A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER

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This is to certify that dissertation entitled **"A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USIMG IT AS PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER"** is a bonafide work done by **Dr. SUREKHA,** Post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfilment of rules and regulations of **The Tamil Nadu Dr. M.G.R Medical University**, for the award of **M.D. Degree Branch I (General Medicine)** during the academic period from **2019 to 2022**.

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DECLARATION

I solemnly declare that this dissertation **"A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof.Dr.P.PARANTHAMAN M.D,** Professor and HOD of General Medicine, Department of General Medicine, Government Kilpauk Medical College and Hospital, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfilment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

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The Institutional Ethics Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application "A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS A PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER" Submitted by Dr. M.SUREKHA II Year Post Graduate in General Medicine, Government Kilpauk Medical College, Chennai – 10.

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Place: Chennai- 10

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CONTENTS

LIST OF ABBREVATIONS USED

NO-NITRIC OXIDE

IVC-INFERIOR VENA CAVA

PaO2-PARTIAL PRESSURE OF OXYGEN

PaCO2-PARTIAL PRESSURE OF CARBON DIOXIDE

HPS-HEPATOPULMONARY SYNDROME

ABG-ARTERIAL BLOOD GAS ANALYSIS

PPH-PORTOPULMONARY HYPERTENSION

NALD -NON ALCOHOLIC LIVER CELL DISEASE

HVPG-HEPATIC VENOUS PRESSURE GRADIENT

ABSTRACT

BACKGROUND AND OBJECTIVES

Cirrhosis of liver has been the most common medical entity among patients..there are various pulmonary manifestations of cirrhosis .The diagnosis of hepatopulmonary syndrome includes impaired oxygenation level which include paO2 less than 80mmhg. As paO2 value decreases child pugh score also increases which correlates with the severity of arterial hypoxemia.. Hence early detection of hypoxemia in patients with cirrhosis leads to early prevention of development of hepatopulmonary syndrome and further complications of cirrhosis.

METHODS

The present study will be carried out at in- patients who will get admitted in General medicine , Government Royapettah Hospital for a duration of 6 months . After explaining about the procedure,Arterial blood will be taken from radial artery under strict aseptic precautions and the sample will be sent for Blood gas Analysis (OPTI CCA –TS BLOOD GAS ANALYSER) on the day of admission.In ABG ,values of PaO2,SaO2, ph and PaCo2 will be noted.For patients having hypoxia on day of admission ,will be repeated every 3rd day… and their grade of hypoxemia will be compared with child pugh score.. and these patients are followuped in medicine opd and gastroenterology opd…

RESULTS

In the present study 11% had hepatopulmonary syndrome and 89% were normal There is statistically significant association between hypoxia and grading of varices($P<0.05$) .There is statistically significant association between child pugh class and Hepatopulmonary syndrome($P<0.05$)

Hypoxia has been identified in one-third of individuals with chronic liver disease, and the presence of hypoxia in these patients may alter their treatment

CONCLUSION

From this study, it has been found out that Arterial Blood Gas analysis has shown abnormalities in patients with Cirrhosis of Liver in the form of Hypoxemia & Hypocapnea. As the severity of Hypoxemia increases, Severity of Hepatic dysfunction increases, both of which are directly proportional. As so the Child Pugh score also worsens. Hence, Hpoxemia can be used as a Prognostic marker in Liver Cirrhotic patients.

“A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS A PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER ”

1. Introduction

A very common disease which the clinicians encounter both at primary and tertiary care is cirrhosis of liver. Cirrhosis is diffuse hepatic fibrosis where normal architecture is replaced by nodules. There are various causes of cirrhosis eg, alcoholic liver disease, hepatitis, nonalcoholic liver disease, etc.

Cirrhosis leads to a variety of complications like ascites ,hepatic encephalopathy, jaundice ,peritonitis, hepatorenal syndrome, hepato pulmonary syndrome, variceal haemorrhage, carcinoma . Hepatopulmonary syndrome is atriad of liver disease, impaired oxygenation, intrapulmonary vascular abnormalities known as intrapulmonary vascular dilatations. Patients presents with dyspnea, platypnea, orthodeoxia and hypoxia. HPS related hypoxemia is due to intrapulmonary dilatations which leads to ventilation perfusion mismatch and oxygen diffusion limitations.[1,2]

The diagnosis of HPS is done by impaired oxygenation detection by arterial blood gas analysis.An arterial oxygen tension paO2 < 80mmhg indicates impaired oxygenation. As the paO2 value decreases the severity of portal hypertension increases. Child pugh score also increases as paO2 value decrease.

The severity of hypoxemia was proportionally increased with severity of hepatic dysfunction. Hence this study was conducted in Government Royapetteh

Hospital/Government Kilpauk Medical College Hospital for the study of arterial blood gas analysis in patients with cirrhosis of liver.[3]

2.Aim and Objectives

Aims :To analyse the prevalence of hypoxemia in patients with cirrhosis of liver with respect to arterial blood gas analysis and correlate paO2 value with the severity of portal hypertension with reference to child pugh score

Objectives:-

1. To study the prevalence of hypoxemia in patients with cirrhosis of liver with reference to arterial blood gas analysis and correlate paO2 value with the severity of portal hypertension

2. Evaluation of patients with Cirrhosis of liver for the presence of Pulmonary manifestations with special reference to arterial hypoxemia.. and to correlate the paO2 with child pugh score .

3.Review Of Literature

Pulmonary symptoms of liver cirrhosis include pulmonary hypertension, acute lung injury, restrictive or obstructive lung disorders, interstitial fibrosis, pleural effusion, consolidation, and a variety of pulmonary gas exchange abnormalities, including Hepatopulmonary Syndrome. The trinity of liver illness, arterial deoxygenation, and pulmonary vascular dilatation is known as the Hepatopulmonary Syndrome (HPS). 4The prevalence of HPS in cirrhotic patients has been observed to range from 4% to 19%. Kennedy and Knudson coined the term hepatopulmonary syndrome in 1977 to describe the disease entity in a patient with alcoholic liver disease, dyspnea, and hypoxemia. However, this was not the first time the trio was defined and described in the literature. Fluckiger documented a 37-year-old woman who acquired cyanosis and clubbing as a result of syphilis-related liver disease in 1884. Following that, in 1956, Rydell and Hoffbauer documented the second case of hepatopulmonary syndrome in the literature.[5] However, in this case, there was a clear demonstration of arterial oxygen desaturation of 73 percent and an estimated shunt calculation of around 40%. Juvenile cirrhosis was the cause of liver failure in this case. A postmortem investigation revealed pulmonary vascular dilatations in both of these patients documented in the early literature, underlining the need of including pulmonary abnormalities in the description of this disease entity. However, in 1994, Krowka and Cortese standardised the diagnosis of HPS, limiting it to a blood oxygen tension of less than 70 mmHg.[6,7]

Liver cirrhosis

Liver Cirrhosis is one of the important health problems in India as well as in Western countries. Cirrhosis of liver is a commonly encountered disease in clinical practice and is responsible for significant morbidity and mortality all over the world. This disease is progressive and chronic in nature, diffusely involves the liver and is associated with degeneration of liver cells, excess collagen deposition resulting in fibrosis, formation of nodules, and distortion of normal vascular architecture resulting in hemodynamic alterations. It is a disease with characteristic clinical findings and diagnosis with histopathology. The leading etiological factors in India are Hepatitis B and C; followed by alcohol and NALD [1], other causes include autoimmune hepatic diseases, Hepatic venous outflow tract obstruction, toxins, drugs, cardiac failure, metabolic abnormalities and genetic abnormalities. There is a significant group where etiology of cirrhosis of liver cannot be detected and this group is called “Cryptogenic Cirrhosis”

Cirrhosis is a pathologically defined entity that is associated with a spectrum of characteristic clinical manifestations. The cardinal pathologic features reflect irreversible chronic injury of the hepatic parenchyma and include extensive fibrosis in association with the formation of regenerative nodules. These features result from hepatocyte necrosis, collapse of the supporting reticulin network with subsequent connective tissue deposition, distortion of the vascular bed, and nodular regeneration of remaining liver parenchyma.[8]

Advanced liver disease is associated with typical hemodynamic changes such as increased cardiac output and regional organ blood flow, decreased arterial pressure and low peripheral vascular resistance. This pattern identifies the so called “hyper dynamic syndrome” Peripheral vasodilatation by reducing cardiac “after load” may prevent any clinical evidence of cardiac dysfunction; however, many studies have demonstrated that under physiological or pharmacological stress the ventricular systolic function may give an inadequate response.

Cirrhotic cardiomyopathy is a pathological condition defined as “a chronic cardiac dysfunction in patients with cirrhosis characterized by blunted contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of known cardiac disease” In cirrhosis, cardiac output increases while systemic vascular resistance and arterial pressure decreases. Overall there seems to be a link between progression of liver function impairment, the development of portal hypertension and the degree of hyper dynamic circulation which is the hallmark of the deranged cardiovascular function in advanced liver disease.[9]

Some cirrhotic patients have obvious features of cardiomyopathy. However most have a normal or supernormal ejection fraction as judged by echocardiography. Thus physicians often assume that cardiac function is often normal in these patients. However further investigations have uncovered multiple problems in cardiac performance that place these patients at risk of heart failure. Early cardiac

decompensation is often missed because the cardiac workload is reduced by peripheral vasodilatation caused by liver failure. Thus cirrhotic patients are dismissed as having normal cardiac function. However when these patients are subjected to physiological or pharmacological stress they are prone to develop clinical signs of suboptimal perfusion including renal failure and acidosis. Most patients with liver disease have subtle defects in myocardial function that are not apparent on cursory examination and these defects become apparent only when these patients are exposed to stress.

Liver cirrhosis is associated with a wide range of cardiovascular abnormalities. It was first reported by Kowalski and Abelmann ,who noted a higher resting cardiac output and decreased systemic vascular resistance in patients with cirrhosis. These abnormalities include hyperdynamic circulation characterized by an increase in cardiac output and a decrease in peripheral vascular resistance .[10,11]

An increase in cardiac output can be attributed to an increase in venous return, heart rate and myocardial contractility, all of which are controlled by the autonomic nervous system. Vasodilatation (low systemic vascular resistance), the presence of arteriovenous communications, expanded blood volume and increased sympathetic nervous activity may further raise the cardiac output; most of these pathophysiological mechanisms are active in advanced cirrhosis . In the early stages, the presence of a hyperdynamic circulation is often not apparent. However, with the progression of the liver disease, there is an overall association

between the severity of the cirrhosis and the degree of hyperdynamic circulation. Studies on circulatory changes with posture suggest that the patients are mostly hyperdynamic in the supine position.Blood and plasma volumes are raised in advanced cirrhosis, but the distribution between central and non-central vascular areas is unequal.[12,13]

In addition to the hyperdynamic circulation, impaired ventricular contractility in response to stimuli was also described in cirrhotic patients. Initially, this was thought to be a manifestation of latent alcoholic cardiomyopathy but later studies in non-alcoholic patients and in experimental animal models revealed the same pattern of blunted cardiac contractile responsiveness. Thus, these cardiovascular changes are now termed cirrhotic cardiomyopathy." Due to the associated systemic vasodilatation, overt heart failure is generally not a feature of cirrhotic cardiomyopathy. In the absence of specific diagnostic criteria, the exact prevalence of cirrhotic cardiomyopathy remains unclear. The characteristic features of cirrhotic cardiomyopathy include (a) an attenuated systolic or diastolic response to stress stimuli, (b) structural or histological changes in cardiac chambers, (c) electrophysiological abnormalities, and (d) serum markers suggestive of cardiac stress. The impaired cardiovascular responsiveness in cirrhosis is likely related to a combination of factors that include cardiomyocyte plasma membrane physicochemical changes, attenuated stimulatory pathways, and enhanced activity of inhibitory systems.Diastolic dysfunction is present in the

vast majority of patients with cirrhotic cardiomyopathy, and that simple echocardiographic indices such as the E/A ratio may detect diastolic dysfunction even at rest. This may therefore represent the best available screening test to diagnose cardiac dysfunction.[14,15,16]

Cirrhosis is a gradually developing, chronic disease of the liver. It is the irreversible consequence and final stage of various chronic liver diseases of different etiology or the result of long-term exposure to various noxious agents. Cirrhosis of liver can be classified either etiologically or morphologically. The etiological classification is based on the underlying cause which includes alcohol, hepatitis B and hepatitis C infections, metabolic disorders like Wilson disease, nonalcoholic fatty liver disease and also due to autoimmune hepatitis. When no cause is found it is called as cryptogenic cirrhosis. Morphological classification is based on the size of 4 the nodules. It could be micronodular if the nodules are less than 3 mm, macronodular if they are more than 3 mm and mixed type if both are found. The mixed type is the transition form , from micronodular to macronodular cirrhosis.

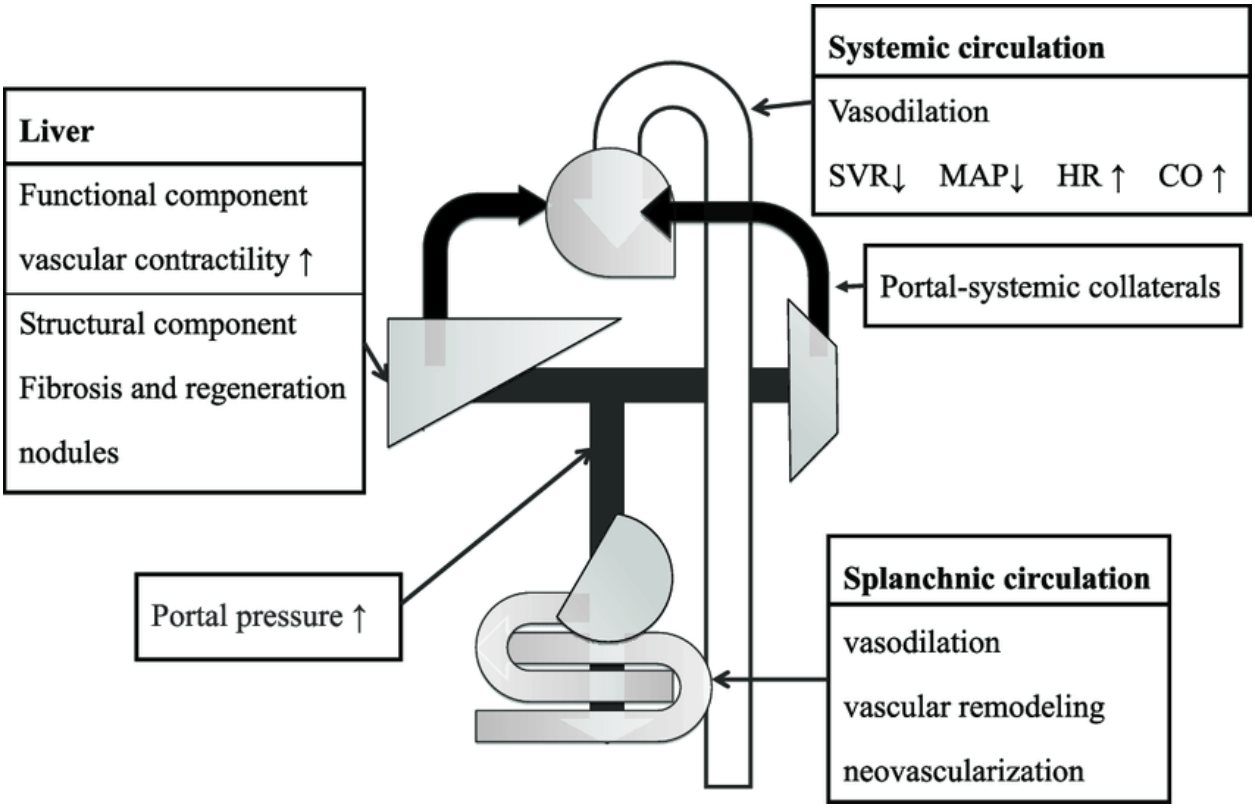
Hemodynamic changes in cirrhosis

- Portal hypertension is one of the salient features of cirrhosis. Cirrhosis of the liver accounts for approximately 90% of cases of portal hypertension. Portal hypertension is a common clinical syndrome defined by a pathologic increase of portal venous pressure. As a consequence, the gradient between portal pressure (PP) and inferior vena cava pressure (IVC) (portal pressure gradient, PPG) is increased above the upper normal value of 5 mm Hg. The importance of portal hypertensive syndrome is defined by the frequency and severity of its complications, including upper gastrointestinal bleeding from ruptured gastroesophageal varices, ascites, and hepatorenal Syndrome, which represent the leading causes of death and of liver transplantation in patients with cirrhosis.
- Portal hypertension is considered to be clinically significant (CSPH) when PPG, or its clinical equivalent hepatic venous pressure gradient (HVPG), exceeds 10 to 12 mm Hg, since this is the threshold for the clinical manifestations of portal hypertensive syndrome to appear. The vast majority of patients with cirrhosis develop CSPH along the course of the disease, and data from a recent multicentric study indicate that CSPH is already present at diagnosis in approximately 60% of histologically proven, wellcompensated cirrhosis case.
- Portal hypertension is related both to vascular resistance and to portal blood flow. The fundamental hemodynamic abnormality is an increased resistance to portal flow. This may be mechanical due to the disturbed

architecture and nodularity of cirrhosis or due to an obstructed portal vein. Other intra-hepatic factors such as collagenosis of the space of Disse, hepatocyte swelling and the resistance offered by portal-systemic collaterals 6 contribute. There is also a dynamic increase in intra-hepatic vascular resistance.

- Stellate (Ito) cells have contractile properties that can be modulated by vaso-active substances. These include nitric oxide (NO) which is vasodilatory and endothelin which is a vaso-constrictor. These may modulate intra-hepatic resistance and blood flow especially at a sinusoidal level.
- As the portal venous pressure is lowered by the development of collaterals deviating portal blood into systemic veins, portal hypertension is maintained by increasing portal flow in the portal system which becomes hyperdynamic. It is uncertain whether the hyperdynamic circulation is the cause or the consequence of the portal hypertension or both. It is related to the severity of liver failure. Cardiac output increases and there is generalized vasodilatation. Arterial blood pressure is normal or low. Splanchnic vasodilatation is probably the most important factor in maintaining the hyperdynamic circulation. Azygous blood flow is increased. Gastric mucosal blood flow rises. The increased portal flow raises the oesophageal variceal transmural pressure. The increased flow refers to total portal flow (hepatic and collaterals).The actual portal flow

reaching the liver is, of course, reduced. The factors maintaining the hyperdynamic splanchnic circulation are multiple. There seems to be interplay of vasodilators and vaso-constrictors. These might be formed by the hepatocyte, fail to be inactivated by it or be of gut origin and pass through intra-hepatic or extrahepatic venous shunts. Endotoxins and cytokines, largely formed in the gut, are important triggers. NO and endothelin-1 are synthesized by vascular endothelium in response to endotoxin. Prostacyclin is produced by portal vein endothelium and is a potent vasodilator. It may play a major role in the circulatory changes of portal hypertension due to chronic liver disease. Glucagon is vasodilatory after pharmacological doses but does not seem to be vaso-active at physiological doses. It is probably not a primary factor in the maintenance of the hyperkinetic circulation in established liver disease.



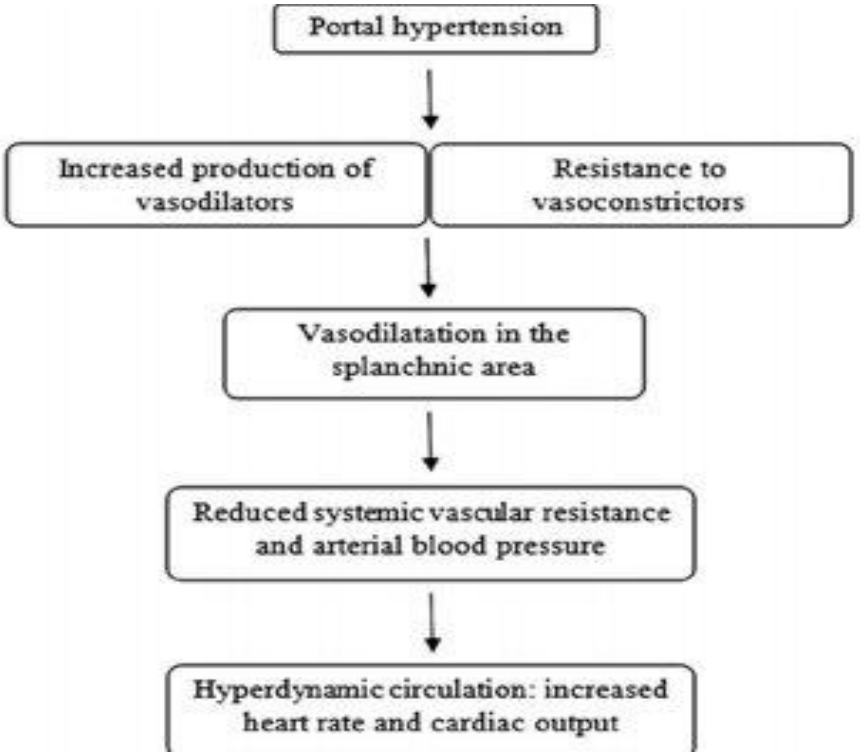
Cardiac and vascular changes in cirrhosis [17,18]

The cardiovascular system in patients with cirrhosis or portal hypertension is abnormal. The circulation becomes hyperdynamic, characterized by increased cardiac output and decreased peripheral vascular resistance and arterial pressure. Moreover, despite the increased cardiac output at rest, with stressful stimuli such as hemorrhage, surgery or vasoactive drug administration, the ventricular response is blunted, a condition known as cirrhotic cardiomyopathy. These cardiovascular abnormalities have been suggested to induce or aggravate several complications of cirrhosis such as renal salt and water retention, variceal bleeding, hepatopulmonary syndrome, and increased cardiovascular fragility

under stress. Recent reviews have detailed the clinical aspects of hyperdynamic circulation and cirrhotic cardiomyopathy.

HYPERDYNAMIC CIRCULATION

Peripheral vasodilatation is central to hyperdynamic circulation and portal hypertension in cirrhosis. However, the factors directly initiating vasodilatation remain obscure. A hypothesis that has received much attention over the past three decades is the "humoral factor" theory. In cirrhosis, increased intrahepatic resistance induces portosystemic collateral formation, allowing gut-derived humoral substances to directly enter the systemic circulation without detoxification by the liver. The following gut derived or locally-produced humoral factors have been implicated as possible mediators of peripheral vasodilatation in cirrhosis or portal hypertension



CLASSIFICATION OF CIRRHOSIS

Cirrhosis is classified either anatomically or etiologically

MORPHOLOGIC CLASSIFICATION:

Micronodular Cirrhosis: Histologically, the liver has tiny, homogenous 2mm nodules that are evenly distributed throughout the organ and divided by thin fibrous septae. A chemical substance, such as alcohol, is usually the etiology

Macronodular Cirrhosis: Larger nodules separated by broader scars, irregularly dispersed throughout the liver, histologically. An infectious agent, such as viral hepatitis, is usually to blame.

Mixed: Has both micronodular and macronodular features.

HISTOLOGIC classification:

Portal, Post-necrotic, Post Hepatitic, Biliary, Congestive.

ETIOLOGICAL CLASSIFICATION6:

(1) Alcoholic.

(2) Cryptogenic and posthepatitic.

(3) Biliary

(4) Cardiac.

(5) Metabolic, inherited, and drug-related

CLINICAL FEATURES OF CIRRHOSIS[19,20,21]

Cirrhosis can cause the following signs and symptoms, which can occur in the absence of cirrhosis or as a result of cirrhosis complications. Many are generic and can occur in other conditions, thus they aren't always indicative of cirrhosis. In the same way, the lack of any does not rule out the likelihood of cirrhosis.

Spider Angiomata or Spider Nevi - An increase in estradiol causes vascular lesions with a core arteriole surrounded by many smaller arteries. About 33% of the time, this happens.

Palmar Erythema- Due to changes in sex hormone metabolism, natural speckled mottling of the palm is exaggerated.

Muehrcke's nails - paired horizontal bands separated by normal color due to hypoalbuminemia (low production of albumin).

Terry's nails - Hypoalbuminemia causes the proximal two-thirds of the nail plate to appear white and the distal one-third to appear red.

Clubbing- Angle between the nail plate and proximal nail fold > 180 degrees.

Hypertrophic osteoarthropathy - Chronic proliferative periostitis of the long bones that can cause considerable pain.

Dupuytren's Contracture - Palmer fascia thickening and shortening causes flexion abnormalities in the fingers. Fibroblastic proliferation and disordered collagen deposition are thought to be the causes. It is fairly prevalent (33 percent of patients).

Fetor Hepaticus - Increased dimethyl sulphide, which is detected in severe portal-systemic shunting, causes a sweet pungent odour in the breath.

Jaundice – Increased bilirubin levels (at least 2-3 mg/dL or 30 mmol/L) cause yellowish discoloration of the skin, eyes, and mucous membranes. Urine can also be dark in colour.

Asterixis - Bilateral asynchronous flap of outstretched, dorsiflexed hands seen in patients with hepatic encephalopathy.

Gynecomastia - Benign proliferation of glandular tissue of male breasts. Patients present with a rubbery or firm mass extending concentrically from the nipples. This is due to increased estradiol and can occur in upto 66% of patients.

Hypogonadism – Manifested as impotence, infertility, loss of sexual drive, and testicular atrophy due to primary gonadal injury or suppression of hypothalamic or pituitary function.

Others - Weakness , fatigue, anorexia, weight loss.

Liver Size - Can be enlarged, normal, or shrunken.

Splenomegaly - Due to congestion of the red pulp as a result of portal hypertension.

Ascites - Accumulation of fluid in the peritoneal cavity giving rise to flank dullness (about 1500 mL is needed to elicit flank dullness).6

Caput medusa - The umbilical vein may open as a result of portal hypertension.Caput medusa occurs when blood from the portal venous system is

shunted from the periumbilical veins through the umbilical vein and into the abdominal wall veins. Patients may show signs and symptoms of consequences or aetiology.

COMPLICATIONS OF CIRRHOSIS[22,23,24]

The clinical course of patients with advanced cirrhosis is often complicated by a number of important sequelae that are independent of the etiology of the underlying liver disease. These include

- Portal hypertension and its consequences (e.g., gastroesophageal varices and splenomegaly)
- Pulmonary manifestations (pleural effusion , hepatopulmonary syndrome , portopulmonary hypertension etc)
- Ascites
- Hepatic encephalopathy
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome
- Hepatocellular carcinoma.

PORTAL HYPERTENSION[25,26]

Because the vascular resistance in the hepatic sinusoids is low, the normal pressure in the portal vein is low (5 to 10 mmHg). Increased resistance to portal blood flow is the most common cause of portal hypertension (>10 mmHg). The increased resistance is frequently sinusoidal when cirrhosis is accompanied with

portal hypertension. The most prevalent cause of portal hypertension is cirrhosis. More than 60% of cirrhotic patients have clinically significant portal hypertension.

Clinical Features:

The major clinical manifestations of portal hypertension include

- Hemorrhage from gastroesophageal varices
- Splenomegaly with hypersplenism
- Ascites
- Acute and chronic hepatic encephalopathy

VARICEAL BLEEDING[27,28]

While any of the porto-systemic venous collaterals can cause severe bleeding, varices near the gastroesophageal junction are the most prevalent source.

Clinical Features[29,30]

Variceal bleeding often occurs without any obvious precipitating factors and usually presents with painless yet massive hematemesis with or without melena.

PORTAL HYPERTENSIVE GASTROPATHY[31]

Due to portal venous hypertension, many patients develop congestive gastropathy. The mucosa appears engorged and friable in this condition, which is detected by endoscopic examination. Instead of the rapid haemorrhage typical of a variceal source, indolent mucosal bleeding develops.

SPLENOMEGALY AND HYPERSPLENISM

In patients with severe portal hypertension, congestive splenomegaly is prevalent. Although splenomegaly is usually asymptomatic, it is large and leads to cirrhosis-related thrombocytopenia or pancytopenia.

ASCITES

Ascites is a condition in which there is an excess of fluid in the peritoneal cavity. Cirrhosis and other forms of severe liver disease are the most common causes, but a variety of other conditions can result in either transudative or exudative ascites.

Pathogenesis:

The accumulation of ascitic fluid indicates an excess of total body water and sodium, although the cause of this imbalance is unknown.

There are three theories that have been offered. According to the "underfilling" idea, the underlying issue is improper fluid sequestration within the splanchnic vascular bed as a result of portal hypertension, resulting in a decrease in effective circulating blood volume. The kidney detects an apparent drop in intravascular volume (underfilling) and responds by holding salt and water, according to this idea. According to the "overflow" theory, the primary problem is excessive salt and water retention in the kidneys in the absence of voluminous urine. The peripheral arterial vasodilatation hypothesis, a third, more appealing explanation, may bring the prior hypotheses together. It explains the pattern of arterial hypotension and increased cardiac output seen in individuals with cirrhosis and ascites, as well as the presence of high amounts of vasoconstrictor chemicals. Sodium retention is again thought to be caused by arterial vascular underfilling,

which is caused by a disproportionate increase in the vascular compartment due to arteriolar vasodilation rather than a decrease in intravascular volume. According to this idea, portal hypertension causes nitric oxide-mediated splanchnic arteriolar vasodilation, which causes arterial vascular space underfilling and baroreceptor-mediated activation of reninangiotensin, sympathetic output, and antidiuretic hormone release.

A multitude of causes contribute to the buildup of fluid in the abdominal cavity, regardless of the triggering event. Elevated adrenaline and norepinephrine levels in the blood have been widely reported. Patients with cirrhosis plus ascites have increased central sympathetic outflow, whereas those with cirrhosis alone do not. Increased sympathetic output reduces natriuresis and reduces sensitivity to atrial natriuretic peptide via activating the renin-angiotensin system. By increasing hydrostatic pressure within the splanchnic capillary bed, portal hypertension aids in the production of ascites. Hypoalbuminemia and a lower plasma oncotic pressure encourage fluid extravasation into the peritoneal cavity. Ascites is uncommon in cirrhotic patients unless they have both portal hypertension and hypoalbuminemia.

Due to the distortion and obstruction of the hepatic sinusoids and lymphatics, hepatic lymph may weep freely from the surface of the cirrhotic liver, contributing to the formation of ascites. Renal variables can have a role in the persistence of ascites. Patients with ascites are unable to eliminate a normal water load. They exhibit enhanced proximal and distal tubule sodium reabsorption, the

latter owing to elevated plasma renin activity and subsequent hyperaldosteronism. Many individuals' insensitivity to circulating atrial natriuretic peptide, which is typically present un high concentrations in patients with cirrhosis and ascites, could be a contributing cause. Increased serum prostaglandin or catecholamine levels may cause renal vasoconstriction, which can lead to salt retention. Endothelin, a powerful vasoconstrictor peptide, has recently been suggested to play a role. While some people have reported elevated levels, others haven't noticed anything.

Clinical Features and Diagnosis:

Ascites is usually first observed by the patient as an increase in abdominal circumference. Because the diaphragm is elevated, a more prominent collection of fluid may cause shortness of breath. Ascites can be detected on physical examination by the presence of changing dullness, a fluid wave, or bulging flanks when peritoneal fluid accumulation surpasses 500 mL. Smaller amounts of ascites can be detected with an ultrasound scan, particularly with a Doppler study.

SPONTANEOUS BACTERIAL PERITONITIS (SBP)

Without an evident primary source of infection, patients with ascites and cirrhosis can develop acute bacterial peritonitis. SBP is more common in patients with severe liver disease, which indicates a poor prognosis.

HEPATORENAL SYNDROME

In the absence of recognised specific causes of renal impairment, hepatorenal syndrome is a significant consequence in a patient with cirrhosis and ascites. It is characterised by progressive azotemia with excessive salt retention and oliguria.

HEPATIC ENCEPHALOPATHY

Hepatic (portal-systemic) encephalopathy is a complicated neuropsychiatric condition marked by changes in awareness and behaviour, personality changes, fluctuating neurologic symptoms, asterixis (flapping tremor), and electroencephalographic alterations. Acute reversible encephalopathy or chronic and progressive encephalopathy are also possible.

Pathogenesis:

Hepatic encephalopathy's exact cause is unknown. Severe hepatocellular dysfunction and/or intrahepatic and extrahepatic shunting of portal venous blood into the systemic circulation, which mostly bypasses the liver, are the most essential elements in the aetiology. Various hazardous compounds taken from the intestine are not detoxified by the liver as a result of these processes, resulting in metabolic abnormalities in the central nervous system (CNS). Hepatic encephalopathy can present in a variety of ways, with any neurologic abnormalities, including localised impairments, being possible. Cerebral edoema, which is common, adds to the clinical presentation and overall mortality rate.

COAGULOPATHY

Cirrhotic patients' clotting function, both cellular and humoral, commonly shows a variety of abnormalities. Hypersplenism can cause thrombocytopenia. The alcoholic patient's bone marrow may be directly suppressed by ethanol. Reduced protein synthesis can result in less fibrinogen (factor I), prothrombin (factor II), and factors V, VII, IX, and X being produced. Reduced levels of all of these factors, save factor V, may be exacerbated by cholestasis-related malabsorption of the fat-soluble cofactor vitamin K.

PULMONARY MANIFESTATIONS OF CIRRHOSIS

HYPOXEMIA AND HEPATOPULMONARY SYNDROME

There is a well-documented causal relationship between hepatic and pulmonary disease.2 Although complications of liver disease commonly cause changes in pulmonary mechanics that affect blood flow and consequently arterial oxygenation , some patients who have liver disease experience hypoxemia as a result of abnormalities in the pulmonary vessels. With minimal treatment options, HPS has been only a medical curiosity, but the success of transplantation in treating complications of liver disease has intensified the interest HPS as a potentially curable condition in HPS as a potentially curable disease.

Definition

The hepatopulmonary syndrome (HPS) is defined as the triad of liver disease, arterial deoxygenation and pulmonary vascular dilatation.

PATHOPHYSIOLOGY

Vasodilatation

The most important alteration in HPS is the dilatation of the precapillary and postcapillary pulmonary vasculature27, which leads to impaired oxygenation of venous blood as it passes through the lung.Human studies have demonstrated increased pulmonary production of nitric oxide (NO).Exhaled NO levels are increased in patients with cirrhotic HPS and normalize after liver transplantation30,32 as HPS resolves. In addition, inhibition of the production of NO with N G -nitro -L arginine methyl ester (L-NAME) and methlyene blue, transiently alleviates HPS . In rats, common bile duct ligation (CBDL) reliably produces a triad of cholestatic liver disease, intrapulmonary shunting, and hypoxemia similar to that observed in HPS.29 Studies show that CBDL initiates a cascade of molecular events in the pulmonary circulation that causes an imbalance in mediators regulating vascular diameter.

After CBDL, increasing levels of intravascular endothelin-1 have been shown to bind endothelin-1 type B receptors located on the luminal surface of pulmonary vessels throughout the lung. Normally a vasoconstrictor, endothelin-1, facilitates vasodilation when bound to luminal endothelial B-type receptors by increasing the synthesis of endothelial nitric oxide. The resulting production of large amounts of nitric oxide in the pulmonary circulation overrides the local regulatory feedback mechanisms controlling vascular diameter.

The vessels are thus rendered insensitive to stimuli that normally facilitate

the dynamic matching between ventilation and perfusion, causing an excess of perfusion compared to the ventilation and hypoxemia caused by the resulting venous admixture.

That receptor binding correlates closely with the production of endothelial nitric oxide synthase, development of intrapulmonary vascular dilatation, and severity of pulmonary gas exchange, thus supporting hypothesis.

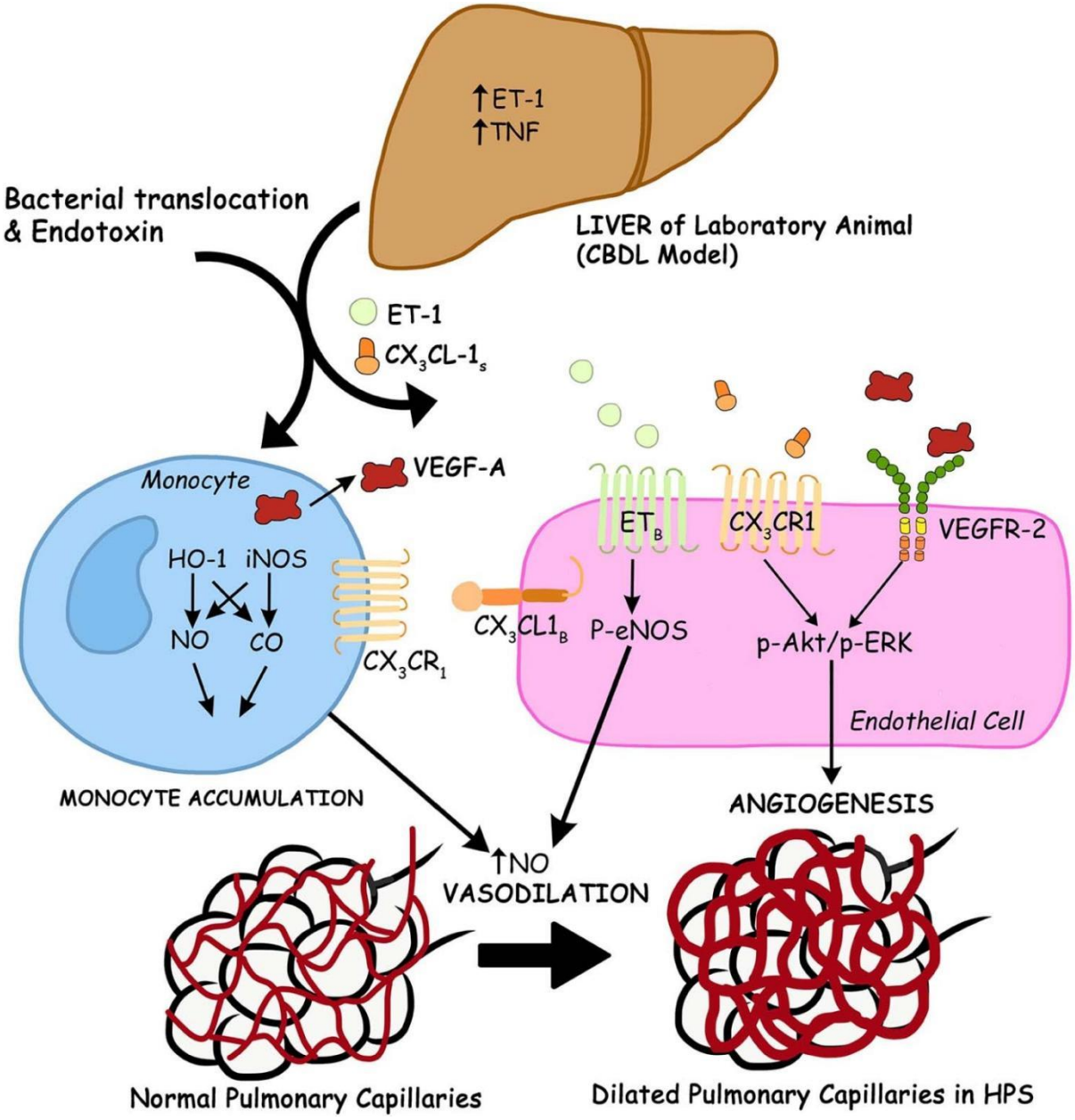


Fig 1. Proposed mechanisms of HPS based on findings in experimental models. Liver injury and/or portal hypertension trigger the production of cytokines and vasoactive mediators that increase vascular shear stress. Pulmonary microvascular dilatation is initiated by hepatic endothelin-1 production and release and endothelial nitric oxide synthase (Enos)-derived nitric oxide(NO) production through an increased number of endothelial endothelin B receptors. Macrophages that accumulate in the microvasculature also contribute to vasodilatation by producing NO from inducible nitric oxide synthase (iNOS) and carbon monoxide (CO) from heme oxygenase-1(HO-1).

HYPOXEMIA[32.33]

Three physiologic mechanisms commonly used to explain why hypoxemia occurs in patients who have HPS are (1) enhanced mismatching of alveolar ventilation to pulmonary vascular perfusion (VA/Q), (2) diffusion perfusion, and (3) the flow of deoxygenated blood through abnormal dilated vessels that join pulmonary arteries directly to the pulmonary veins, bypassing the pulmonary capillary alveolar surface. That a significant improvement in arterial oxygenation is observed in most patients who have HPS and who are given supplemental oxygen supports the hypothesis that VA/Q is the predominant cause of hypoxemia. Some investigators suggest that hypoxemia is also caused by a ‘‘diffusion-perfusion defect’’. The researchers think that in individuals with liver disease, pulmonary blood flow is raised to the point where there is inadequate time for proper oxygen exchange at the capillary–alveolar interface. Because a component of the red blood cell mass would not make touch with the alveolar

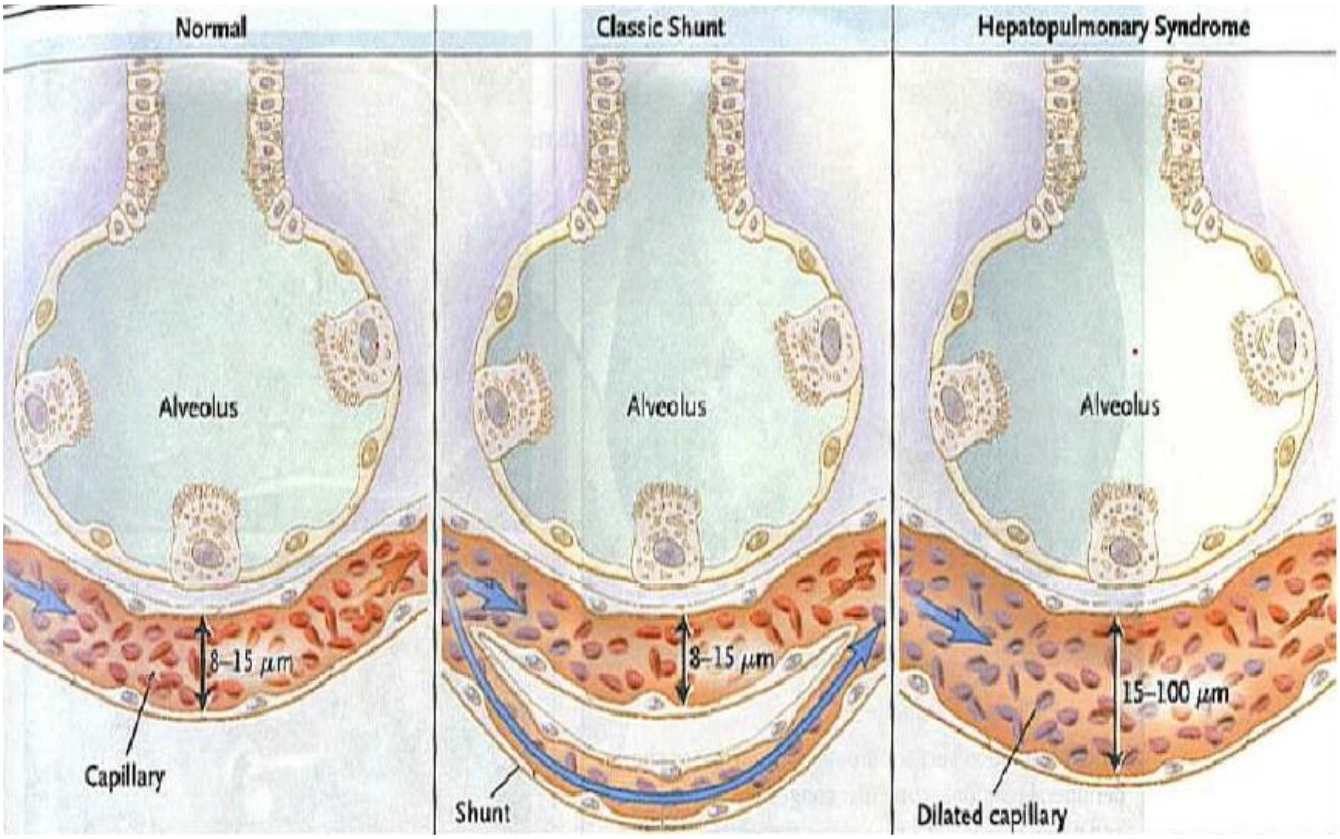
surface, this condition is considered an unusual type of anatomic shunt. Some researchers believe that a diffusion-perfusion deficiency occurs in all individuals with liver illness, whereas others believe that this mechanism of decreased gas exchange is only seen in HPS patients. Researchers have discovered a link between impaired oxygenation and the transit time for blood flow via the pulmonary circulation in individuals with liver illness but no hypoxemia, which supports this notion. However, there is inadequate evidence to support whether or not this process contributes to hypoxemia in HPS and, if so, to what extent. Anatomic shunts that connect the pulmonary artery and venous circulation directly, on the other hand, are a well-documented source of venous mixing and hypoxemia in HPS. These enormous shunts, which resemble spider angiomata, are mostly found on the hilar and pleural surfaces. They differ from echocardiographically discovered intraparenchymal dilated vessels. Because many patients with echocardiographic shunts do not develop hypoxemia, the role of the latter in generating hypoxemia is less clear. All patients' arterial oxygen saturation is affected by their position, but this effect is amplified in individuals with HPS. In the supine position, arterial oxygenation falls due to gravity pushing the stomach contents into the diaphragm, limiting functional residual capacity and causing venous mixing due to decreased VA/Q mismatching. Because of the additional effects of ascites and increased intrathoracic blood volume on functional reserve capacity, oxygen desaturation in the supine position is frequently increased in patients with liver disease. When compared to the supine

posture, individuals with HPS frequently exhibit orthodeoxia and platypnea, deoxygenation, and dyspnea in the sitting and standing positions. The gravity-dependent redirection of pulmonary blood flow to dilated arteries in the base of the lung while standing causes these findings. As a result, pulmonary blood is directed to dilated arteries that are unable to adjust their diameter in response to ventilation. Similar findings are reported for diabetics who have severe autonomic neuropathy who develop orthodeoxia and platypnea. As in patients who have HPS, autonomic neuropathy is thought to cause profound pulmonary vascular energy that leads to pooling of blood in areas of the lung with the ventilation. According to some researchers, orthodeoxia is a sufficiently distinct symptom that it can be used to confirm a diagnosis of HPS. Orthodeoxia, on the other hand, occurs in a wide range of diseases in which blood is shifted from the right to the left side of the circulatory system. 24,26 Furthermore, people with mild liver illness who do not have oxygen desaturation27 and so do not have HPS show a drop in oxygen saturation while assuming the standing position. The latter finding suggests that orthodeoxia's diagnostic and prognostic value is a separate finding that requires additional investigation. Researchers employ three different definitions for HPS-related orthodeoxia: a drop in PaO2 of 4%, 5%, or 10%. The figures of a 4% and 5% decrease in oxygenation upon taking the upright position were taken from research that linked arterial oxygenation to a demonstrable rise in shunt fraction; the 10% value was chosen based on clinical impression. Although these figures are intriguing, they must first be tested in study participants to

discover if they have any clinical significance. Because vascular anergy might produce gravity-dependent alterations in pulmonary blood flow and, as a result, oxygen saturation in patients with or without suspected HPS, it's recommended that blood oxygen and saturation measurements be documented in a single position for all patients with liver illness. Evidence suggests that a loss of pulmonary autoregulation leads to arterial dilatation in arteries ranging in diameter from 15 to 150 mm. Because failure to regulate perfusion in response to ventilation causes hypoxemia, a loss or insensitivity of normal autoregulatory systems in the pulmonary circulation gives a reasonable explanation for each of the three postulated hypoxemia processes. Although the exact source of this vascular anergy is unknown, there is enough evidence to link an imbalance in the neurogenic or vasoactive mediators responsible for the integrity of reactive alterations in pulmonary vascular tone to the genesis of hypoxemia in HPS. Investigators explored the pulmonary circulation in animal models that develop a disease that mirrors HPS in humans to better describe the alterations in vascular tone that lead to hypoxemia in HPS. Some researchers believe that portal hypertension causes a vasoactive mediator imbalance, resulting in downstream vascular dilatation that is characteristic of both HPS and the hyperdynamic circulation. Others, on the other hand, contend that this idea is invalidated by the failure of all patients with portal hypertension to acquire both HPS and hyperdynamic circulation. Furthermore, whereas hyperdynamic alterations are frequently associated with hepatic synthetic function, the severity of hypoxemia

in HPS is not, and HPS has been detected in patients with relatively little portal hypertension. Alternative ideas contend that HPS and hyperdynamic circulation are not caused by the same insult or follow the same molecular pathways, and that the fundamental problem in HPS is found in the lung rather than the portal circulation.

Fig 2: In a normal lung, the capillary diameter is 8 to15 µm and oxygen diffuses rapidly into the capillary. In a classical shunt, blood bypasses the alveolus, whereas in the hepatopulmonary syndrome, the capillaries are dilated to 15 to 100µm in diameter, and oxygen fails to diffuse into the center of the dilated capillary.



CLINICAL FEATURES[34,35,36,37]

Because many patients with HPS are asymptomatic or their respiratory symptoms might be attributed to intrinsic lung disease, the diagnosis of HPS may be ignored or delayed; consequently, a high index of suspicion is required to establish the diagnosis. The most common complaint in symptomatic patients is the gradual onset of dyspnea. Platypnea (increased dyspnea when standing) is a common symptom of HPS, and it's caused by a preponderance of vasodilation in the lung bases. Hypoxemia results from increased shunting across these areas in the upright position. Platypnea's prevalence, sensitivity, and specificity, however, are unknown. Spider angiomata, digital clubbing, and cyanosis have all been reported in HPS patients, although they have not been studied as diagnostic signs.

INVESTIGATIONS

To identify intrapulmonary vasodilation, methods such as contrast echocardiography, lung perfusion scanning, pulmonary angiography, and high resolution chest computed tomography (CT) scanning are used. The most sensitive and widely used screening approach is two-dimensional transthoracic contrast echocardiography. On echocardiography, the contrast agent used is agitated saline, which produces microbubbles. A positive test is the observation of intravenously given saline microbubbles in the left heart chambers after three cardiac cycles. Microbubbles should not be seen on the left side of the heart in normal circumstances, however instant visibility of injected contrast indicates

intracardiac shunting. When compared to transthoracic echocardiogram, transesophageal contrast echocardiography may improve the sensitivity of detecting intrapulmonary vasodilation, but the former is a more intrusive and expensive method.

Material and method:-

Study design – prospective observational study

Study period:- 6 months

Study centre :- Govt. Kilpauk Medical College/ Government Royapettah hospital Chennai

Study population :chronic liver disease patients admitted in the Medicine ward, Govt. Royapettah hospital/Govt. Kilpauk Medical College, Chennai .

Sample Size:- 105

The sample size was calculated based on previous study conducted in areas of Amritsar among which 50% of the chronic liver disease patients had hypoxemia and an absolute precision of 10%, sample size was derived.

Sample size was calculated using the formula:

N = sample size

Z value for α at 0.05=1.96

P = prevalence=50%

q = 100-p=100-50=50%

d = absoluteprecision of 10%

Sample size **N = 3.84 X pq / d^2**

3.84X50X50 / 10×10 = 96

Considering 10% non-response rate, sample size, **N= 105**

Authored by : Khushvinder sherry,pashaura singh

Published in: 2016

Sample procedure: Convenience sampling method

Inclusion criteria:-

1. Proven cases of cirrhosis of liver.(by clinical, laboratory investigations, endoscopic and sonographic evidence).
2. Age above 18 years, including males and females.

Exclusion criteria:-

1. Patients of Age below 18 years.
2. Patients with coexisting primary pulmonary diseases like COPD, Bronchial asthma, ILD etc.
3. Coexisting intrinsic heart disease.

4. Patients with life threatening complications of cirrhosis like active upper gastrointestinal haemorrhage, hepatic encephalopathy.
5. Smokers.

Methodology:-

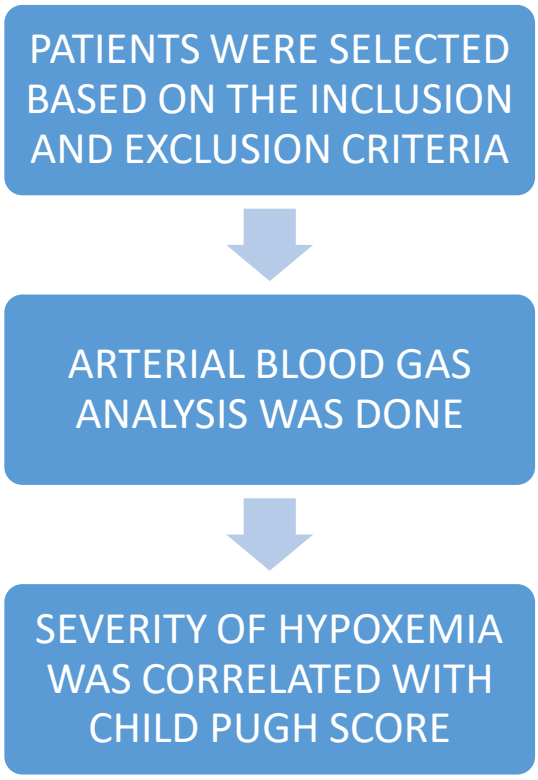
The present study was carried out at in- patients who were admitted in General medicine , Government Royapettah Hospital for a duration of 6 months . After explaining about the procedure,Arterial blood was taken from radial artery under strict aseptic precautions and the sample was sent for Blood gas Analysis (OPTI CCA –TS BLOOD GAS ANALYSER) on the day of admission. In ABG, values of PaO2,SaO2, ph and PaCo2 was noted. For patients having hypoxia on day of admission, was repeated every 3rd day. and their grade of hypoxemia was compared with child pugh score. and these patients are followed in medicine OPD and gastroenterology OPD.

The presence of hypoxemia and orthodeoxia was also detected. Orthodeoxia was defined as fall in PaO2 levels more than 3mmHg on changing position from supine to standing and hypoxemia if PaO2 was less than 70mmHg breathing room air in any position at rest (supine, sitting or standing). Alveolar-Arterial gradient of partial pressure of oxygen was taken as elevated if it were elevated more than 30mmHg (calculated as P (A-a) O2=PaO2-150-1.25xPaCO2).

PaO2 determines were done while breathing 100% oxygen.The severity of paO2 was compared with child pugh score.

the variables of child pugh score include serum bilirubin,serum albumin,PT,INR,ascites ,hepatic encephalopathy score include 5-15.

A 5-7,B 7-9,C >10.



Statistical Analysis

Analysis done by using SPSS Version 20.Descriptive analysis was used. P value of less than 0.05 will be taken as statistically significant .

Investigations needed:

- Arterial blood gas analysis

- Complete blood count
- Liver function test
- Renal function test
- PT, INR

Results

Table 1:Age wise distribution of study participants

Age in years	Frequency	Percentage	Mean ±SD
≤30	15	14	
31- 40	42	40	
41-50	23	22	38.5±5.68
51-60	21	20	
>60	4	4	
Total	105	100	

In the present study 40% belong to age group of 31 to 40 years. About 22% belong to age group of 41 to 50 years. About 20% belonged to age of 51 to 60 years .And 14% were in the age group of less than 30 years .mean age is 38.5 years and standard deviation is 5.68 years

Figure 1:Age wise distribution of study participants

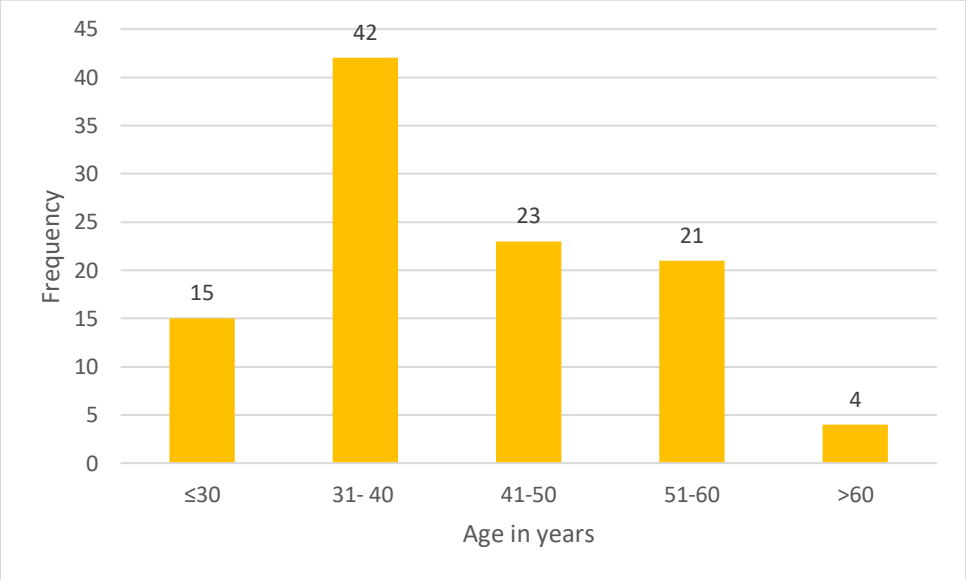


Table 2:Sexwise distribution of study participants

Sex	Frequency	Percentage
Male	86	82
Female	19	18
Total	105	100

In the present study 82% were males and 18% were females

Figure 2:Sexwise distribution of study participants

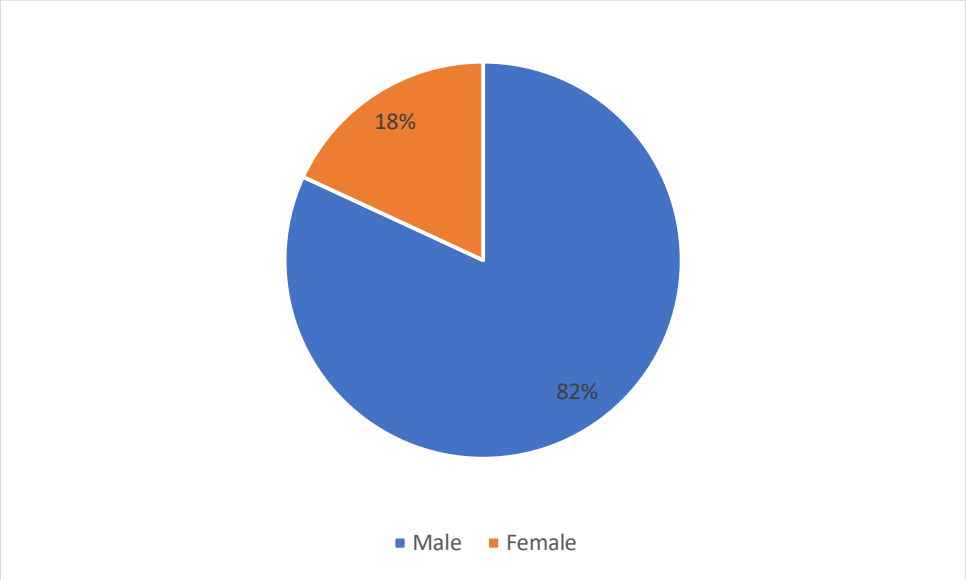


Table 3:Distribution of etiology of cirrhosis among study participants

Etiology	Frequency	Percentage
Hepatitis B	12	11.4
Hepatitis C	8	7.6
Alcohol	72	68.5
Others	13	12.5
Total	105	100

In the present study 69% were alcoholics,11% had Hepatitis B infection ,8% ha d Hepatitis C infection and 12.5% were from other causes .

Figure 3:Distribution of etiology of cirrhosis among study participants

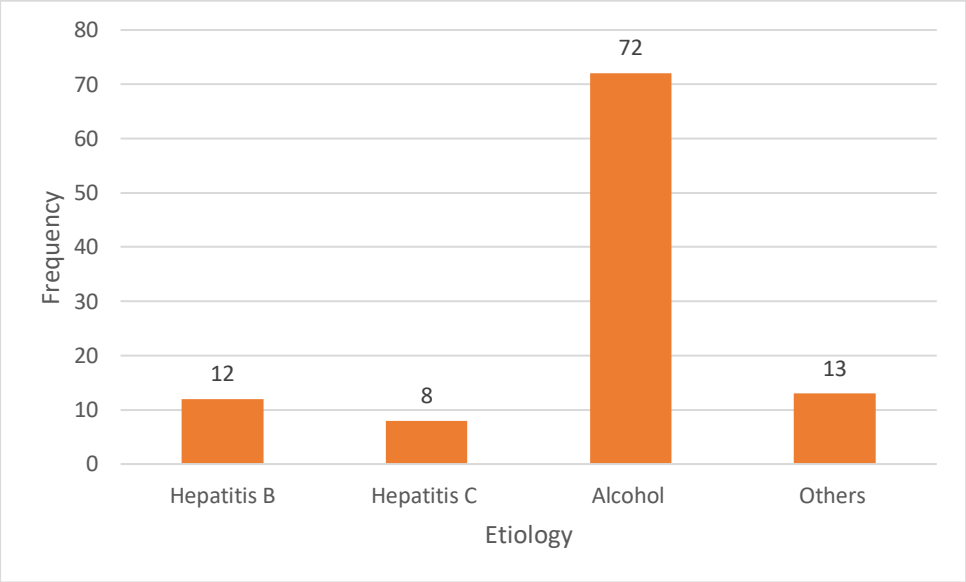


Table 4:Distribution of clinical signs among study participants

Clinical signs	Frequency	Percentage
Cyanosis	8	7.6
Clubbing	22	2.1
Spider naevi	12	11.42
Pedal edema	22	20.95
Jaundice	8	7.61
Ascites	60	5.71

Splenomegaly	76	72.3

In the present study 21% had pedal edema ,11% had spider naevi ,7% had cyanosis,6% had splenomegaly.

Figure 4:Distribution of clinical signs among study participants

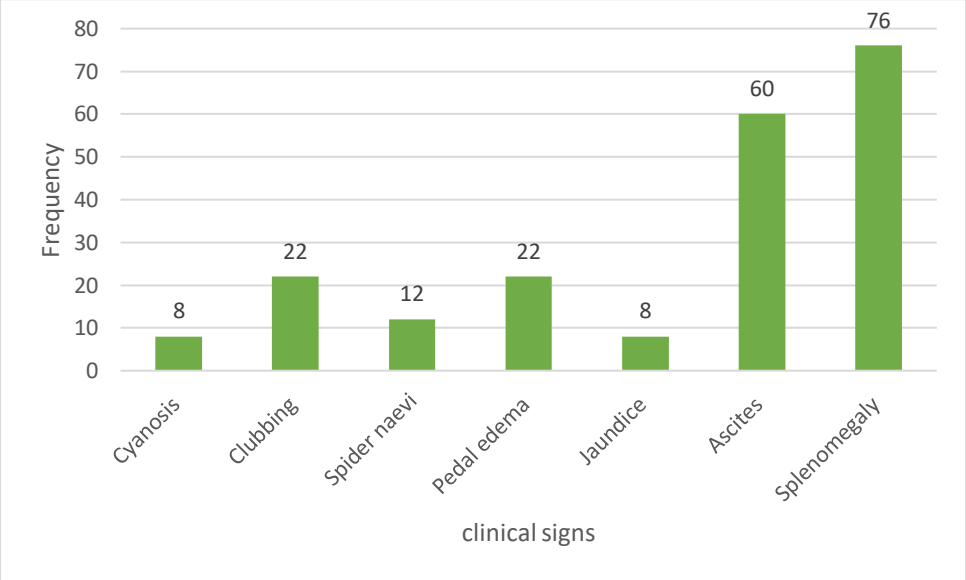


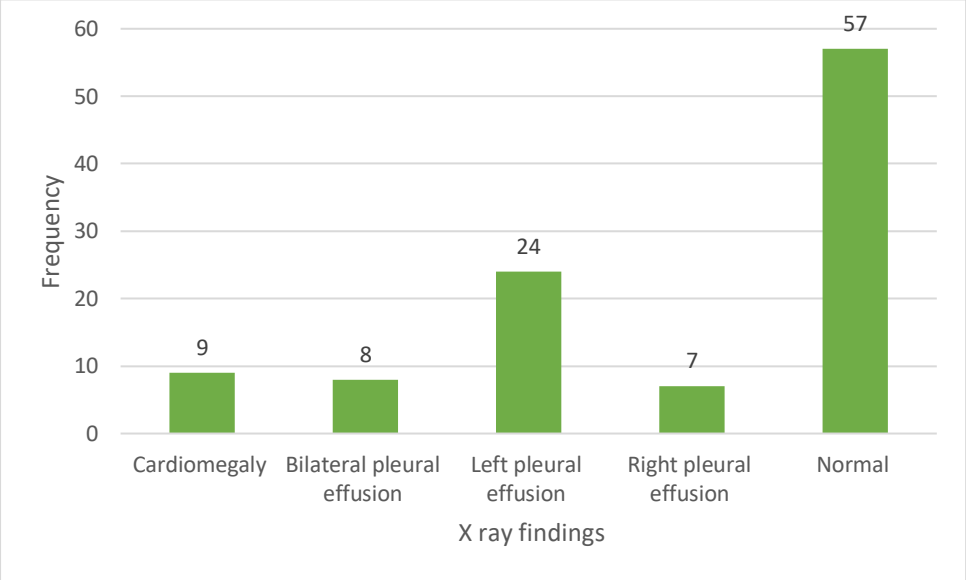
Table 5:Distribution of chest X Ray findings among study participants

X Ray findings	Frequency	Percentage
Cardiomegaly	9	8.6
Bilateral pleural effusion	8	7.6
Left pleural effusion	24	22.9

Right pleural effusion	7	6.7
Normal	57	54.2
Total	105	100

In our study 23% had left pleural effusion,9% had cardiomegaly ,8% had bilateral pleural effusion and 7% had right pleural effusion

Figure 5:Distribution of chest X Ray findings among study participants



In the present study 79% had normal Pulmonary function test and 21% had restrictive pulmonary function test

Table 6:Distribution of CVS findings among study participants

CVS	Frequency	Percentage

ESM	25	24
Normal	80	76
Total	105	100

In the present study 76% had normal CVS finding. About 24% had ejection systolic murmur

Figure 6:Distribution of CVS findings among study participants

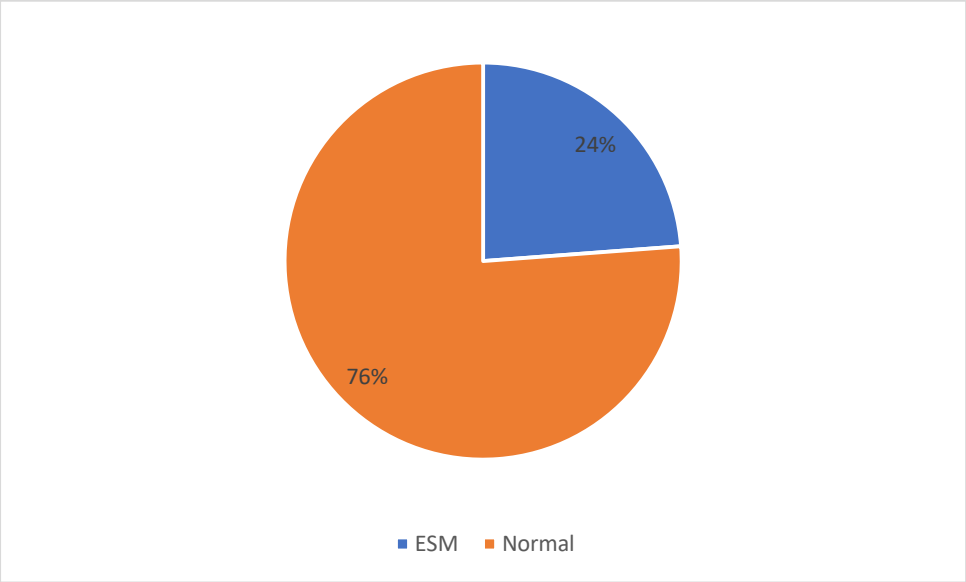


Table 7:Distribution of Hypoxia among study participants

Hypoxia	Frequency	Percentage
Yes	16	15
No	89	85

Total	105	100

In the present study 15% had hypoxia and 85% did not have hypoxia

Figure 7:Distribution of Hypoxia among study participants

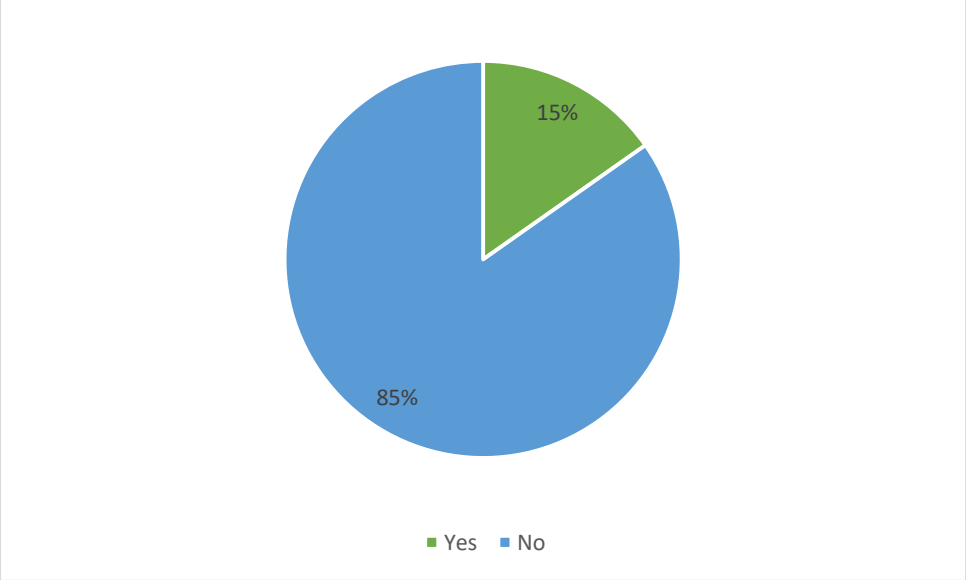


Table 8:Child Pugh class among study participants

Child pugh class	Frequency	Percentage
A	31	29
B	50	48
C	24	23

Total	105	100

In the present study 48% had child pugh class B ,29% had Child pugh class A, and 23% had Child Pugh class C

Figure 8:Child Pugh class among study participants

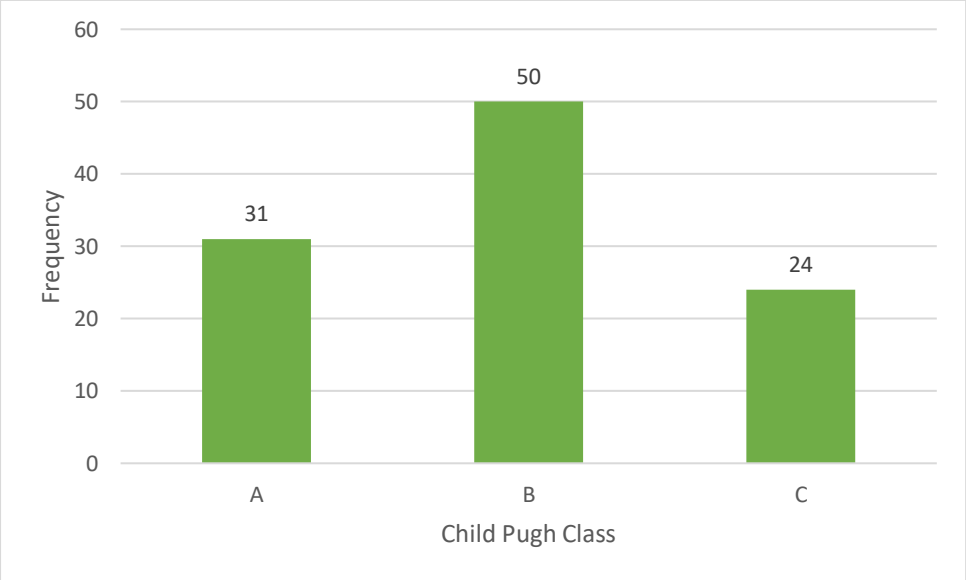


Table 9:Distribution of hepatopulmonary syndrome among study participants

HPS	Frequency	Percentage
Yes	12	11

No	93	89
Total	105	100

In the present study 11% had hepatopulmonary syndrome and 89% were normal

Figure 9:Distribution of hepatopulmonary syndrome among study participants

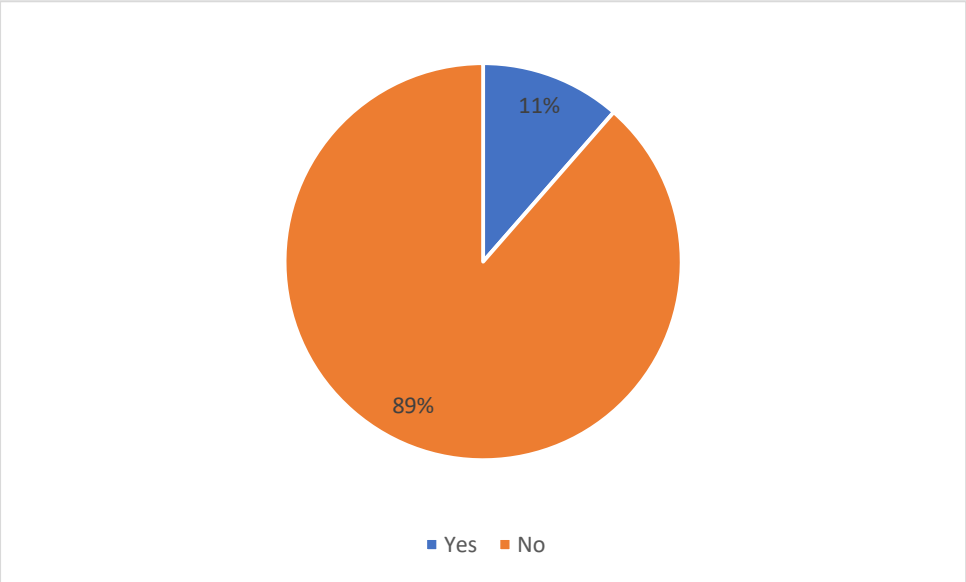


Table 10:Association between hypoxia and grading of varices

Hypoxia	A	B	C	Total	Chisquare	P value
Yes	0	4	12	16		
No	31	46	12	89	24.23	0.0001

Total	31	50	24	105		

There is statistically significant association between hypoxia and grading of varices($P<0.05$)

Figure 10:Association between hypoxia and grading of varices

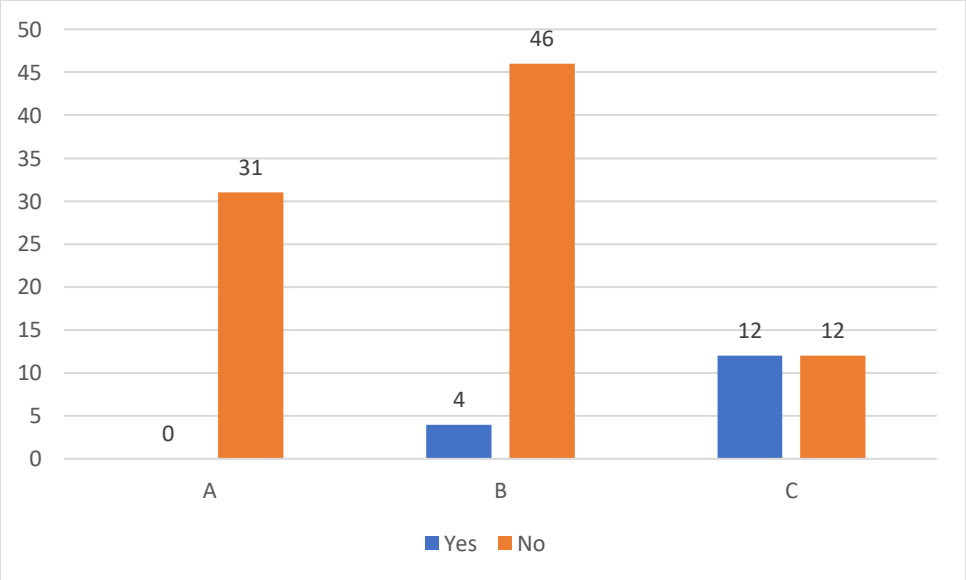


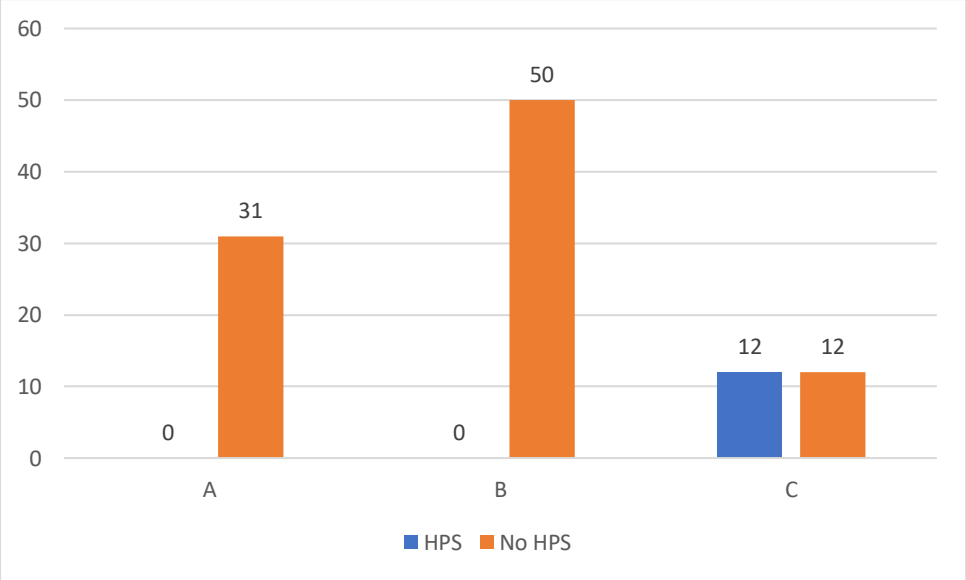
Table 11:Association between child pugh class and Hepatopulmonary syndrome

Child Pugh class	HPS	No HPS	Total	Chi square	P value
A	0	31	31		

B	0	50	50	21.26	0.0001
C	12	12	24		
Total	12	93	105		

There is statistically significant association between child pugh class and Hepatopulmonary syndrome(P<0.05)

Figure 11:Association between child pugh class and Hepatopulmonary syndrome



Discussion

Age

In the present study 40% belong to age group of 31 to 40 years.About 22% belong to age group of 41 to 50 years. About 20% belonged to age of 51 to 60 years .And 14% were in the age group of less than 30 years .mean age is 38.5 years and standard deviation is 5.68 years

Sex

In the present study 82% were males and 18% were females

Risk factors

In the present study 69% were alcoholics,11% had Hepatitis B infection ,8% ha d Hepatitis C infection and 12.5% were from other causes .

Symptoms

In the present study 21% had pedal edema ,11% had spider naevi ,7% had cyanosis,6% had splenomegaly.

Chest Xray findings

In our study 23% had left pleural effusion,9% had cardiomegaly ,8% had bilateral pleural effusion and 7% had right pleural effusion

Cardiovascular finding

In the present study 76% had normal CVS finding. About 24% had ejection systolic murmur

Hypoxia

In the present study 15% had hypoxia and 85% did not have hypoxia

Child Pugh classification

In the present study 48% had child pugh class B ,29% had Child pugh class A, and 23% had Child Pugh class C

Hepatopulmonary syndrome

In the present study 11% had hepatopulmonary syndrome and 89% were normal There is statistically significant association between hypoxia and grading of varices($P<0.05$)

Association between risk factors and outcome

There is statistically significant association between pulmonary function test and grading of varices($P<0.05$) There is statistically significant association between child pugh class and Hepatopulmonary syndrome($P<0.05$)

Pulmonary dysfunction is frequent in patients with a lengthy history of liver disease, and more than 70% of patients with liver cirrhosis experience dyspnea. Hypoxia has been identified in one-third of individuals with chronic liver disease, and the presence of hypoxia in these patients may alter their treatment

There is no one mechanism that explains the link between liver disease and hypoxia, and several factors contribute to its aetiology.

Despite the fact that none of them has been established to be the primary cause, ascites, hepatopulmonary syndrome, excessive hepatomegaly, low albumin levels, anaemia, increased closing volume, and respiratory muscle weakness are still thought to have a role in the pathogenesis of hypoxemia in cirrhosis

Many causes have been identified as contributing to pulmonary abnormalities in liver illness, including cardiopulmonary issues unrelated to hepatic affection as well as distinct problems linked with hepatic disease and/or portal hypertension

Cirrhosis is linked to impairments in pulmonary function, which can affect 45-50 percent of patients. Although an intra or extrapulmonary shunt, ventilation-perfusion mismatch, and diffusion defect are all potential causes of decreased pulmonary function, there is no consensus on which reasons are most likely. Hepatopulmonary syndrome (HPS) is a devastating complication of cirrhosis that affects 5-32 percent of cirrhotic individuals.

Dyspnea is a prevalent symptom of chronic liver illness, according to Krowka et al. [46]. Before the proper diagnosis of HPS, the dyspnea had been present for an average of five years. This suggests that dyspnea is a common complaint among cirrhotic patients. Furthermore, pulmonary hypertension, hypoxemia, ascites anaemia, abdominal distention, and pleural effusion are all consequences of liver disease that can produce dyspnea [47,48]Advanced liver disease cardiomyopathy can also cause dyspnea.

In a study of 120 patients with hepatic cirrhosis, Vachiery et al. [49] discovered that 70% of patients with HPS were in the C stage, and he documented that the Child-Pugh classification, which indicates the degree of liver cell failure, is the most valuable criterion used in determining the prognosis in cirrhotic patients. The degree of hepatic affection is related to the pulmonary abnormalities found in cirrhotic patients [50]

Helmy and Awadallah [51]found that hypoxemic individuals had a statistically significant lower serum albumin than non-hypoxic patients. These findings are also consistent with those of Melot et al. [52] who found a reduction in serum albumin in hypoxemic patients. Low blood albumin levels may contribute to hypoxemia by producing mild interstitial edoema, which impairs alveolar O2 diffusion [53]

Conclusion

From this study, it has been found out that Arterial Blood Gas analysis has shown abnormalities in patients with Cirrhosis of Liver in the form of Hypoxemia & Hypocapnea. As the severity of Hypoxemia increases, Severity of Hepatic dysfunction increases, both of which are directly proportional. As so the Child Pugh score also worsens. Hence, Hpoxemia can be used as a Prognostic marker in Liver Cirrhotic patients.

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PROFORMA

A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS A PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER”

NAME:

AGE :

SEX:

OCCUPATION:

IP.NO/ HOSPITAL NO:

ADDRESS:

DATE OF ADMISSION:

DATE OF DISCHARGE:

STATUS AT DISCHARGE:

PRESENTING COMPLAINTS

ABDOMINAL DISTENSION

ABDOMINAL PAIN

BREATHLESSNESS

YELLOWISH DISCOLOURATION OF EYES

SWELLING OF LEGS

COUGH

PRURITIS

ANOREXIA

VOMITING

ALTERED BLADDER AND BOWEL HABITS

GENERALIZED WEAKNESS

ALTERED SENSORIUM

CONVULSIONS

HISTORY OF PRESENT ILLNESS

PAST HISTORY:

DIABETES MELLITUS HYPERTENSION

RENAL DISEASE DRUG HISTORY

ISCHEMIC HEART DISEASE PULMONARY TB

CIRRHOSIS LIVER DISEASE BRONCHIAL ASTHMA

JAUNDICE

OTHERS

ANY OTHER SYSTEMIC ILLNESS IN THE PAST

PERSONAL HISTORY

SLEEP

DIET

APPETITE

BOWEL

BLADDER

HABITS

SMOKING

TOBACCO CHEWING

ALCOHOL

FAMILY HISTORY

DIABETES

HYPERTENSION

ISCHAEMIC HEART DISEASE

CEREBROVASCULAR ACCIDENTS

ALCOHOLISM

OBESITY

GENERAL PHYSICAL EXAMINATION

BUILT , PALLOR , OEDEMA: PEDAL/FACIAL/GENERALIZED

ICTERUS LYMPHADENOPATHY

CYANOSIS HEIGHT

CLUBBING WEIGHT

BMI

VITALS SIGNS

PULSE

BP

RESPIRATORY RATE

TEMPERATURE

JVP

SIGNS OF HEPATOCELLULAR FAILURE

GASTROINTESTINAL SYSTEM

RESPIRATORY SYSTEM

CARDIOVASCULAR SYSTEM

NERVOUS SYSTEM

PROVISIONAL DIAGNOSIS

INVESTIGATIONS

I. HAEMATOLOGY

HAEMOGLOBIN Gm/dl

TC Cells/mm3

DC

NEUTROPHILS %

LYMPHOCYTES %

EOSINOPHILS %

MONOCYTES %

ESR mm/1hr

II. BIOCHEMISTRY

RENAL FUNCTION TEST

LIVER FUNCTION TEST

ARTERIAL BLOOD GAS ANALYSIS

III. PT,INR

IV.ELECTROCARDIOGRAM

V.CHILD PUGH SCORE

VI. DIAGNOSIS

MASTERCHART

age	sex	alcohol int	icterus	pallor	clubbing	cyanosis	orthodexia	edal edem
25	M	+	-	-	+	-	-	+
36	M	+	+	-	+	-	-	-
56	M	-	+	-	-	-	-	-
35	M	+	+	+	-	-	-	+
40	F	-	+	-	-	-	-	+
51	M	+	+	+	+	-	-	-
45	M	+	+	-	-	-	-	+
26	M	+	-	-	-	-	-	-
43	F	-	+	+	-	-	-	+
55	M	+	+	-	+	+	+	+
40	M	-	-	-	-	-	-	-
54	M	+	+	-	-	-	-	+
60	M	+	+	-	+	+	+	+
44	M	-	-	-	-	-	-	-
30	F	-	-	+	+	-	-	+
27	M	+	+	-	-	-	-	+
42	M	+	+	-	-	-	-	-
40	F	-	-	+	-	-	-	+
25	M	+	-	-	+	-	-	+
36	M	+	+	-	+	-	-	-
56	M	-	+	-	-	-	-	-
35	M	+	+	+	-	-	-	+
40	F	-	+	-	-	-	-	+
51	M	+	+	+	+	-	-	-
45	M	+	+	-	-	-	-	+
26	M	+	-	-	-	-	-	-
43	F	-	+	+	-	-	-	+
55	M	+	+	-	+	+	+	+
40	M	-	-	-	-	-	-	-
54	M	+	+	-	-	-	-	+
60	M	+	+	-	+	+	+	+
44	M	-	-	-	-	-	-	-
30	F	-	-	+	+	-	-	+
27	M	+	+	-	-	-	-	+
42	M	+	+	-	-	-	-	-
40	F	-	-	+	-	-	-	+
25	M	+	-	-	+	-	-	+
36	M	+	+	-	+	-	-	-
56	M	-	+	-	-	-	-	-
35	M	+	+	+	-	-	-	+
40	F	-	+	-	-	-	-	+
51	M	+	+	+	+	-	-	-
45	M	+	+	-	-	-	-	+
26	M	+	-	-	-	-	-	-
43	F	-	+	+	-	-	-	+
55	M	+	+	-	+	+	+	+
40	M	-	-	-	-	-	-	-
54	M	+	+	-	-	-	-	+
60	M	+	+	-	+	+	+	+

44 M	-	-	-	-	-	-	-
30 F	-	-	+	+	-	-	+
27 M	+	+	-	-	-	-	+
42 M	+	+	-	-	-	-	-
40 F	-	-	+	-	-	-	+
35 M	+	-	-	+	-	-	+
35 F	+	+	-	+	-	-	-
40 M	-	+	-	-	-	-	-
65 F	+	+	+	-	-	-	+
52 M	-	+	-	-	-	-	+
46 M	+	+	+	+	-	-	-
38 M	+	+	-	-	-	-	+
34 M	+	-	-	-	-	-	-
48 F	-	+	+	-	-	-	+
50 F	+	+	-	+	+	+	+
55 M	-	-	-	-	-	-	-
26 M	+	+	-	-	-	-	+
42 F	+	+	-	+	+	+	+
40 M	-	-	-	-	-	-	-
70 M	-	-	+	+	-	-	+
36 M	+	+	-	-	-	-	+
55 M	+	+	-	-	-	-	-
51 M	-	-	+	-	-	-	+
29 M	+	-	-	+	-	-	+
45 M	+	+	-	+	-	-	-
37 M	-	+	-	-	-	-	-
45 M	+	+	+	-	-	-	+
35 M	-	+	-	-	-	-	+
35 F	+	+	+	+	-	-	-
40 M	+	+	-	-	-	-	+
65 F	+	-	-	-	-	-	-
52 M	-	+	+	-	-	-	+
46 M	+	+	-	+	+	+	+
38 M	-	-	-	-	-	-	-
34 M	+	+	-	-	-	-	+
48 F	+	+	-	+	+	+	+
50 F	-	-	-	-	-	-	-
55 M	-	-	+	+	-	-	+
26 M	+	+	-	-	-	-	+
42 F	+	+	-	-	-	-	-
40 M	-	-	+	-	-	-	+
70 M	-	+	-	-	-	-	+
36 M	+	+	+	+	-	-	-
55 M	+	+	-	-	-	-	+
51 M	+	-	-	-	-	-	-
29 M	-	+	+	-	-	-	+
45 M	+	+	-	+	+	+	+
37 M	-	-	-	-	-	-	-
45 M	+	+	-	-	-	-	+
40 M	+	+	-	+	+	+	+

70 M	-	-	-	-	-	-	-
36 M	-	-	+	+	-	-	+
55 M	+	+	-	-	-	-	+
51 M	+	+	-	-	-	-	-
29 M	-	-	+	-	-	-	+
45 M	-	-	+	-	-	-	+

spider nae	CVS	RS	ascites	splenomeg	HB (g%)	s.albumin	s.bilirubin	PT/INR
-	N	PLE	+	+	9.2	2.1	2.4	16.5/1.4
-	N	N	-	+	10.2	4.3	3.1	12.9/1.2
-	N	PLE	-	+	9.6	4.4	2.6	15.4/1.4
-	ESM	N	+	+	6.5	3.2	2.8	14.4/1.4
-	N	N	+	+	8.9	2.8	3	18.6/1.7
+	N	N	+	+	8	3.9	3.2	15.4/1.5
-	N	N	+	+	10.6	2.5	3.1	13.3/1.0
-	N	N	-	+	11.2	1.2	3.4	16.5/1.5
-	ESM	N	+	+	6.7	2.2	2.5	14.4/1.3
+	N	PLE	+	+	9	3.4	2.1	16.4/1.4
-	N	N	-	+	10.4	1.4	3.5	17.6/1.6
-	N	N	+	+	11	4.6	2	18.1/1.8
+	N	N	+	+	9.5	6.5	2.9	19.9/2.1
-	N	N	-	-	10.2	1.3	3	15.7/1.4
-	ESM	N	+	+	7.2	1.2	3.2	16.6/1.6
+	N	N	+	+	9.8	3.2	2.4	15.6/1.4
-	N	PLE	+	+	10.4	4.1	2.8	14.9/1.4
-	ESM	N	+	+	7	2	3	16.3/1.5
-	N	N	+	+	9.2	2.1	2.4	16.5/1.4
-	N	N	-	+	10.2	4.3	3.1	12.9/1.2
-	N	N	-	+	9.6	4.4	2.6	15.4/1.4
-	ESM	N	+	+	6.5	3.2	2.8	14.4/1.4
-	N	PLE	+	+	8.9	2.8	3	18.6/1.7
+	N	N	+	+	8	3.9	3.2	15.4/1.5
-	N	PLE	+	+	10.6	2.5	3.1	13.3/1.0
-	N	N	-	+	11.2	1.2	3.4	16.5/1.5
-	ESM	N	+	+	6.7	2.2	2.5	14.4/1.3
+	N	N	+	+	9	3.4	2.1	16.4/1.4
-	N	N	-	+	10.4	1.4	3.5	17.6/1.6
-	N	N	+	+	11	4.6	2	18.1/1.8
+	N	N	+	+	9.5	6.5	2.9	19.9/2.1
-	N	PLE	-	-	10.2	1.3	3	15.7/1.4
-	ESM	N	+	+	7.2	1.2	3.2	16.6/1.6
+	N	N	+	+	9.8	3.2	2.4	15.6/1.4
-	N	N	+	+	10.4	4.1	2.8	14.9/1.4
-	ESM	N	+	+	7	2	3	16.3/1.5
-	N	N	+	+	9.2	2.1	2.4	16.5/1.4
-	N	N	-	+	10.2	4.3	3.1	12.9/1.2
-	N	PLE	-	+	9.6	4.4	2.6	15.4/1.4
-	ESM	N	+	+	6.5	3.2	2.8	14.4/1.4
-	N	N	+	+	8.9	2.8	3	18.6/1.7
+	N	N	+	+	8	3.9	3.2	15.4/1.5
-	N	N	+	+	10.6	2.5	3.1	13.3/1.0
-	N	N	-	+	11.2	1.2	3.4	16.5/1.5
-	ESM	PLE	+	+	6.7	2.2	2.5	14.4/1.3
+	N	N	+	+	9	3.4	2.1	16.4/1.4
-	N	PLE	-	+	10.4	1.4	3.5	17.6/1.6
-	N	N	+	+	11	4.6	2	18.1/1.8
+	N	N	+	+	9.5	6.5	2.9	19.9/2.1

-	N	N	-	-	10.2	1.3	3 15.7/1.4
-	ESM	N	+	+	7.2	1.2	3.2 16.6/1.6
+	N	N	+	+	9.8	3.2	2.4 15.6/1.4
-	N	N	+	+	10.4	4.1	2.8 14.9/1.4
-	ESM	PLE	+	+	7	2	3 16.3/1.5
-	N	N	+	+	9.2	2.1	2.4 16.5/1.4
-	N	N	-	+	10.2	4.3	3.1 12.9/1.2
-	N	N	-	+	9.6	4.4	2.6 15.4/1.4
-	ESM	N	+	+	6.5	3.2	2.8 14.4/1.4
-	N	N	+	+	8.9	2.8	3 18.6/1.7
+	N	N	+	+	8	3.9	3.2 15.4/1.5
-	N	PLE	+	+	10.6	2.5	3.1 13.3/1.0
-	N	N	-	+	11.2	1.2	3.4 16.5/1.5
-	ESM	N	+	+	6.7	2.2	2.5 14.4/1.3
+	N	N	+	+	9	3.4	2.1 16.4/1.4
-	N	N	-	+	10.4	1.4	3.5 17.6/1.6
-	N	N	+	+	11	4.6	2 18.1/1.8
+	N	PLE	+	+	9.5	6.5	2.9 19.9/2.1
-	N	N	-	-	10.2	1.3	3 15.7/1.4
-	ESM	PLE	+	+	7.2	1.2	3.2 16.6/1.6
+	N	N	+	+	9.8	3.2	2.4 15.6/1.4
-	N	N	+	+	10.4	4.1	2.8 14.9/1.4
-	ESM	N	+	+	7	2	3 16.3/1.5
-	N	N	+	+	9.2	2.1	2.4 16.5/1.4
-	N	N	-	+	10.2	4.3	3.1 12.9/1.2
-	N	N	-	+	9.6	4.4	2.6 15.4/1.4
-	ESM	PLE	+	+	6.5	3.2	2.8 14.4/1.4
-	N	N	+	+	8.9	2.8	3 18.6/1.7
+	N	N	+	+	8	3.9	3.2 15.4/1.5
-	N	N	+	+	10.6	2.5	3.1 13.3/1.0
-	N	N	-	+	11.2	1.2	3.4 16.5/1.5
-	ESM	N	+	+	6.7	2.2	2.5 14.4/1.3
+	N	N	+	+	9	3.4	2.1 16.4/1.4
-	N	PLE	-	+	10.4	1.4	3.5 17.6/1.6
-	N	N	+	+	11	4.6	2 18.1/1.8
+	N	N	+	+	9.5	6.5	2.9 19.9/2.1
-	N	N	-	-	10.2	1.3	3 15.7/1.4
-	ESM	N	+	+	7.2	1.2	3.2 16.6/1.6
+	N	N	+	+	9.8	3.2	2.4 15.6/1.4
-	N	PLE	+	+	10.4	4.1	2.8 14.9/1.4
-	ESM	N	+	+	7	2	3 16.3/1.5
-	N	PLE	+	+	9.2	2.1	2.4 16.5/1.4
+	N	N	-	+	10.2	4.3	3.1 12.9/1.2
-	N	N	-	+	9.6	4.4	2.6 15.4/1.4
-	ESM	N	+	+	6.5	3.2	2.8 14.4/1.4
-	N	N	+	+	8.9	2.8	3 18.6/1.7
+	N	N	+	+	8	3.9	3.2 15.4/1.5
-	N	N	+	+	10.6	2.5	3.1 13.3/1.0
-	N	PLE	-	+	11.2	1.2	3.4 16.5/1.5
+	ESM	N	+	+	6.7	2.2	2.5 14.4/1.3

-	N	N	+	+	9	3.4	2.1 16.4/1.4
-	N	N	-	+	10.4	1.4	3.5 17.6/1.6
+	N	N	+	+	11	4.6	2 18.1/1.8
-	N	N	+	+	9.5	6.5	2.9 19.9/2.1
-	N	N	-	-	10.2	1.3	3 15.7/1.4
-	ESM	PLE	+	+	7.2	1.2	3.2 16.6/1.6

viral marke	chest Xray	PaO2	child pugh class	PCO2	sa02
Neg	RPE	60	B	40	96
Neg	N	60	B	42	98
Neg	N	60	B	32	90
Neg	RPE	60	B	36	96
Neg	N	60	B	35	88
Neg	N	60	C	40	92
Neg	RPE	68	B	41	91
Neg	N	68	A	41	90
HBV	CM	68	B	36	88
Neg	N	68	C	34	84
Neg	N	68	A	40	90
Neg	RPE	68	C	42	91
Neg	N	72	C	35	82
Neg	N	72	A	42	96
Neg	N	72	A	45	96
Neg	RPE	72	C	38	96
Neg	N	72	B	36	90
HBV	BPE	72	B	41	92
Neg	RPE	72	B	40	96
Neg	N	72	B	42	98
Neg	N	72	B	32	90
Neg	RPE	72	B	36	96
Neg	N	72	B	35	88
Neg	N	72	C	40	92
Neg	RPE	72	B	41	91
Neg	N	72	A	41	90
HBV	CM	72	B	36	88
Neg	N	72	C	34	84
Neg	N	72	A	40	90
Neg	RPE	76	C	42	91
Neg	N	76	C	35	82
Neg	N	76	A	42	96
Neg	N	76	A	45	96
Neg	RPE	76	C	38	96
Neg	N	77	B	36	90
HBV	BPE	77	B	41	92
Neg	RPE	77	B	40	96
Neg	N	77	B	42	98
Neg	N	77	B	32	90
Neg	RPE	77	B	36	96
Neg	N	78	B	35	88
Neg	N	78	C	40	92
Neg	RPE	78	B	41	91
Neg	N	78	A	41	90
HBV	CM	78	B	36	88
Neg	N	78	C	34	84
Neg	N	78	A	40	90
Neg	RPE	78	C	42	91
Neg	N	78	C	35	82

Neg	N	78 A	42	96
Neg	N	78 A	45	96
Neg	RPE	78 C	38	96
Neg	N	78 B	36	90
HBV	BPE	78 B	41	92
Neg	RPE	78 B	40	96
Neg	N	78 B	42	98
Neg	N	78 B	32	90
Neg	RPE	78 B	36	96
Neg	N	78 B	35	88
Neg	N	78 C	40	92
Neg	RPE	78 B	41	91
Neg	N	78 A	41	90
HBV	CM	78 B	36	88
Neg	N	78 C	34	84
Neg	N	78 A	40	90
Neg	RPE	78 C	42	91
Neg	N	78 C	35	82
Neg	N	78 A	42	96
Neg	N	78 A	45	96
Neg	RPE	78 C	38	96
Neg	N	78 B	36	90
HBV	BPE	78 B	41	92
Neg	RPE	81 B	40	96
Neg	N	81 B	42	98
Neg	N	81 B	32	90
Neg	RPE	82 B	36	96
Neg	N	82 B	35	88
Neg	N	82 C	40	92
Neg	RPE	82 B	41	91
Neg	N	82 A	41	90
HBV	CM	82 B	36	88
Neg	N	84 C	34	84
Neg	N	84 A	40	90
Neg	RPE	84 C	42	91
Neg	N	84 C	35	82
Neg	N	84 A	42	96
Neg	N	84 A	45	96
Neg	RPE	86 C	38	96
Neg	N	86 B	36	90
HBV	BPE	86 B	41	92
Neg	RPE	86 B	40	96
Neg	N	86 B	42	98
Neg	N	86 B	32	90
Neg	RPE	86 B	36	96
Neg	N	86 B	35	88
Neg	N	86 C	40	92
Neg	RPE	86 B	41	91
Neg	N	86 A	41	90
HBV	CM	86 B	36	88
Neg	N	86 C	34	84
Neg	N	86 A	40	90
Neg	RPE	86 C	42	91
Neg	N	86 C	35	82
Neg	N	86 A	42	96
Neg	N	86 A	45	96

PATIENT CONSENT FORM

" A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS A PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER "

Study centre : GOVERNMENT ROYAPETTAH HOSPITAL/ GOVT. KILPAUK MEDICAL COLLEGE, CHENNAI

Patients Name :

Patients Age and sex :

Identification Number :

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression:

Patients Name and Address: Place Date

Signature of investigator :

Study investigator's Name : Place Date

நோயாளி ஒப்புதல் படிவம்

ஆய்வு விவரம் **A STUDY OF HYPOXEMIA IN PATIENTS WITH CIRRHOSIS OF LIVER AND USING IT AS A PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER**

ஆய்வு மையம்: அரசு கீழ்ப்பாக்கம் மருத்துவக் கல்லூரி, சென்னை நோயாளி பெயர்:
நோயாளி வயது:
புறநோயாளி எண்:
நோயாளி இந்தப் பெட்டிகள் உள்ளே டிக் செய்யலாம்

-மேலே உள்ள ஆய்வின் நடைமுறையின் நோக்கத்தை நான் புரிந்துகொண்டேன் என உறுதிப்படுத்துகிறேன். கேள்வி கேட்பதற்கு எனக்கு வாய்ப்பு உள்ளது, எனது முழு திருப்திக்கு எனது கேள்விகளும் சந்தேகங்களும் பதிலளிக்கப்பட்டன. ☐

-இந்த ஆய்வில் நான் பங்கேற்பது தன்னார்வத்திலானது மற்றும் எனது சட்டபூர்வ உரிமைகள் பாதிக்கப்படாமல் எந்த நேரத்திலும் எந்தக் காரணமும் கூறாமல் விலகிக்கொள்வதற்கு நான் சுதந்திரமாக உள்ளேன் என்பதை நான் புரிந்துகொண்டேன். ☐

-சிகிச்சையக ஆய்வை வழங்கும் நிறுவனம், ஆய்வை வழங்கும் நிறுவனத்தின் சார்பாக பணிபுரியும் மற்றவர்கள், நெறிமுறைக் குழு மற்றும் ஒழுங்குமுறை அமைப்புகள், தற்போதைய ஆய்வு மற்றும் அவற்றில் இருக்கக் கூடிய எந்த ஒரு ஆராய்ச்சியிலும் எனது உடல்நலப் பதிவேடுகளைப் பார்ப்பதற்கு எனது அனுமதி தேவையில்லை என்று நான் புரிந்துகொண்டேன். அது தொடர்பாக நடத்தப்படும், நான் ஆய்விலிருந்து விலகினாலும் கூட இந்த அணுகலை ஒப்புக்கொள்கிறேன். எனினும், சட்டத்தின் கீழ் தேவைப்பட்டால் ஒழிய, மூன்றாம் தரப்பினருக்கு வெளியிடப்படும் அல்லது பிரசுரிக்கப்படும் எந்தத் தகவல்களில் எனது அடையாளம் வெளிப்படுத்தப்படாது என்பதை நான் புரிந்துகொண்டேன். இந்த ஆய்விலிருந்து எழும் தரவுகள் அல்லது முடிவுகளின் பயன்பாட்டை கட்டுப்படுத்தாமல் இருக்க நான் ஒப்புக்கொள்கிறேன் ☐

.-மேலே உள்ள ஆய்வில் பங்கேற்க நான் ஒப்புக்கொள்கிறேன், ஆய்வின் போது அளிக்கப்பட்ட அறிவுரைகளுக்கு இணங்க வேண்டும், ஆய்வுக் குழுவுடன்

விசுவாசத்துடன் ஒத்துழைக்கவும், எனது உடல்நலத்தில் அல்லது நல்வாழ்வுத் தில் ஏதேனும் சீர்கேடு ஏற்பட்டால் அல்லது எதிர்பாராத அல்லது வழக்கத்திற்கு மாறான அறிகுறிகள். ☐

-இந்த ஆய்வில் பங்கேற்பதற்கு நான் ஒப்புதல் அளிக்கிறேன்.

-இரத்தவியல், உயிர்வேதியியல், ரேடியோலாஜிக்கல் பரிசோதனைகள் உட்பட முழுமையான மருத்துவ பரிசோதனை மற்றும் பகுப்பாய்வு பரிசோதனைகளை மேற்கொள்ள நான் அனுமதி கொடுக்கிறேன். ☐

கையொப்பம்/கட்டைவிரல் ரேகை:

நோயாளியின் பெயர் மற்றும் முகவரி:

ஆய்வாளரின் தேதி கையொப்பம்:

ஆய்வு ஆய்வாளரின் பெயர், இடம், தேதி: