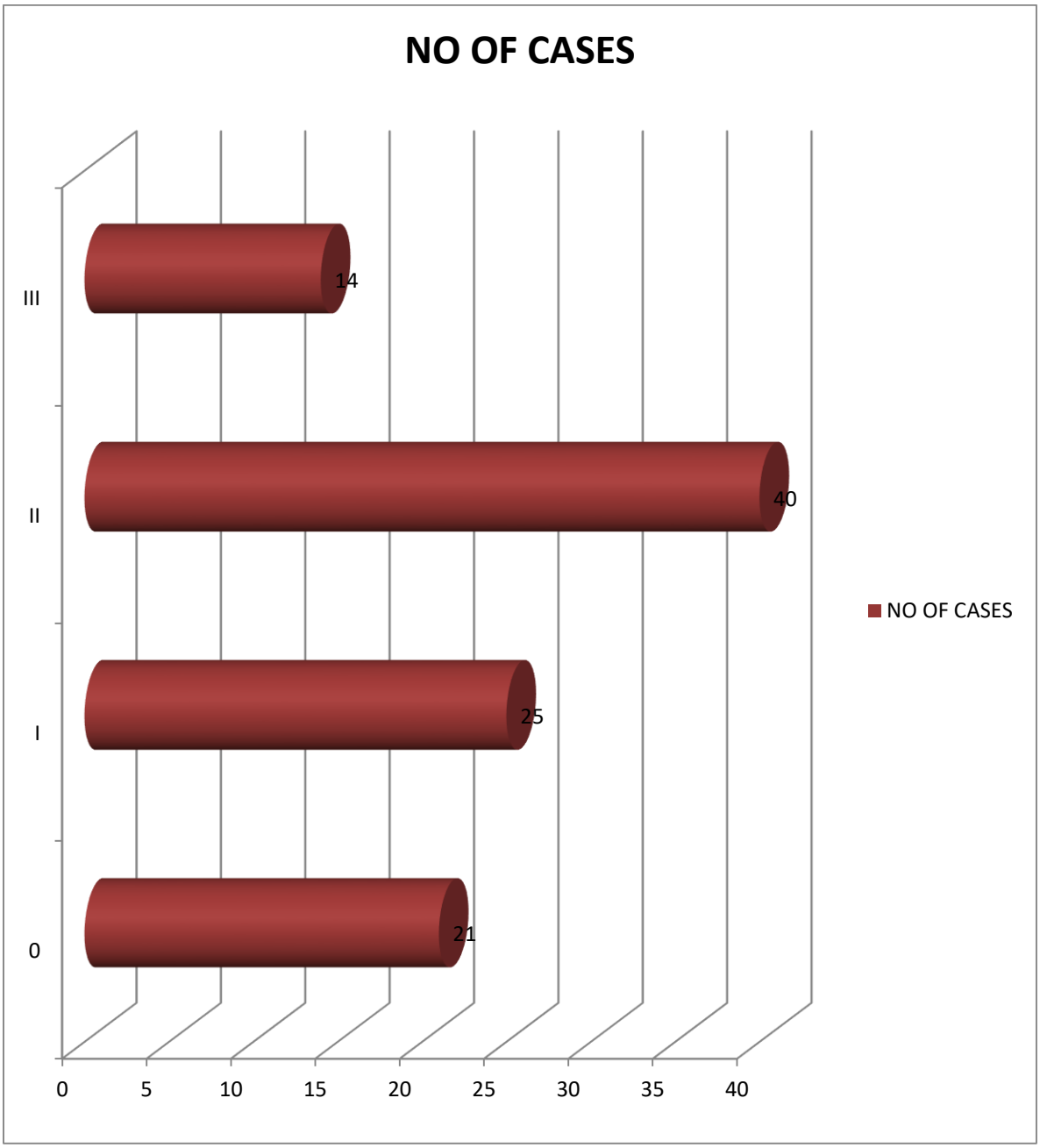


The F/H ratio of about 42% of patients falls between 5-7.

TABLE 9: VARICEAL GRADE WISE DISTRIBUTION

VARICEAL GRADE	NO OF CASES
0	21
I	25
II	40
III	14
Total	100

CHART 9: VARICEAL GRADE WISE DISTRIBUTION

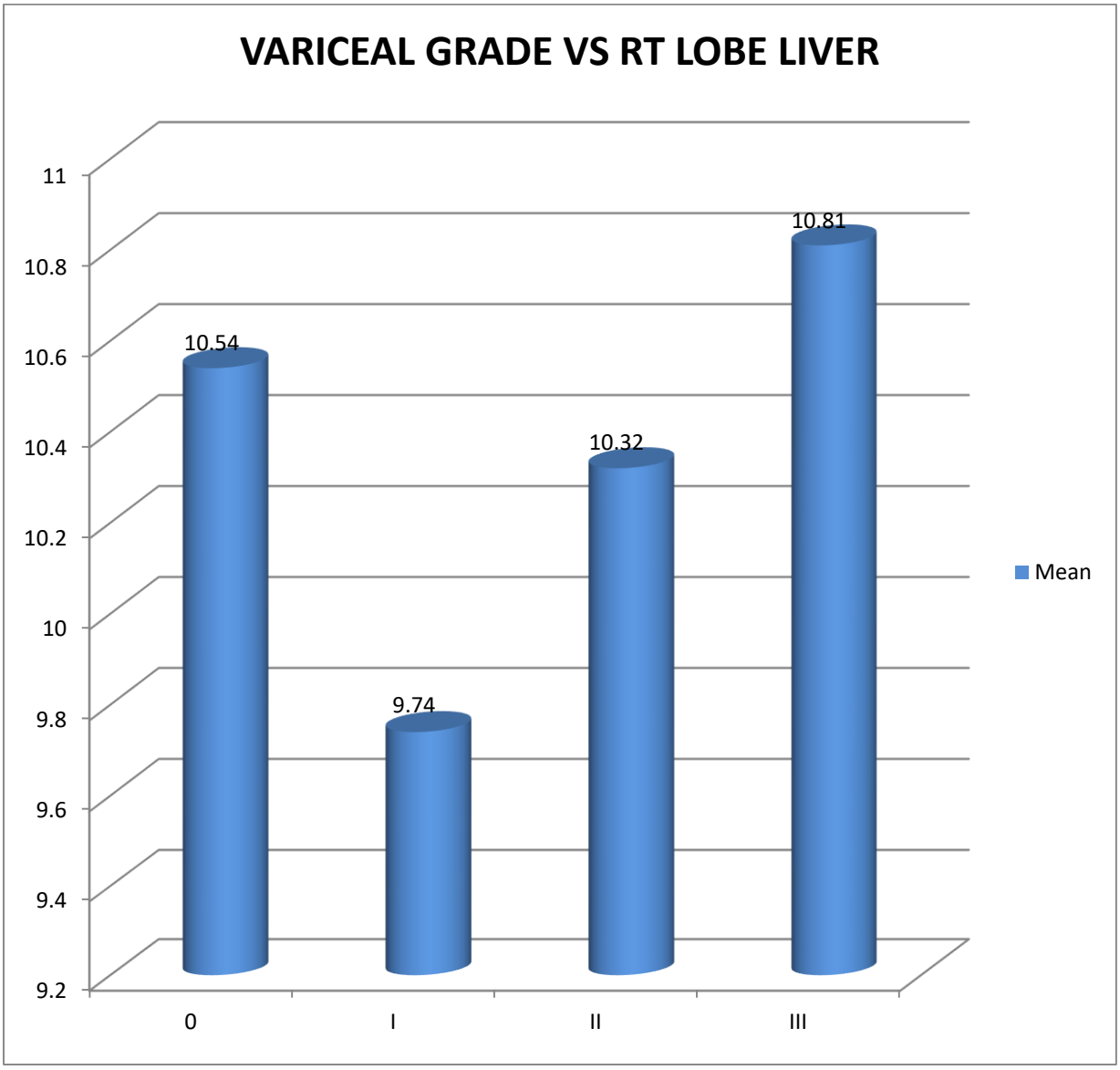


About 40% of the study population have been found to have grade 2 varices.

TABLE 10: VARICEAL GRADE VS RT LOBE LIVER DIAMETER

VARICEAL GRADE VS RT LOBE LIVER			
variceal grade vs rt lobe liver	Mean	SD	p' value
0	10.54	1.15	
I	9.74	1.02	
II	10.32	1.22	
III	10.81	1.42	0.033
		P VALUE	Significant

CHART 10: VARICEAL GRADE VS RT LOBE LIVER

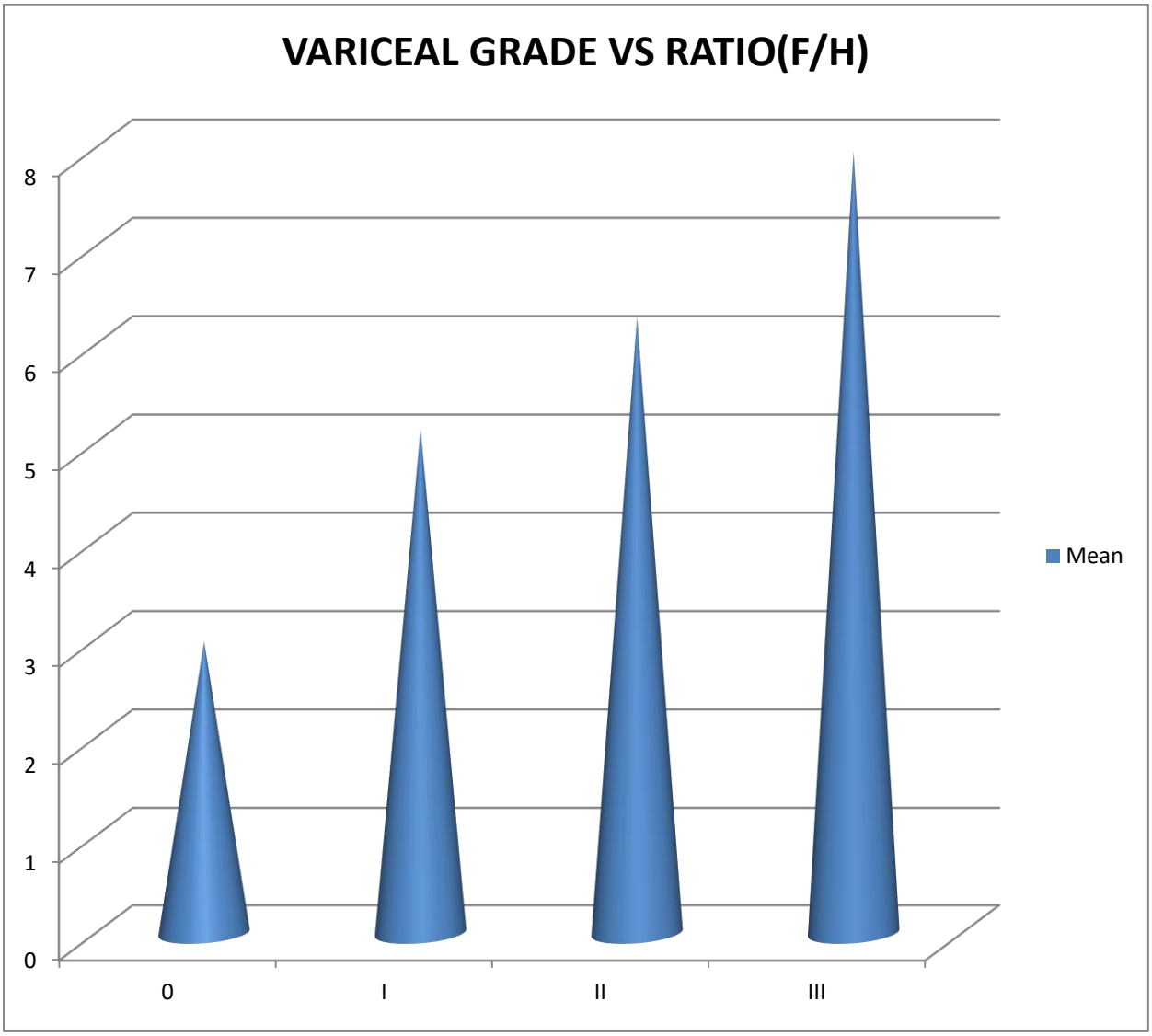


For those with grade 3 varices when compared with right lobe liver diameter the standard deviation obtained is 1.42 which corresponds to a p value of 0.033 which is significant. It proves that there is direct correlation between right lobe liver diameter and oesophageal varices.

TABLE 11: VARICEAL GRADE VS RATIO(F/H)

VARICEAL GRADE VS RATIO(F/H)			
variceal grade vs Ratio (F/H)	Mean	SD	p' value
0	2.98	0.52	
I	5.14	0.59	
II	6.28	1.05	
III	7.96	1.34	<0.001
			Significant

CHART 11: VARICEAL GRADE VS RATIO (F/H)



For those with grade 3 varices when compared to F/H ratio with a mean value of 7.96 the standard deviation obtained is 1.34 which corresponds to the p value of <0.001which is significant.

TABLE 12: VARICEAL GRADE VS BILIRUBIN

VARICEAL GRADE VS BILIRUBIN			
variceal grade vs sr bilirubin	Mean	SD	p' value
0	7.35	2.27	
I	8.40	2.13	
II	8.45	1.86	0.164
III	7.76	1.55	Not sig

CHART 12: VARICEAL GRADE VS BILIRUBIN

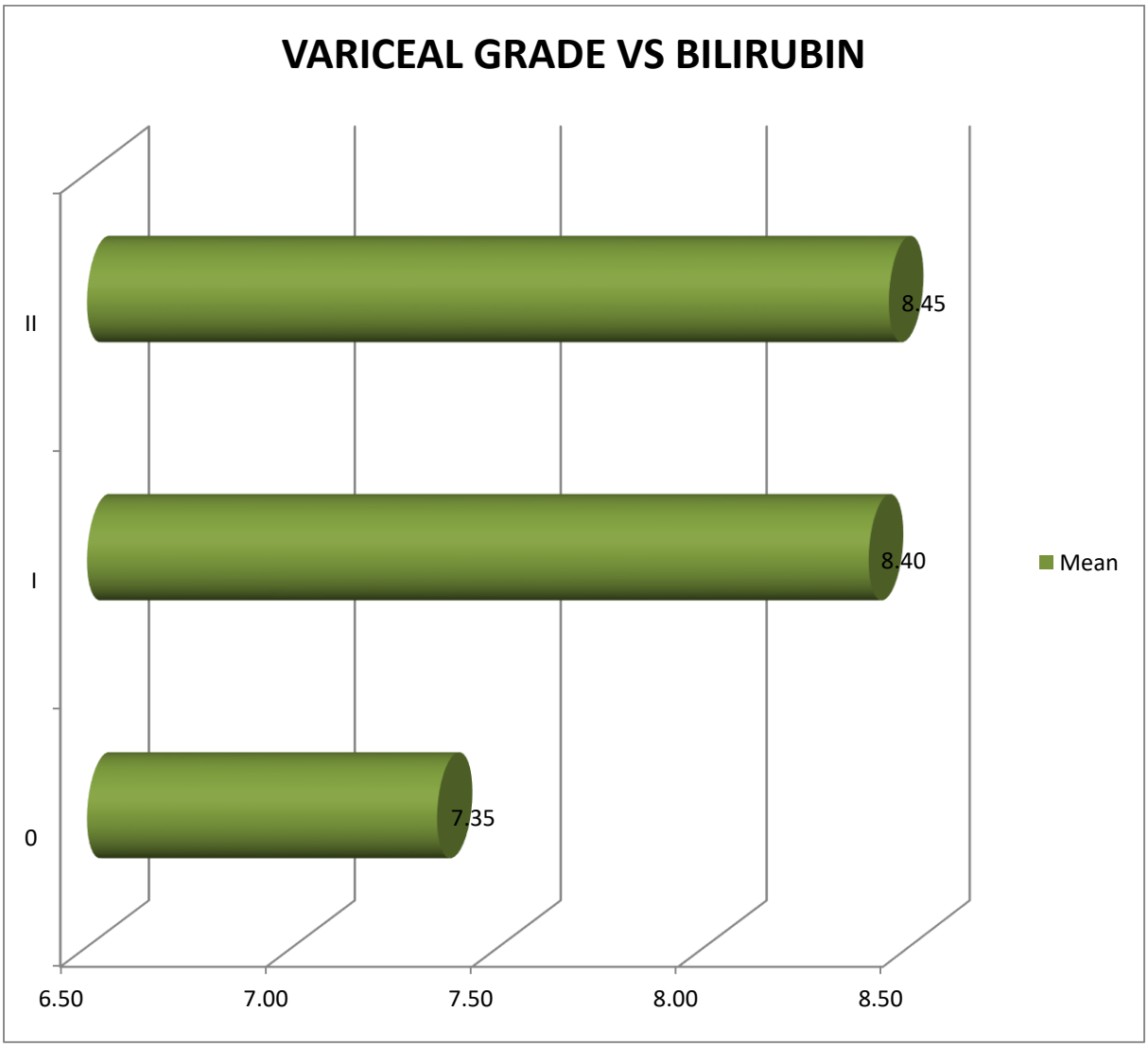


TABLE13: VARICEAL GRADE VS ALBUMIN

VARICEAL GRADE VS ALBUMIN			
variceal grade vs albumin	Mean	SD	p' value
0	3.64	0.75	
I	3.54	0.93	
II	3.66	0.66	0.151
III	3.1	0.98	Not sig

CHART 13: VARICEAL GRADE VS ALBUMIN

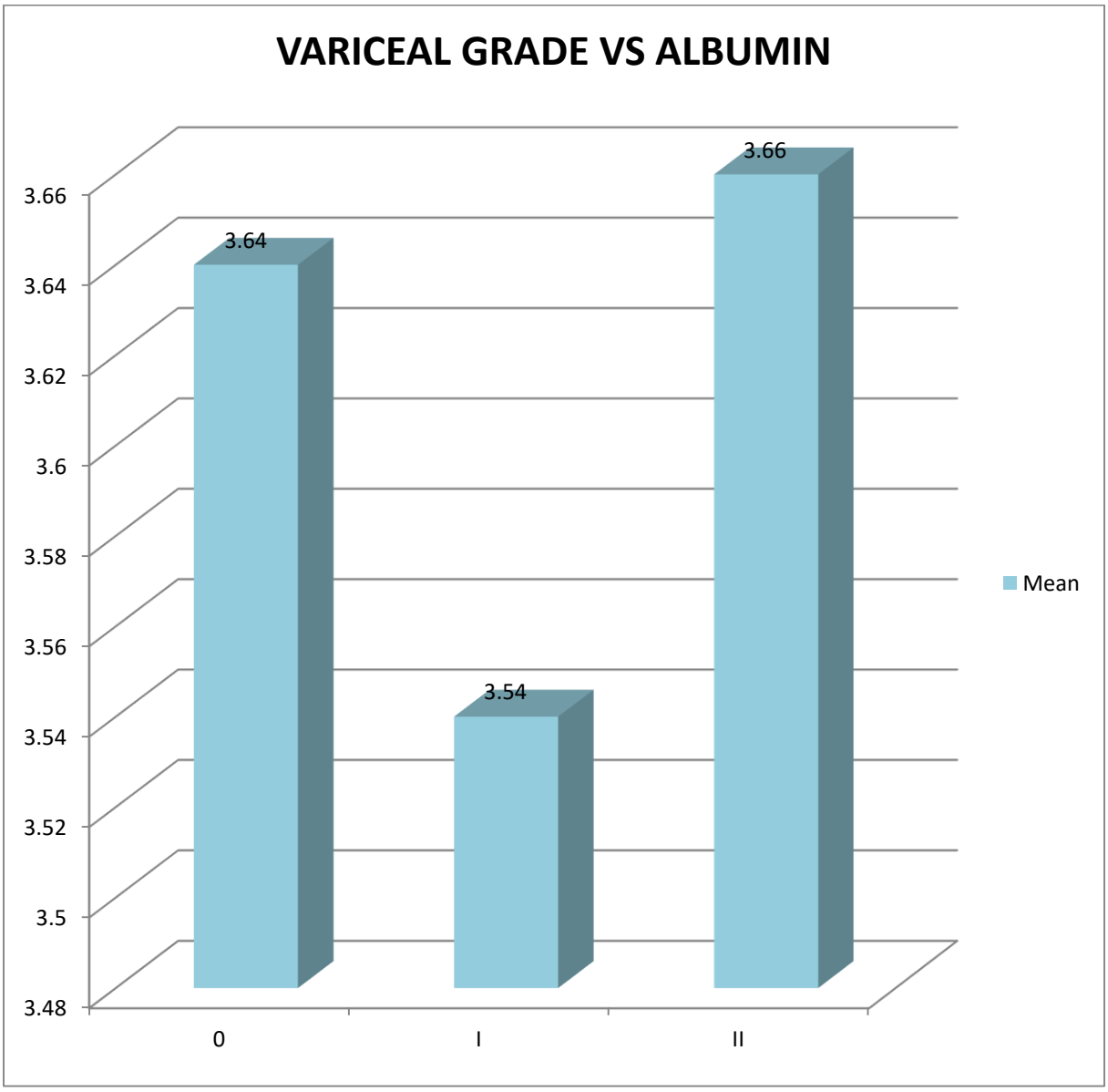
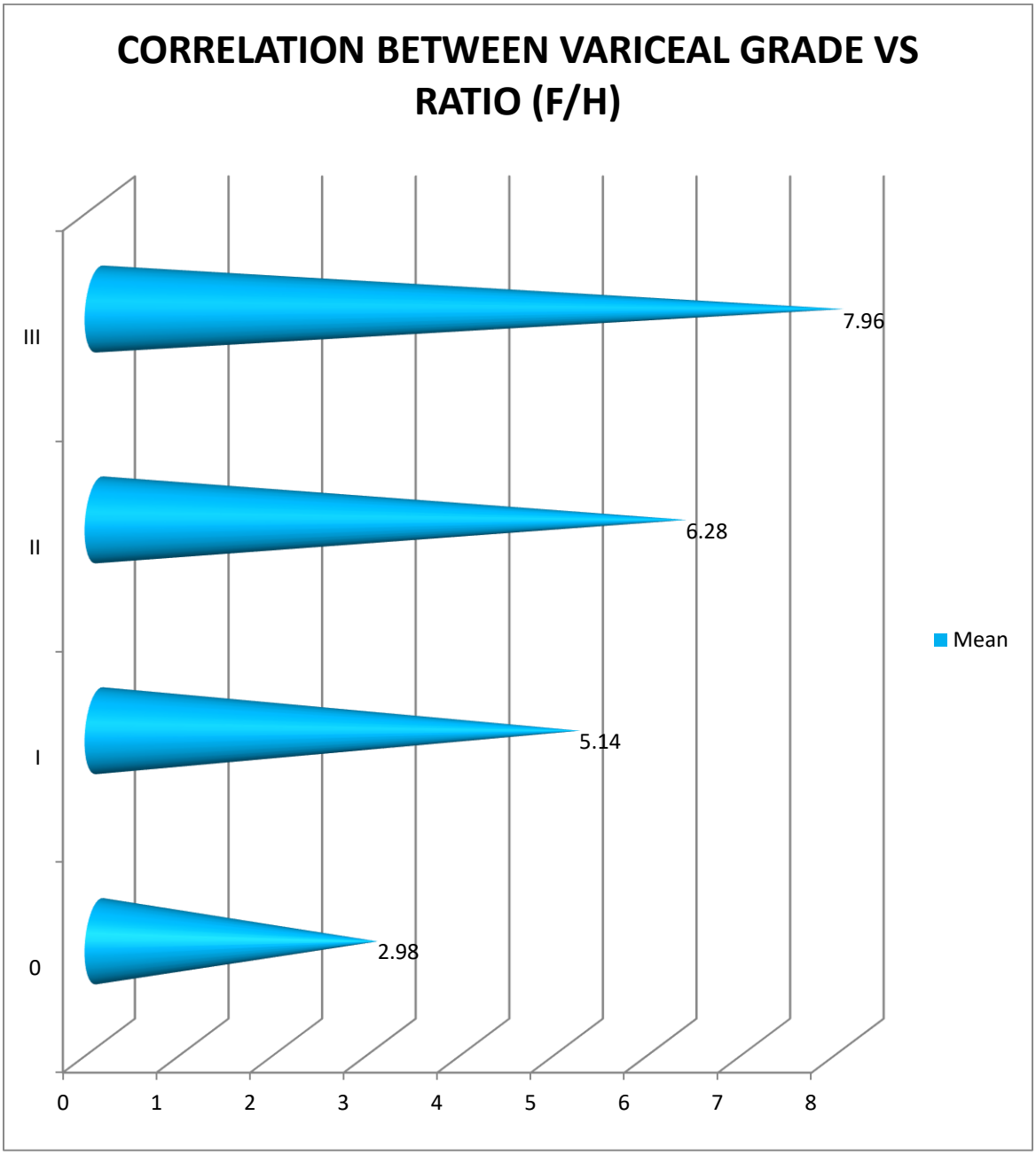


TABLE 14: CORRELATION BETWEEN VARICEAL GRADE VS RATIO (F/H)

CORRELATION BETWEEN VARICEAL GRADE VS RATIO (F/H)			
variceal grade vs Ratio (F/H)	Mean	SD	p' value
0	2.98	0.52	
I	5.14	0.59	
II	6.28	1.05	
III	7.96	1.34	<0.001

Significant

CHART 14: CORRELATION BETWEEN VARICEAL GRADE VS RATIO (F/H)



The correlation coefficient is found to be 0.86 which is a good correlation.

DISCUSSION

Among the study population of 100, about 42% belong to the age group of 40 to 50. Among 100, there were 90 male and 10 females. In this study , Alcoholism is the most common etiology contributing about 56% which is followed by viral 32%. The serum bilirubin values of most patients about 48% lie between 7-9 mg/dl . Serum albumin levels of most of the patients about 38% fall between 3-4 g/dl. About 38% fall under category B of Child Pugh classification. The right lobe liver diameter of about 44% of patients fall between 9-11cm.

The F/H ratio of about 42% of patients falls within 5-7. About 40% of the study population have been found to have grade 2 varices. The standard deviation of the study population of 42% whose values fall with within F/H ratio of 5-7 is found to be 1.36. For those with grade 3 varices when compared with right lobe liver diameter the standard deviation obtained is 1.42 which corresponds to a p value of 0.033 which is significant.

It proves that there is direct correlation between right lobe liver diameter and oesophageal varices. For those with grade 3 varices when compared to F/H ratio with a mean value of 7.96 the standard deviation obtained is 1.34 which corresponds to the p value of <0.001which is significant.

The correlation coefficient is found to be 0.86 which is a good correlation. The right lobe liver diameter is a very easy parameter that can be measured simply as a part of ultrasound abdomen and serum albumin levels are measured as routine biochemical investigation.

Thus this method requires parameters which can be easily detected without any additional efforts and thereby carries increased compliance.

CONCLUSION

Higher grades of oesophageal varices was noted with higher right lobe of liver diameter to albumin ratios. Thus the Right lobe of liver to albumin ratio can be used as a screening tool to diagnose the presence of oesophageal varices.

Hence, this can identify subset of patients who require prophylactic endoscopic management. Therefore, this reduces the economic burden on the patients and reduces the cost of management

LIMITATIONS

- It is a small scale study.
- Long term follow up is not done.
- Liver biopsy which is gold standard for diagnosis of cirrhosis has not been done.

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PROFORMA

Name:

Age / Sex:

Occupation:

Presenting complaints:

H/O jaundice

H/O abdominal distension/pedal edema

H/O hematochezia/melena/hematemesis

H/O altered sensorium/altered sleep habit

H/O fever

H/O abdominal pain

H/O oliguria/dysuria/hematuria

Past History:

H/o DM, HT, CKD, CVD, DRUG INTAKE, CAD, Thyroid disorders, CLD,renal transplantation and blood transfusion.

PERSONAL HISTORY:

Alcohol intake/smoking/high risk behavior

Clinical Examination:

General Examination:

Consciousness,

Orientation to time,place,person

Pallor,

Jaundice,

Clubbing,

Lymphadenopathy,

Hydration status

Pedal edema

Other signs of hepatocellular failure

Vitals:

PR

BP

RR

SpO2

Urine output

Systemic examination:

CVS:

RS:

ABDOMEN:

Presence of distended and dilated veins

Direction of flow

Free fluid

Hepatomegaly/splenomegaly

CNS:

Laboratory investigations:

a) Complete blood count,

b) Renal function test,

c) Liver function test,

d) PT-INR

e) Serum albumin

f) ultrasonography abdomen

g) esophagoduodenoscopy

ABBREVIATIONS

- RFT - RENAL FUNCTION TEST
- AKI - ACUTE KIDNEY INJURY
- CLD - CHRONIC LIVER DISESASE
- CAD - CORONARY ARTERY DISEASE
- CCF - CONGESTIVE CARDIAC FAILURE
- Scr - SERUM CREATININE
- ECG – ELECTROCARDIOGRAM
- LFT - LIVER FUNCTION TEST
- HRS - HEPATORENAL SYNDROME
- MI - MYOCARDIAL INFARCTION
- RRI - RENAL RESISTIVE INDEX
- HPS - HEPATOPULMONARY SYNDROME
- PPH - PORTO PULMONARY HYPERTENSION

CONSENT FORM

ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர்: தேதி:

வயது: நோயாளிஎண்:

ஆராய்ச்சிசேர்க்கைஎண்:

இந்தஆராய்ச்சியின்விவரங்களும்அதன்நோக்கங்களும்முழுமையாகஎனக்குவிளக்கபட்டது.

எனக்குவிளக்கபட்டவிஷயங்களைநான்புரிந்துகொண்டுஎனதுமுழுமனதுடன்சம்மதிக்கிறேன்.

இந்தஆராய்ச்சியில்பிறரின்நிர்பந்தமின்றிஎன்சொந்தவிருப்பத்தின்பேரில்தான்பங்குபெறுகிறேன்மற்றும்நான்இந்தஆராய்ச்சியில்இருந்துஎந்தநேரமும்பின்வாங்கலாம்என்றும்அதனால்எந்தபாதிப்பும்எனக்குஏற்படாதுஎன்பதையும்புரிந்துகொண்டேன்.

நான்என்னுடையசுயநினைவுடன்மற்றும்முழுசுதந்திரத்துடன்இந்தமருத்துவஆராய்ச்சியில்பங்குகொள்ளசம்மதிக்கிறேன்.

MASTER CHART

S.No	Age	Sex	Etiology	Sr Bilirubin	Albumin	Child Pugh	Rt Lobe Liver	Ratio (F/H)	Variceal Grade
1	55	F	VIRAL	7.4	4.4	A	11.1	3.3	0
2	48	M	ALCOHOL	8.2	3	B	12.1	4.5	II
3	28	M	ALCOHOL	3	2.3	C	11.5	3.6	0
4	46	M	ALCOHOL	5	3.3	A	10.1	4.3	I
5	47	M	ALCOHOL	8	2.4	C	11.2	5.5	III
6	55	M	ALCOHOL	9	2.5	B	12.5	6.5	I
7	55	M	VIRAL	11	2.2	C	9.7	7.6	III
8	58	M	ALCOHOL	13	2.3	A	9.8	4.6	I
9	50	M	ALCOHOL	9	3.3	B	9.9	3.4	0
10	54	M	ALCOHOL	4	2.5	C	8.9	5.5	I
11	35	M	VIRAL	8.5	3.1	A	10.7	6.6	II
12	41	M	VIRAL	7.4	2.5	C	11.8	9.9	III
13	64	M	VIRAL	7.9	2.6	B	10	7.7	II
14	43	M	ALCOHOL	8.6	2.6	B	9.8	6.6	II
15	40	M	ALCOHOL	8.3	4.4	A	8.9	5.5	I
16	45	M	ALCOHOL	7.4	3.3	C	12.3	4.5	I
17	52	M	ALCOHOL	6.5	2.8	A	9.7	8.8	III
18	51	M	VIRAL	5.5	3.7	B	9.5	7.8	II
19	46	M	ALCOHOL	8	2.9	A	9.9	3.4	0
20	56	M	VIRAL	9	3.9	C	8.9	7.7	II
21	60	M	ALCOHOL	12.8	3.8	B	12	6.6	II
22	62	M	ALCOHOL	4.5	3.7	A	11.1	2.4	0
23	41	M	ALCOHOL	6.9	4.4	B	12.1	5.5	II
24	43	M	VIRAL	7.8	4.6	C	9.8	3.6	0
25	47	M	VIRAL	8	4.7	A	9.9	4.5	I
26	46	M	ALCOHOL	7.7	4.4	B	10.9	6.6	II
27	32	F	AUTOIMMUNE	9.9	3.3	C	11.2	7.2	II
28	21	F	AUTOIMMUNE	10	4.4	A	8.8	5.6	I
29	58	M	ALCOHOL	10.8	3.4	B	9.1	2.3	0
30	33	M	ALCOHOL	9.4	4.7	C	9.8	5.5	I
31	53	M	CRYPTOGENIC	9.6	3.3	A	8.8	4.6	II
32	44	M	ALCOHOL	8.4	2.9	B	9.9	6.6	II
33	50	M	ALCOHOL	6.3	3.4	B	8.8	4.5	II
34	39	M	VIRAL	6.4	4.4	C	9.9	5.8	II
35	35	F	AUTOIMMUNE	10.5	3.9	B	8.8	5.5	II

36	55	M	ALCOHOL	6.3	2.9	A	7.7	3.1	0
37	46	M	VIRAL	6.7	3.9	A	8.9	7.6	II
38	34	M	VIRAL	6.8	4.4	B	10.6	8.8	III
39	26	M	WILSON	7	4.7	C	12.6	7.4	III
40	42	M	VIRAL	6	4.4	A	11.6	5.5	II
41	50	M	ALCOHOL	9	3.8	C	12.1	6.6	II
42	33	M	WILSON	9.9	4.4	C	9.9	4.7	I
43	50	M	ALCOHOL	7.6	3.3	B	8.9	4.8	I
44	50	M	ALCOHOL	8.4	4	A	9.9	5.3	I
45	39	M	VIRAL	8	2.9	B	8.7	4.8	I
46	53	M	VIRAL	9.6	3.3	C	9.3	5.5	II
47	59	M	ALCOHOL	9.8	4.4	A	12.1	2.7	0
48	44	M	ALCOHOL	11.5	5.1	C	11.1	6.7	II
49	58	M	ALCOHOL	7.8	2.2	B	10.8	4.7	I
50	55	F	VIRAL	7.4	4.4	A	11.1	3.3	0
51	46	M	ALCOHOL	7.7	4.4	B	10.9	6.6	II
52	32	F	AUTOIMMUNE	9.9	3.3	C	11.2	7.2	II
53	21	F	AUTOIMMUNE	10	4.4	A	8.8	5.6	I
54	58	M	ALCOHOL	10.8	3.4	B	9.1	2.1	0
55	33	M	ALCOHOL	9.4	4.7	C	9.8	5.5	I
56	53	M	CRYPTOGENIC	9.6	3.3	A	8.8	4.6	II
57	44	M	ALCOHOL	8.4	2.9	B	9.9	6.6	II
58	50	M	ALCOHOL	6.3	3.4	B	8.8	4.5	II
59	39	M	VIRAL	6.4	4.4	C	9.9	5.8	II
60	35	F	AUTOIMMUNE	10.5	3.9	B	8.8	5.5	II
61	55	M	ALCOHOL	6.3	2.9	A	7.7	7.6	III
62	46	M	VIRAL	6.7	3.9	A	8.9	7.6	II
63	34	M	VIRAL	6.8	4.4	B	10.6	8.8	III
64	26	M	WILSON	7	4.7	C	12.6	7.4	III
65	42	M	VIRAL	6	4.4	A	11.6	5.5	II
66	50	M	ALCOHOL	9	3.8	C	12.1	6.6	II
67	33	M	WILSON	9.9	4.4	C	9.9	4.7	I
68	50	M	ALCOHOL	7.6	3.3	B	8.9	4.8	I
69	50	M	ALCOHOL	8.4	4	A	9.9	5.3	I
70	39	M	VIRAL	8	2.9	B	8.7	4.8	I
71	53	M	VIRAL	9.6	3.3	C	9.3	5.5	II
72	59	M	ALCOHOL	9.8	4.4	A	12.1	2.7	0
73	44	M	ALCOHOL	11.5	5.1	C	11.1	6.7	II
74	58	M	ALCOHOL	7.8	2.2	B	10.8	4.7	I
75	55	F	VIRAL	7.4	4.4	A	11.1	3.3	0
76	55	F	VIRAL	7.4	4.4	A	11.1	3.3	0

77	48	M	ALCOHOL	8.2	3	B	12.1	4.5	II
78	28	M	ALCOHOL	3	2.3	C	11.5	3.6	0
79	46	M	ALCOHOL	5	3.3	A	10.1	2.6	0
80	47	M	ALCOHOL	8	2.4	C	11.2	5.5	III
81	55	M	ALCOHOL	9	2.5	B	12.5	7.8	III
82	55	M	VIRAL	11	2.2	C	9.7	7.6	III
83	58	M	ALCOHOL	13	2.3	A	9.8	4.6	I
84	50	M	ALCOHOL	9	3.3	B	9.9	3.4	0
85	54	M	ALCOHOL	4	2.5	C	8.9	5.5	I
86	35	M	VIRAL	8.5	3.1	A	10.7	6.6	II
87	41	M	VIRAL	7.4	2.5	C	11.8	9.9	III
88	64	M	VIRAL	7.9	2.6	B	10	7.7	II
89	43	M	ALCOHOL	8.6	2.6	B	9.8	6.6	II
90	40	M	ALCOHOL	8.3	4.4	A	8.9	5.5	I
91	45	M	ALCOHOL	7.4	3.3	C	12.3	2.1	0
92	52	M	ALCOHOL	6.5	2.8	A	9.7	8.8	III
93	51	M	VIRAL	5.5	3.7	B	9.5	7.8	II
94	46	M	ALCOHOL	8	2.9	A	9.9	3.4	0
95	56	M	VIRAL	9	3.9	C	8.9	7.7	II
96	60	M	ALCOHOL	12.8	3.8	B	12	6.6	II
97	62	M	ALCOHOL	4.5	3.7	A	11.1	2.8	0
98	41	M	ALCOHOL	6.9	4.4	B	12.1	5.5	II
99	43	M	VIRAL	7.8	4.6	C	9.8	6.6	I
100	47	M	VIRAL	8	4.7	A	9.9	2.3	0

ETHICAL COMMITTEE APPROVAL LETTER

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

Prof Dr V Nagaraajan MD MNAMS DM (Neuro) DSc.,(Neurosciences) DSc (Hons)
Professor Emeritus In Neurosciences, Tamil Nadu Govt Dr MGR Medical University
Chairman, IEC

Dr.M.Shanthi, MD.,
Member Secretary,
Professor of Pharmacology,
Madurai Medical College, Madurai.

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Professor of Microbiology &
Vice Principal,
Madurai Medical College

2. Dr.Sheela Mallika rani, M.D.,
Anaesthesia , Medical
Superintendent Govt. Rajaji
Hosptial, Maudrai

3.Dr.V.T.Premkumar,MD(General Medicine) Professor & HOD of Medicine, Madurai Medical & Govt. Rajaji Hospital, College, Madurai.

4.Dr.S.R.Dhamotharan, MS.,
Professor & H.O.D I/c, Surgery,
Madurai Medical College & Govt.
Rajaji Hosptial, Madurai.

5.Dr.G.Meenakumari, MD.,
Professor of Pathology, Madurai
Medical College, Madurai

6.Mrs.Mercy Immaculate Rubalatha, M.A., B.Ed., Social worker, Gandhi Nagar, Madurai

7.Thiru.Pala.Ramasamy, B.A.,B.L.,
Advocate, Palam Station Road,
Sellur.

8.Thiru.P.K.M.Chelliah, B.A.,
Businessman,21, Jawahar Street,
Gandhi Nagar, Madurai.

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.P.Sinrasu
Course	:	PG in MD., General Medicine
Period of Study	:	2016-2019
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Study of Right lobe of liver diameter to Albumin Ratio as a non- Invasive predictor of Oesophageal varices in patients with liver cirrhosis
Ethical Committee as on	:	13.04.18

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

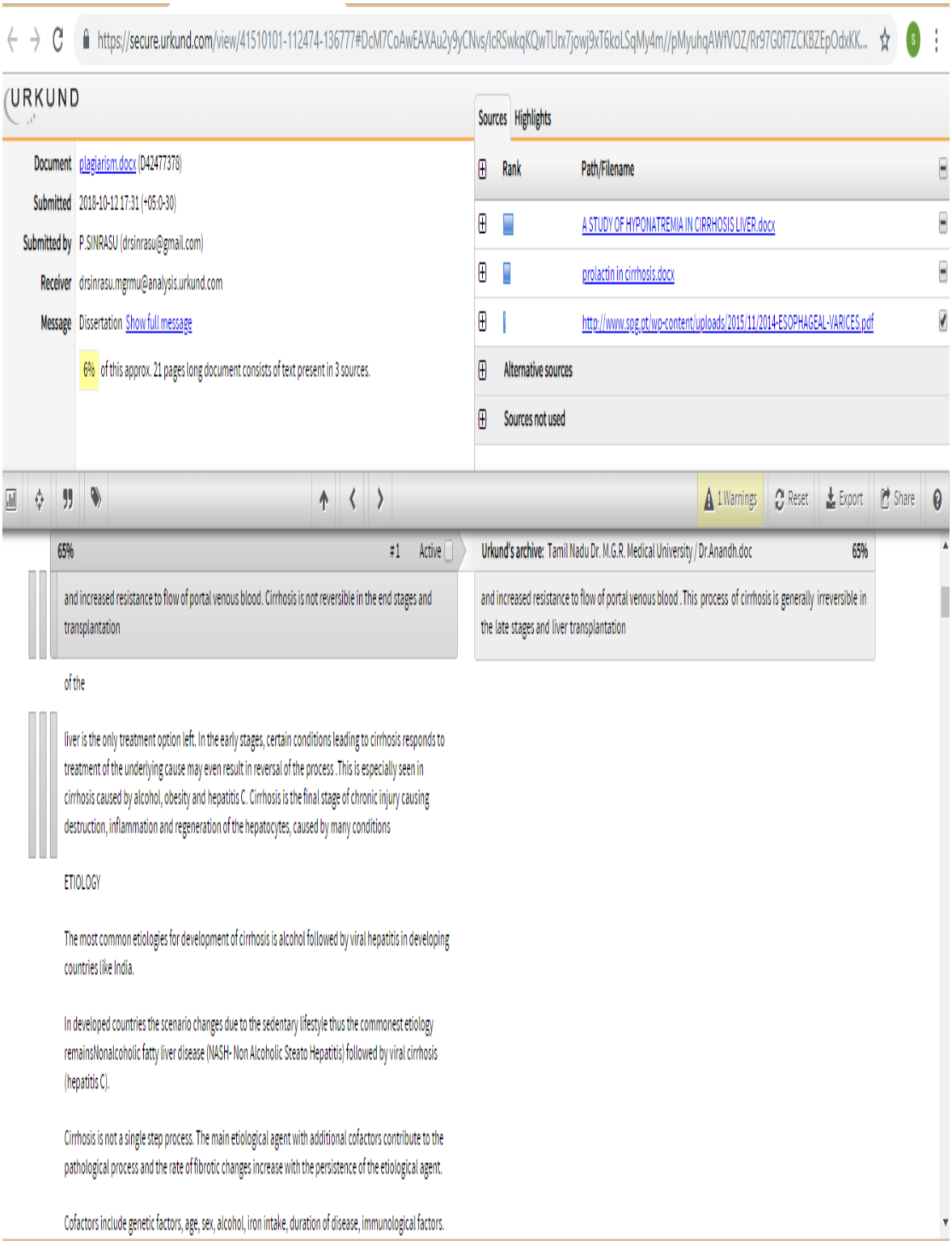
Member Secretary Chairman Dean

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

Dean (Offg)
Madurai Medical College
Madurai-20

16 APR 2018

ANTIPLAGIARISM CERTIFICATE



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