"A STUDY OF CARDIAC DYSFUNCTION IN CIRRHOSIS OF LIVER USING ECG, 2D-ECHO AND NT-proBNP AND ITS CORRELATION WITH CHILD PUGH SCORE- A ONE YEAR CROSS-SECTIONAL STUDY IN KLES DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI."

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A STUDY OF CARDIAC DYSFUNCTION IN CIRRHOSIS OF LIVER USING ECG, 2D-ECHO AND NT-proBNP AND ITS CORRELATION WITH CHILD PUGH SCORE" – A ONE YEAR CROSS –SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL,** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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ABBREVIATIONS

ALT	-	ALANINE AMINOTRANSFERASE
AST	-	ASPARTATE AMINOTRANSFERASE
AT- II	-	ANGIOTENSIN – II
BNP	-	BRAIN NATRIURETIC PEPTIDE
cGMP	-	CYCLIC GUANOSINE MONO PHOSPHATE
CCM	-	CARDIOMYOPATHY
CLD	-	CHRONIC LIVER DISEASE
CVS	-	CARDIOVASCULAR DISEASE
CTP	-	CHILD-PUGH SCORE
CBC	-	COMPLETE BLOOD COUNT
DT	-	DECELERATION TIME
DCLD	-	DECOMPENSATED CHRONIC LIVER DISEASE
2D-ECHO	-	ECHOCARDIOGRAPHY
EF	-	EJECTION FRACTION
e′		EARLY DIASTOLIC MITRAL ANNULAR VELOCITY
EC	-	ENDOGENOUS CANNABINOIDS
ECG	-	ELECTROCARDIOGRAM
GGT	-	GAMMA GLUTAMYL TRANSPEPTIDASE

HBV	-	HEPATITIS B VIRUS
HCV	-	HEPATITIS C VIRUS
INR	-	INTERNATIONAL NORMALISED RATIO
LAP	-	LEFT ATRIAL PRESSURE
LVEDP	-	LEFT VENTRICULAR END DIASTOLIC PRESSURE
LVEF	-	LEFT VENTRICULAR EJECTION FRACTION
LFT	-	LIVER FUNCTION TEST
MELD	-	MODEL FOR END STAGE LIVER DISEASE
PT	-	PROTHROMBIN TIME
RFT	-	RENAL FUNCTION TEST
USG	-	ULTRASONOGRAPHY

ABSTRACT

Background: The relationship between CLD and the cardiovascular system has been defined as cirrhotic cardiomyopathy (CCM) based on echocardiographic and ECG findings in CLD patients. The purpose of this study was to see how useful is NT-proBNP levels, 2D- ECHO, and ECG in ruling out CVS dysfunction in patients of chronic liver disease.

Material & Method: This cross-sectional study was done among the patients with chronic liver disease above age 18yrs at KLES Dr. Prabhakar Kore Hospital and Research Centre, Belagavi. Patients with ischemic heart disease, congenital heart disease, pregnant women and thyroid disorder were excluded from the study. Patients were analysed for liver function test, USG abdomen, NT-proBNP, 2D-ECHO and ECG were conducted and compared with the Child Pugh scoring system. The data were analysed using SPSS v21 operating on windows 10.

Results: In the present study, a total of 92 patients were included with mean age of 51.5±10.75yrs. Among the included patients, there was male preponderance with 96.7% male patients and 3.3% female patients. Our study found significant relation of blood parameters with the severity of the cirrhosis. There is significant correlation of NT-proBNP levels, 2D-ECHO findings and ECG changes with severity of the cirrhosis among the patients ($p<0.05$).

Conclusion: The present study found a significant cardiac dysfunction in the patients of cirrhosis of liver. The association between cardiac dysfunction and severity of liver was strongly seen in patients with Child Pugh Class C. The cardiac dysfunction assessed using NT proBNP, 2D-ECHO and ECG is useful in early detection and management of patients with cirrhotic cardiomyopathy.

Keyword: Child-Pugh score, Cirrhosis, Cardiomyopathy, NT-proBNP, Echocardiography.

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INTRODUCTION

Chronic liver disease (CLD) is common and widespread entity worldwide.[1] The link between CLD and the cardiovascular system has been identified as cirrhotic cardiomyopathy (CCM) based on echocardiographic and ECG findings in CLD patients.[2,3]

Zardi et al and Moller et al., have defined CCM as a chronic cardiac dysfunction in patients with liver cirrhosis and / or portal hypertension, characterized by a sudden decrease in the cardiac contractile response to physical, pathological or pharmacological stress, but with normal cardiac output at rest.[4,5]

"Cirrhotic cardiomyopathy is defined as "a chronic cardiac dysfunction in patients with cirrhosis characterised by blunted contractile responsiveness to stress and /or altered diastolic relaxation with electrophysiological abnormalities in absence of known cardiac disease".[1] It occurs due to decreased beta-adrenergic function, abnormal plasma membrane biophysical characteristics and increased nitric oxide synthesis mediated by cGMP."

Characteristics of cirrhotic cardiomyopathy include an attenuated systolic or diastolic response to stressful stimuli, histological or structural changes in heart chambers, raised serum markers suggestive of stress and abnormalities in the electrophysiology.

Cirrhotic cardiomyopathy and hyperdynamic circulation have been seen in chronic liver disease patients, but still much to be explored. As the correlation between cirrhotic cardiomyopathy and severity of chronic liver disease has not been well established, our study aimed to find the same.

CLD patients unscreened for cardiovascular abnormalities have increase morbidity and mortality. Our research aimed to study the utility of NT-proBNP value, 2D-ECHO and ECG to rule out cardiovascular dysfunction, which can lead to early diagnosis and management of the same. Thus, decreasing the morbidity, mortality and increasing the life expectancy and improving the quality of life of the patient.

AIMS & OBJECTIVES

Aim

The present research aimed to study cardiac dysfunction in cirrhosis of liver using ECG, 2D-ECHO and NT-proBNP and its correlation with CHILD-PUGH score.

Objective

- To evaluate cardiac dysfunction in patients with cirrhosis of liver using NT-proBNP, 2D-ECHO and ECG.
- To correlate cardiac dysfunction with the severity of cirrhosis of liver using Child-Turcotte Pugh (CTP) Score.

REVIEW OF LITERATURE

Globally, chronic liver disorders are a leading cause of morbidity and mortality. Multiple etiological causes contribute to a similar clinic-pathological pathophysiology in CLDs, albeit progression rates and clinical course may differ. Mortality data is usually used to measure the disease burden. Between 1980 and 2013, mortality due to CLD has increased by 46% worldwide, underscoring the growing public health importance of the disease.[6] One of the most common etiologies is alcohol. Alcohol related liver disease is the leading cause of death, accounting for 2.5 million/year. The pathologic aspects of cirrhosis comprise of distortion of architecture of the liver with the creation of regenerating nodules, which indirectly means development of fibrosis. 5-year survival rate in the patients with decompensated cirrhosis is 14 to 35 percent and in the patients with compensated CLD is 84 percent.[7]

Liver cirrhosis:

In late stages of chronic liver disease, progressive liver fibrosis occurs which is characterized by the formation of regenerating nodules and alterations in the liver architecture. It is widely assumed that in its advanced stages, it is irreversible, and that liver transplantation (LT) may be the sole therapeutic option. Cirrhosis of liver due to any etiology is reversible, if done in the initial stages of CLD. People with cirrhosis are vulnerable to variety of problems and have a drastically reduced life expectancy.

Incidence:

Global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% for the general population. Cirrhosis was expected to kill 771,000 people globally in 2001, placing 14th and 10th in the globe and developed nations, respectively, as the main cause of death.[8] Death of the patients secondary to CLD are predicted to rise, making it the 12th leading cause of death by 2020.[9] In India, Cirrhosis of liver is responsible for 22.2 fatalities per 1,00,000 persons, according to World Health Organization (WHO) Global Health Observatory figures.[10]

Etiology:

Cirrhosis can be caused by a variety of liver diseases, including cholestasis and chronic hepatitis. The three most common causes of cirrhosis in the US are hepatitis C, alcoholic liver disease, and non-alcoholic hepatic disease; between 2004 and 2013, they collectively accounted for around 80% of patients on the LT (liver transplant) waiting list.[11]

In developed countries, common causes are[12]:

- Hepatitis C infection and Hepatitis B infection
- Hemochromatosis
- Alcoholic liver disease
- NAFLD

Additionally, cirrhosis can be brought on by:

- Wilson’s disease
- Celiac disease
- Autoimmune hepatitis

- Sclerosing cholangitis
- Biliary cirrhosis
- Medications like Methotrexate and Isoniazid
- Alpha-1 antitrypsin deficiency
- Granulomatous liver disease
- Polycystic portal fibrosis
- Right heart failure
- Veno-occlusion disease

Classification

Cirrhosis of liver was traditionally classified as micronodular, macronodular, or mixed.[13] Micronodular cirrhosis, defined by nodules less than 3 mm in diameter, was thought to be caused by alcohol, hemochromatosis, cholestatic causes of cirrhosis, and hepatic venous outflow obstruction. Macronodular cirrhosis, described by nodules larger than 3 mm in size, was thought to be caused by chronic viral hepatitis.

- Micronodular cirrhosis
- Macronodular cirrhosis
- Mixed type

Pathogenesis

The hallmark pathological characteristic is chronic severe hepatocyte damage accompanied by extensive fibrosis with nodule formation in the normal liver tissue. This is primarily due to hepatocyte necrosis, reticular network degradation, and nodule regeneration of remaining liver tissue.

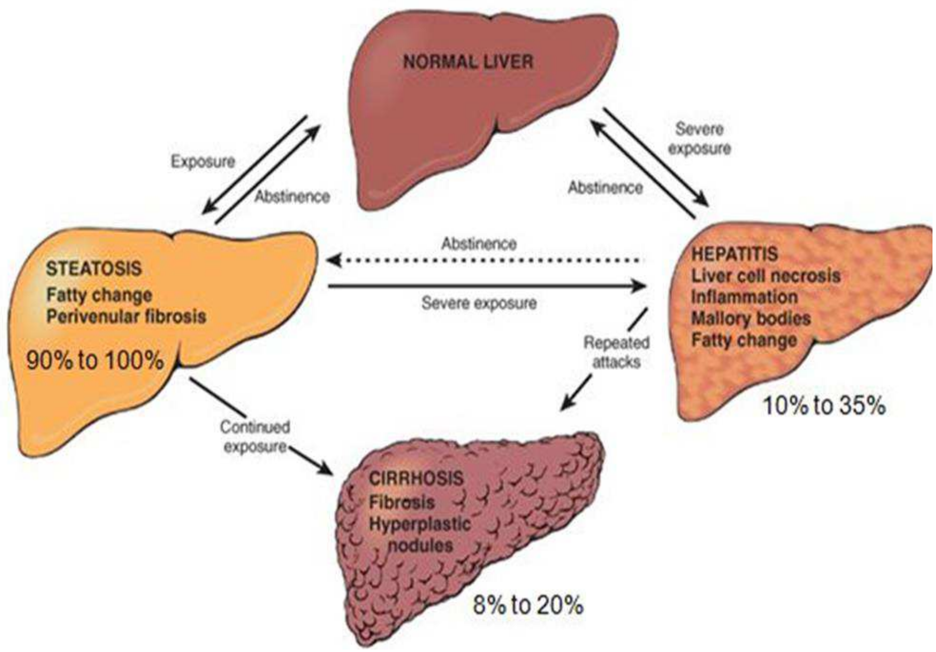

Figure 1: Hepatic repair and regeneration

As a result of the activation of hepatic stellate cells, the development of myofibroblasts causes an increase in the production of collagen and other extracellular matrix components, which distorts the architecture of liver, reduces mass and function.

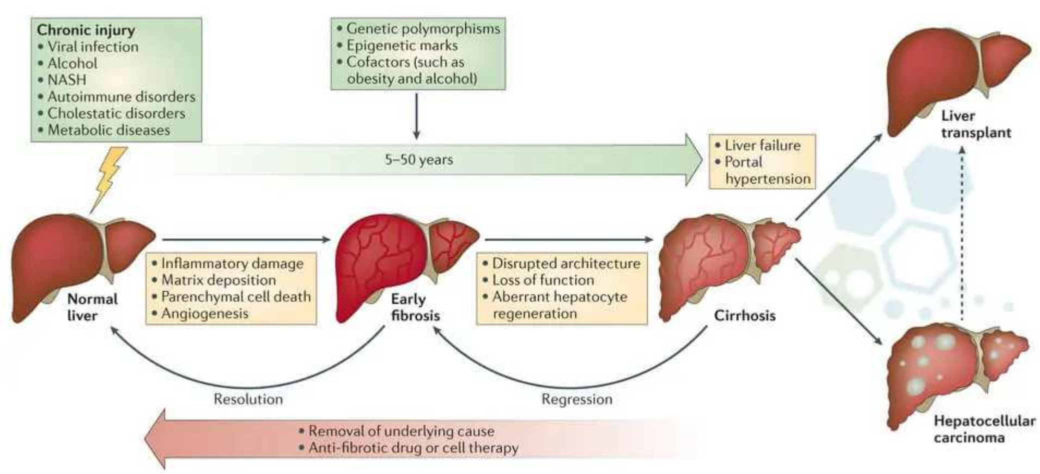

Figure 2: Pathogenesis of hepatic cirrhosis

Clinical manifestations

The clinical manifestations of cirrhosis of liver might include nonspecific symptoms (e.g., anorexia, loss of weight, tiredness, weakness,) as well as signs and symptoms of decompensation of liver disease (pruritus, jaundice, abdominal distension from ascites, confusion due to hepatic encephalopathy and signs of upper gastrointestinal bleeding).

SYMPTOMS
Anorexia
Weight loss
Weakness
Fatigue
Muscle cramps
Easy bruising
Amenorrhea/ oligomenorrhea/ metrorrhagia (women) **Impotence** **Infertility** **Decreased libido (men)**
Jaundice **Dark or "cola-colored" urine** **Pruritus** **Hematemesis/ melena/ hematochezia** **Abdominal distension** **Lower extremity edema**

Cirrhotic patients may exhibit a wide range of signs and symptoms, indicating the critical role of liver in maintaining the homeostasis. Furthermore, they may have characteristics associated with the underlying cause of cirrhosis, such as diabetes mellitus, hepatitis, cryoglobulinemia, and arthropathy in hemochromatosis patients, or extrahepatic autoimmune disorders (such as thyroiditis or hemolytic anemia) in autoimmune hepatitis.

Physical examination

In patients with cirrhosis, a number of physical findings have been described including jaundice, digital clubbing, gynecomastia, spider angiomata, ascites, palmar erythema, splenomegaly, and asterixis.

Table 1: Findings on physical examination

Hepatomegaly
Splenomegaly
Spider angioma / spider telangiectasia
Palmar erythema
Digital clubbing
Hypertrophic osteoarthropathy
Dupuytren's contracture **Terry nails** **Parotid gland enlargement (likely due to alcohol use and not cirrhosis per se)**
Gynecomastia (men) **Loss of chest or axillary hair (men)** **Testicular atrophy (men)** **Caput medusa** **Cruveilheir- Baumgarten murmur (venous hum)**

Individuals with cirrhosis of liver exhibit jaundice as well as spider angiomata. Jaundice is characterized by a yellowish discoloration of the mucous membranes and dermis as a result of an increase in serum bilirubin. Before the bilirubin level hits 0.02 to 0.03 g/L, it is typically undetected. Jaundice can also cause urine to seem dark or "cola" in color.

Spider angiomata are vascular lesions consisting of a central core arteriole which is surrounded on all sides by numerous smaller arteries. They are most commonly present on the upper trunk, ears, and the upper limbs. The central arteriole (body of the lesion) may be observed throbbing when pinched with a glass slide. The blood in the spider angioma first goes to the central arteriole and then, after blanching to the peripheral points of each "neck". Several radiating legs and surrounding erythema are usually present, which may cover the whole lesion or merely the central region.

Figure 3: Showing the spider angioma

Patients with CLD frequently exhibit fetor hepaticus and parotid gland enlargement in the head and neck region. Parotid gland enlargement is prevalent in patients of chronic liver disease and is most likely caused by alcohol rather than cirrhosis. Rather than a hyperactive gland, enlargement is frequently caused by fatty infiltration, fibrosis and edema. The breath of people with cirrhosis has a sweet, pungent odour known as fetor hepaticus.[14] It is caused by high levels of dimethyl sulphide, the presence of which signals severe portal- caval shunting.[15]

Gynecomastia affects up to two-thirds of cirrhotic individuals based on chest findings. It occurs secondary to increase in the androstenedione generated by the adrenal gland, an increase in estrone made by aromatization of androstenedione, or an increase in the synthesis of estradiol from estrone.[16] Men can also have feminization related symptoms such as axillary or chest hair loss and inversion of the typical male pubic hair pattern. In addition to cirrhosis, gynecomastia can arise in a variety of other disorders.

Hepatomegaly is very commonly seen in patients of cirrhosis. The liver in CLD may be enlarged, normal or small in size. Although, hepatomegaly or palpable liver may indicate the presence of liver disease, the absence of an enlarged liver cannot not rule out liver disease. The liver in cirrhosis has a firm and nodular consistency when palpated. In humans, liver is the largest internal organ, measuring twenty-one to twenty-three centimeters horizontally and fourteen to seventeen centimeters vertically. Size of the liver varies individually.

Caput medusa- lower abdominal wall veins typically drain inferiorly into the iliofemoral system, whereas the upper abdominal wall veins drain superiorly into the axillary veins and the thoracic wall. When cirrhosis produces portal hypertension, the umbilical vein, which is ordinarily vestigial in infancy, may reopen. Blood from the portal system may be diverted to the umbilical vein from the periumbilical veins and finally into the abdominal veins, making them visible. This look has been compared to the head (caput) of the fabled Gorgon Medusa.

Dupuytren's contracture is produced by the palmar fascia thickening and shortening, resulting in finger flexion abnormalities (Figure 4). Pathologically, it is distinguished by disorganized collagen deposition, fascial thickness, and fibroblastic proliferation. The pathophysiology is unknown, however it may be connected to free radical generation induced by hypoxanthine oxidative metabolism.[17]

Figure 4: Showing Dupuytren's contracture

Major complications

The common complications of cirrhosis include:

Esophageal Variceal hemorrhage
Ascites
Spontaneous bacterial peritonitis
Hepatic encephalopathy
Hepatocellular carcinoma
Hepatorenal syndrome
Hepatopulmonary syndrome
Hepatic hydrothorax
Portopulmonary hypertension
Cirrhotic cardiomyopathy
Portal vein thrombosis

Patients with decompensated cirrhosis, experience these complications. Multiple factors can predispose a cirrhotic patient to decompensation. Bleeding, inflammation, alcohol use, medications, dehydration, and constipation are all risk factors for decompensation.[18–20] Furthermore, patients who are obese are at a higher risk of decompensation.[21] Patients that have developed decompensation should be considered for liver transplantation.

Many complications of cirrhosis are the result of portal hypertension which is increased pressure within the portal venous system. This leads to the formation of venous collaterals as well as the circulatory, vascular, functional and biochemical abnormalities that contribute to the pathogenesis of ascites and other complications.

Complications of portal hypertension include:

Hepatic encephalopathy
Ascites
Spontaneous bacterial peritonitis
Variceal bleeding
Portal hypertensive gastropathy
Hepatorenal syndrome
Hepatopulmonary syndrome
Hepatic hydrothorax
Portopulmonary hypertension
Cirrhotic cardiomyopathy

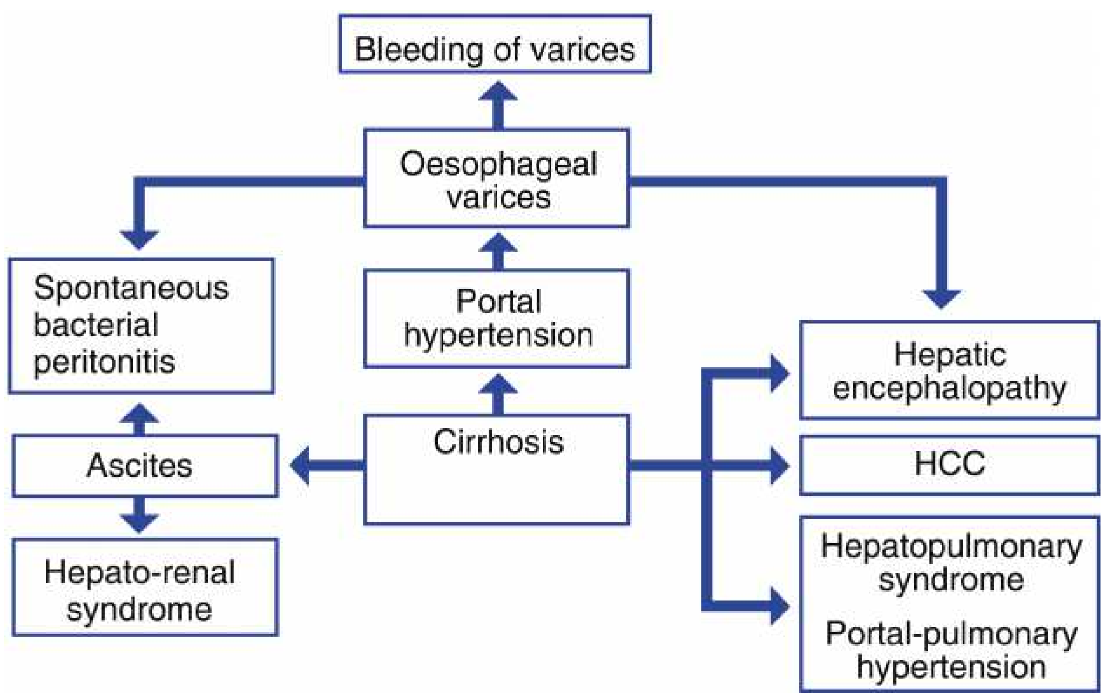

Figure 5: Complications of cirrhosis

As a consequence of the portal hypertension, there occurs ascites and variceal bleeding. The causes of portal hypertension are divided into pre-hepatic, intra-hepatic and post-hepatic.

Around 60% of cirrhotic patients have portal hypertension. Ascites, bleeding varices, Splenomegaly, and other primary complications of portal hypertension are common. Splenomegaly is caused by congestion, which occurs due to increased portal pressure. Even before ascites develops, hypersplenism with thrombocytopenia can be the first symptom of portal hypertension.

Pathogenesis:

"Portal hypertension" occurs as a result of increased intra-hepatic resistance and increased portal blood flow. Hepatic compliance decreases as hepatic resistance increases. Tiny variations in blood flow are caused by a rise in the portal pressure. A healthy liver can adapt to change in portal pressure. However, it can have a strong stimulatory impact on portal pressure in the cirrhotic liver.

Mechanical factors include hepatic fibrosis and nodularity, as well as distortion of vascular architecture and remodeling in the splanchnic and systemic vascular systems, which occurs in response to the hyperdynamic circulatory state's sustained increases in flow and shear stress.

The hyperdynamic circulation is characterized by splanchnic and peripheral vasodilation, increased cardiac output and decreased MAP (mean arterial pressure). Vasodilation, especially in the splanchnic bed, allows more systemic blood to enter into the portal venous circulation. Vasodilation in the splanchnic vessels is primarily caused by relaxation of the splanchnic arteriole and the resulting splanchnic hyperemia.

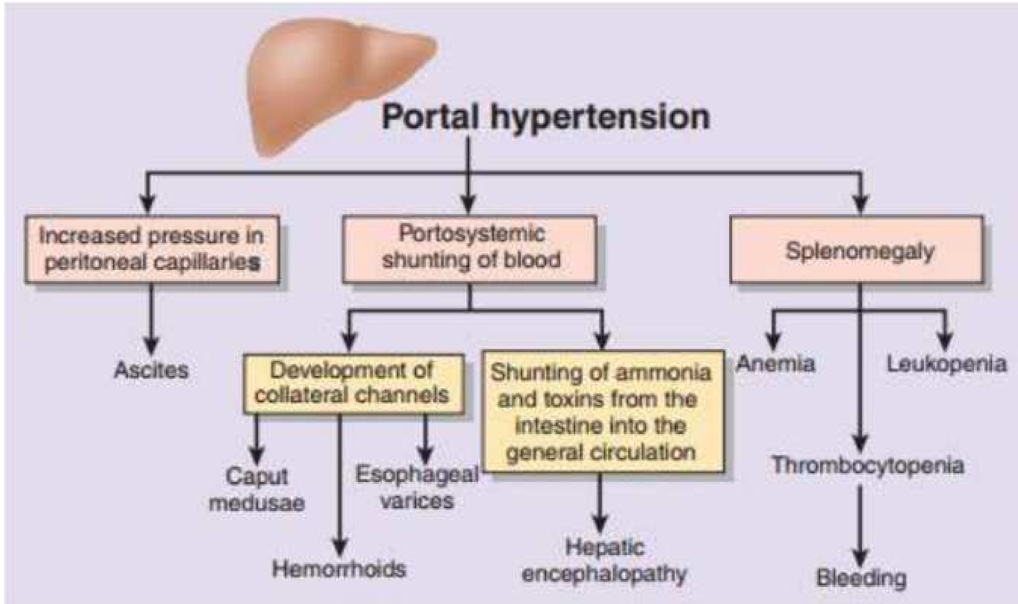

Figure 6: Portal Hypertension

Laboratory findings

Patients with cirrhosis may experience several lab test abnormalities. Laboratory abnormalities may also be the first sign that a patient has cirrhosis, since, panels of liver function tests are frequently sent for screening or examination of particular symptoms. Derangement in the blood parameters include hyponatremia, higher international normalized ratio (INR)/ an extended prothrombin time, increased ALP (alkaline phosphatase) or GGT (gamma-glutamyl transpeptidase), aberrant aminotransferases, and thrombocytopenia.

Table 2: Laboratory tests used in cirrhosis patients

Moderately elevated aminotransferases (often with an AST:ALT ratio >1)
Elevated alkaline phosphatase (2 to 3 times the ULN)
Elevated gamma-glutamyl transpeptidase
Thrombocytopenia
Leukopenia/neutropenia
Anemia
Low serum albumin
Prolonged prothrombin time / elevated INR
Hyperbilirubinemia
Hyponatremia
Elevated serum creatinine

Liver function tests

The most common laboratory measures include the enzyme testing, specifically the serum aminotransferases, gamma-glutamyl transpeptidase, and alkaline phosphatase, serum bilirubin and the synthetic testing which includes the serum albumin concentration and Prothrombin time.

Aminotransferases – ALT (Alanine aminotransferase) and AST (Aspartate aminotransferase) both are commonly elevated in patients with CLD. The aspartate aminotransferase (AST) is more often raised more than the alanine aminotransferase (ALT). The ratio of AST/ALT is typically less than one in chronic hepatitis that isn't caused by alcoholism. Reversing the AST to ALT ratio in cases of chronic hepatitis that proceed to cirrhosis. [22,23]

Alkaline phosphatase (ALP) - ALP levels in cirrhosis are often higher than normal, albeit they seldom exceed two or three times the upper limit. Patients with underlying cholestatic liver disease had higher values.

GGT - stands for gamma-glutamyl transpeptidase. Although they are nonspecific, the levels of this enzyme in liver illness generally correlate with alkaline phosphatase. Compared to other causes of CLD, ethanol-related CLD often has much higher GGT levels. This can be because alcohol makes hepatic microsomal GGT leak[24] or because alcohol makes hepatocytes release GGT.[25]

Bilirubin – Bilirubin levels in well-compensated cirrhosis can be normal. They do, however, rise as the cirrhosis progresses. An increase in serum bilirubin predicts a poor prognosis in patients with primary biliary cirrhosis.[25]

Prothrombin time (PT) – The bulk of the clotting-related proteins are produced by the liver. Therefore, the prothrombin time period is a good indicator of the severity of hepatic synthetic malfunction. As the ability of cirrhotic livers to synthesis clotting factors decreases, PT rises in cirrhosis. As a result, the severity of hepatic dysfunction is correlated with coagulopathy that is getting worse.

Albumin - The liver is the sole organ where albumin is synthesized. Albumin levels decrease as cirrhosis progresses and the liver's capacity for synthesis declines. Thus, the severity of cirrhosis can be better classified by serum albumin levels. In addition to liver illness, other medical diseases such as heart failure, the nephrotic syndrome, protein-losing enteropathy, and malnutrition can also cause hypoalbuminemia.

The most frequent cause of thrombocytopenia is portal hypertension with congestive splenomegaly. Up to 90% of the circulating platelet mass may temporarily be sequestered as a result of splenic enlargement. Platelets less than 50,000/mL are infrequent, nevertheless, and unless they are compounded by a concurrent coagulopathy, they are rarely a cause for clinical concern.

Hematological disorders seen in Cirrhosis of liver

Cirrhosis of liver or chronic liver failure is usually associated with presence of hypersplenism and diminished erythrocyte cell life. Dietary deficiencies, alcoholism, defective protein synthesis, bleeding and coagulation disorders worsen the situation.

Blood volume: the plasma volume is increased in the patients with cirrhosis, those with ascites. This may lead to low peripheral hemoglobin or erythrocyte levels. The total hemoglobin circulating will be reduced to half in the patients.

Cirrhosis of liver and Cardiac dysfunction[26]

Cirrhotic cardiomyopathy is 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 absence of known cardiac disease”.[7] It occurs due to decreased beta-adrenergic function, abnormal plasma membrane biophysical characteristics and increased nitric oxide synthesis mediated by cGMP.

Diagnostic and supportive criteria for cirrhotic cardiomyopathy as follows: (1) systolic dysfunction : blunted increase in cardiac output on exercise, volume challenge or pharmacological stimuli or resting ejection fraction <55%, (2) diastolic dysfunction: the ratio of early to late (atrial) phases of ventricular filling or E/A ratio <1.0 (age related), prolonged deceleration time (> 200ms), or prolonged isovolumetric relaxation time (>80ms), (3) supportive criteria: electrophysiological abnormalities, abnormal chronotropic response, electromechanical uncoupling/ dys-synchrony, prolonged QTc interval enlarged, left atrium, increased myocardial mass, increased brain natriuretic peptide (BNP) and pro-BNP. Or increased troponin I. [5]

Clinical manifestations and pathophysiology:

Systolic dysfunction: The majority of cirrhotic individuals have normal or enhanced systolic function at rest, with hyperdynamic circulation defined by excessive cardiac output and tachycardia. In these individuals, physical or pharmacological stress frequently revealed underlying systolic dysfunction.[27,28] some data suggests that systolic dysfunction may play a role in the development of hepatorenal syndrome (HRS). Hypotension develops when splanchnic vasodilation is extremely severe that the rise in CO is insufficient to bring hemostasis in the bloodstream. At that point, the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS) are stimulated, causing salt and water retention as well as the beginning of abdominal distention that leads to ascites. The severe vasoconstriction brought on by the aforementioned operation results in HRS.[29,30]

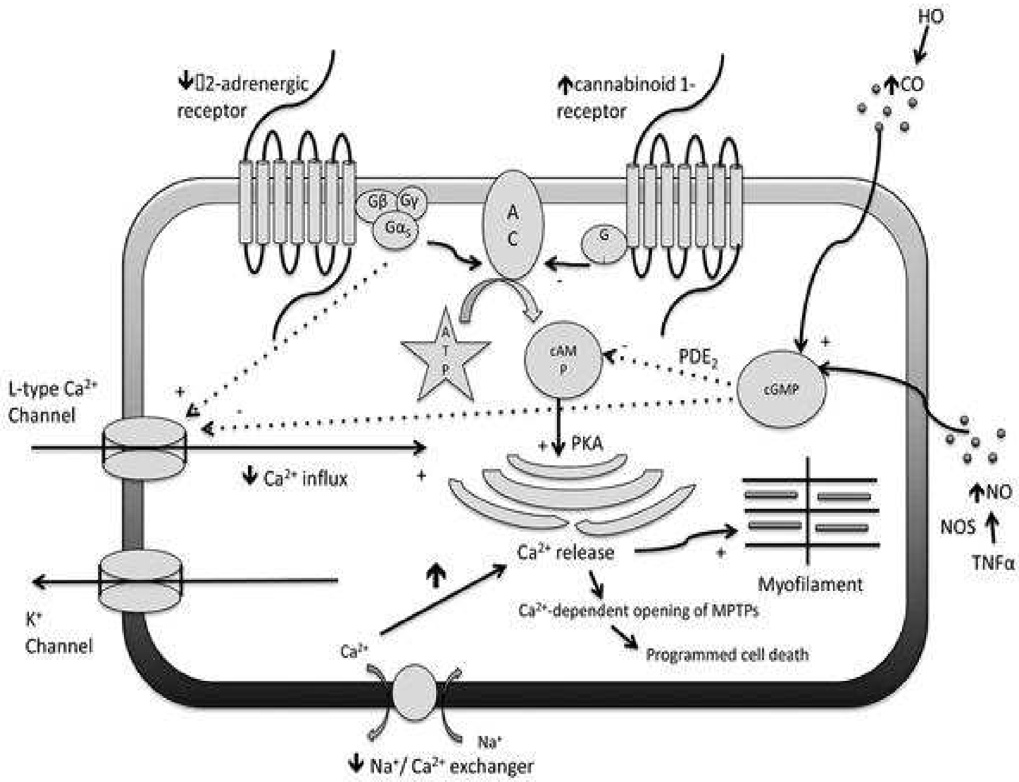

Figure 7: The pathophysiologic process of systolic dysfunction.

Another mechanism of interest in recent study is the influence of endogenous cannabinoids (EC) on the heart function, particularly AEA (anandamide). Anandamide is produced by the membrane phospholipids and it is released from the cell. It acts by activating the cannabinoid-1 or CB1 receptor, which is a GPCR (G-protein coupled receptor). [31]

Another possible mechanism is the presence of substances which depresses the cardiac function such as carbon monoxide (CO) and nitric oxide (NO). According to one research, TNF-α (Tissue necrotic factor) and IL-1β (interleukin) may play a crucial role in the activation of NOS (NO synthases) and which leads to NO formation. NO inhibits cardiac contraction by stimulating cyclic guanosine monophosphate (cGMP), which hastens the degradation of cyclic adenosine monophosphate (cAMP), protein kinase G activation occurs, which in result inhibits the L-type of calcium channel in the sarcolemma, and inhibits the release of calcium from the sarcoplasmic reticulum.[32,33]

Additionally, recent studies have revealed that the Na^{+}/Ca^{2+} exchanger is essential for the growth of CCM. Steady-state intracellular free Ca^{2+} concentration depends on the Na^{+}/Ca^{2+} exchanger to maintain the balance between Ca^{2+} input and outflow. Defects in the Na^{+}/Ca^{2+} exchanger in cirrhotic individuals cause an excessive Ca^{2+} influx, which causes cardiomyocyte death.[4,34]

Diastolic dysfunction: It is defined by aberrant relaxation of left ventricular, which restricts blood flow into ventricles, increases LVEDP (left ventricular end-diastolic pressure),"and enhances contribution of atria to late ventricular filling. On 2-dimensional Doppler echocardiography, these abnormalities are shown by an elevated E/A ratio and a longer deceleration time. As per the latest recommendations from the American Society of Echocardiography, measurement of e′ (early diastolic mitral annular velocity)"is a more reliable diagnostic method of"diastolic"dysfunction.[35]

Some evidence suggests that retention of water and salt in cirrhosis of liver may play a role in the pathogenesis of diastolic dysfunction. High salt consumption has been proven in animal models to cause concentric hypertrophy of the left ventricle and increase the filling pressure of left ventricular without increasing BP. Salt overload promotes cardiac hypertrophy by activating cardiac aldosterone synthesis independently of circulating RAAS.[36,37]

Electrophysiological abnormalities: In Cirrhosis of liver electrophysiological abnormalities includes QT interval prolongation and electromechanical coupling disruption. The abnormalities are attributed to a dysfunction of the sympathetic nervous system as well as vagal dysfunction (autonomic dysfunction). QT interval prolongation affects roughly 40-50% of people.[4,38,39]

Bernardi et al. found that the prevalence of prolonged QT interval increased significantly from CTP (Child Turcott Pugh) class A to B, but didn't differ among cirrhosis etiologies.[39] Trevisani et al. studied QT interval in cirrhotic patients after TIPS and NCPH (non-cirrhotic portal hypertension) and discovered that individuals with non-cirrhotic portal hypertension had a longer QT interval. Another intriguing finding from that research was a worsening of the QT interval following TIPS. The combination of both findings suggested that QT interval prolongation could be caused by the delivery of cardioactive substances from the splanchnic circulation to the systemic circulation and porto-systemic shunt.[38]

Alterations in the fluidity of the plasma membrane and, consequently, changes in the function of membrane receptors and ion channels are the main causes of electrophysiological abnormalities in CCM. Plasma membrane alterations may also result in ion channel deficiencies, resulting in a significant lengthening of the action potential and QT interval. Cirrhosis-induced decrease in K^+ current (both delayed rectifying K^+ current and Ca^{2+} independent transient outward K^+ current) resulted in a prolongation of repolarization phase and action potential in a rat model.[40]

Various article discussing the cardiac dysfunction in Liver cirrhosis:

A significant proportion of cirrhotic patients with volume overload, ascites, and signs of hyperdynamic circulation have normal resting 2D-ECHO parameters but abnormal cardiac responses during exertion, stress, TIPS, or liver transplantation, according to a study by Zardi EM et al., published in 2010, which is consistent with the existence of a cirrhotic cardiomyopathy.[4]

A study conducted by Mota VG et al., (2013) showed that echocardiography should be part of CLD stratification for screening portopulmonary hypertension, and cirrhotic cardiomyopathy, because, most of the time, such complications are diagnosed only when patients are already waiting for a liver transplant.[41]

According to a research conducted by Licata A, et al. (2013), 58 cirrhotic individuals (72% males) with a mean age of 62 years (31% with type 2 diabetes and 11% with moderate arterial hypertension) showed normal function of kidney (mean creatinine 0.9 mg/dl, range 0.7-1.06). CLD patients showed greater plasma value of NT-proBNP (365.23+-65.2 vs 70.8+-70.6) than controls (p0.001). Left atrial volume (LAV)” (61.82+-6.4 vs 43.51+-4.2) and left ventricular ejection fraction (LVEF) (62.7+-6.9 vs. 65.54%, p = 0.05) were also changed in the patients of cirrhosis as compared to controls. The E/A ratio was higher in patients with F2-F3 esophageal varices (1.21±0.46 vs. 0.89±0.33 m/s, p = 0.006) due to their higher e' velocity (0.91+-0.23 vs. 0.66+-0.19 m/s, p0.001). These results show that NT-pro-BNP plasma levels increase directly with the severity of chronic liver disease.[42]

A study conducted by Fede G et al., (2015) Cirrhosis-related circulatory dysfunction has clinical repercussions after insertion of transjugular intrahepatic portosystemic shunt and also during and after liver transplantation. Cardiovascular problems are common after these surgeries, with pulmonary edema being the most common. Other problems include overt heart failure, arrhythmias, pulmonary hypertension, pericardial effusion, and development of cardiac thrombus. This study had shown that during and after liver transplantation, the clinical consequences of cirrhosis-related cardiovascular dysfunction are evident.[43]

Pourafkari L et al., (2017) discovered that independent of disease severity electrocardiographic alterations are prevalent in patients of cirrhosis. Low-voltage complexes of QRS in these individuals may be associated with anthropometric changes and the development of ascites.[2]

In a study by Roy CK et al (2018) it was found that patients who had left ventricular diastolic dysfunction (LVDD) had significantly more severe liver cirrhosis ($p < 0.05$). Grade 2 and Grade 3 left ventricular diastolic dysfunction (LVDD) were associated with increased plasma renin activity and ascites compared to Grade 1 LVDD or without LVDD, indicating a direct association between LVDD and circulatory disorders. In all cases, systolic function and heart rate were normal. In three groups of patients, survival did not change as a function of the degree of left ventricular diastolic dysfunction (LVDD) ($p = 0.739$). In cirrhosis, LVDD develops along with other changes in cardiac structure and function and is related to circulatory dysfunction. This suggests that patients with cirrhosis primarily have left ventricular diastolic dysfunction (LVDD) with normal systolic function at rest. Tissue Doppler imaging (TDI) and standard 2D echocardiography (EDE) both are real-time imaging technologies, non-invasive, and rapid with good accuracy for identifying Cardiovascular abnormalities, suggestive of, for example, cirrhotic cardiomyopathy.[3]

In a research done in 2019, Wiese S et al. evaluated the cardiac dysfunction in cirrhotic individuals. 25 participants in the research developed AD, 4 had LT, and 20 passed away. In a univariate analysis, the model for age and end-stage liver disease and age were the main predictors, while mean arterial pressure (MAP) was the sole cardiovascular measure related with death (p= 0.037). Low cardiac index was independently connected with death in individuals with AD (P = 0.01), whereas last-visit myocardial ECV was substantially linked with the combined end point LT/death (p= 0.001). Heart function appears to deteriorate with the progression of cirrhosis and affects prognosis, especially in those with Alzheimer's disease. Patients with stable cirrhosis, on the other hand, show minimal advancement in cardiac dysfunction over a 2-year period, with only a minor influence on survival. The findings advocate for vigilant cardiac monitoring in advanced cirrhosis. [44]

In a study by Toma L et al., (2020) prolonged QT interval was linked to advanced liver disease. In addition, individuals with decompensated cirrhosis had smaller QRS amplitudes than those with compensated liver disease. Cirrhotic individuals had an increased slowing of the T wave. These findings were linked to serum albumin, cholesterol, and ammonia levels. A study found that advanced liver illness was linked to longer QT intervals. In addition, individuals with decompensated cirrhosis had smaller QRS amplitudes than those with compensated liver disease.[45]

In a study by Gregolin C et al., (2021) to assess the myocardial dysfunction in CCM associated with cirrhosis. Thioacetamide causes cirrhosis of liver, associated with CCM, which included left ventricular diastolic and systolic dysfunction and cardiac hypertrophy in vivo. Cirrhosis reduced baseline cardiac contractility in vitro. Myocardial response to post-rest contraction stimuli was also reduced. The expression of NCX, RYR2, pPBL Ser16, SERCA2 and L-type calcium channel protein were quantitatively similar, but pPBL Thr17 was significantly less, whereas IL-6 (interleukin) was significantly greater.

Cirrhotic cardiomyopathy is related with lower ventricular contractility, altered phospholamban phosphorylation, and greater cardiac pro-inflammatory interleukin (IL-6) levels, according to a new study. These findings shed light on the molecular and physiological impact of liver cirrhosis on heart function.[46]

MATERIAL & METHOD

Source of data: A cross-sectional study in the patients at KLE Dr. Prabhakar Kore Hospital and Research Centre, Belagavi.

Study design-A Cross-Sectional study

Study period- January 2021 to December 2021

Sample size-90

calculated using formula

n=Z2pq/d2

(n= sample size, z= confidence interval, p=prevalence q=100-p, d=absolute error)

Sample method: Cross-sectional study, all study participants who met the inclusion criteria were enrolled in the study. SPSS using descriptive analysis and chi-square test will be used for statistical analysis.

Inclusion Criteria

- Chronic liver disease patients.
- Patients above the age group of 18 years.

Exclusion Criteria

- K/C/O Ischemic Heart Disease
- K/C/O Congenital Heart Disease
- K/C/O Thyroid disorders
- Pregnant women

METHODOLOGY

- Informed consent was obtained and then patients were enrolled in the study.
- All patients who met the inclusion criteria were subjected to a questionnaire and thorough clinical examination, to identify possible etiology of cirrhosis of liver and to identify presence of complications of chronic liver disease.
- Complete blood counts (CBC), renal function tests (RFT) were done.
- Liver function tests (LFT) including coagulation profile.
- Routine workup for chronic liver disease was done.
- USG abdomen including echotexture and size of liver, spleen and portal vein diameter.
- NT-proBNP, 2D-ECHO and ECG done.
- Patients were then classified into CTP Classes A, B and C based on the Child-Turcotte-Pugh score.

CHILD PUGH SCORE-

		POINTS		
FACTOR	**UNITS**	**1**	**2**	**3**
SERUM BILIRUBIN	Mg/dl	<2.0	2.0-3.0	>51
SERUM ALBUMIN	g/dl	>3.5	3.0-3.5	<3.0
PROTHROMBIN TIME	INR	<1.7	1.7-2.3	>2.3
ASCITES		None	Easily controlled	Poorly controlled
HEPATIC ENCEPHALOPATHY		None	Minimal	Advanced

- Child Pugh class A (a score of 5-6)
- Child Pugh class B (a score of 7-9)
- Child Pugh class C (a score of >/=10)

MELD score:(MODEL FOR END-STAGE LIVER DISEASE)

MELD = 0.957 x ln (Sr. Creatinine) + 0.378 x ln (total bilirubin) +1.120 x ln (INR) + 0.643

Maximum MELD = 40

Interpretation:

MELD Score	Mortality
≤ 9	1.9%
10-19	6.0%
20-29	19.6%
30-39	52.6%
≥ 40	71.3%

STATISTICAL ANALYSIS

All data were collected in proforma and entered into an Excel sheet. The demographic data collected were summarized as frequency, percentage, mean, and SD (standard deviation”. The summarised data were represented using tables, figures, pie charts and bar diagram. The difference in means between the continuous data was analysed with t-test, for follow-up data paired t-test and chi-square test was used for categorical data to determine the significance between the parameters observed in this study. A P <0.05 was accepted as significant. Statistical analysis was performed using SPSS version 22.0 (IBM SPSS, US) software operating on windows 10.

RESULTS

A total of 92 patients who met the inclusion criteria were enrolled in the study, after obtaining informed consent.

Table 3: Showing the mean age of patients

	N	Maximum	Minimum	Mean	Standard Deviation
AGE (years)	92	78	28	51.5	10.75

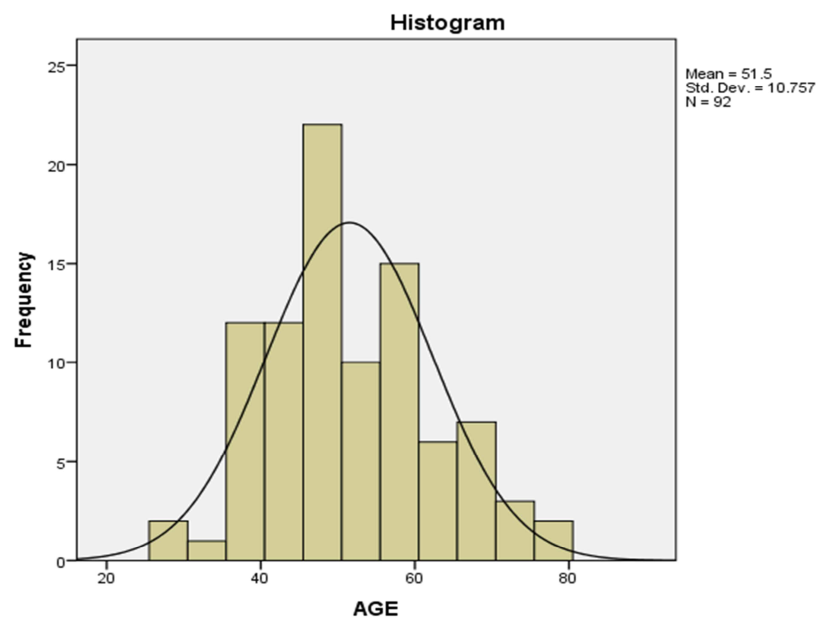

Figure 8: Showing the mean age of patients

The mean age of the study participants was 51.5±10.75 years. The maximum age of the patient was 78 years and minimum was 28 years.

Table 4: Showing the gender distribution among study participants

		Frequency	Percentage
GENDER	Male	89	96.7
	Female	3	3.3
	Total	92	100.0

Among the 92 patients enrolled, the number of male participants were 89 and female participants were 3. In our study, there was male predominance with 96.7% male patients and 3.3% female patients.

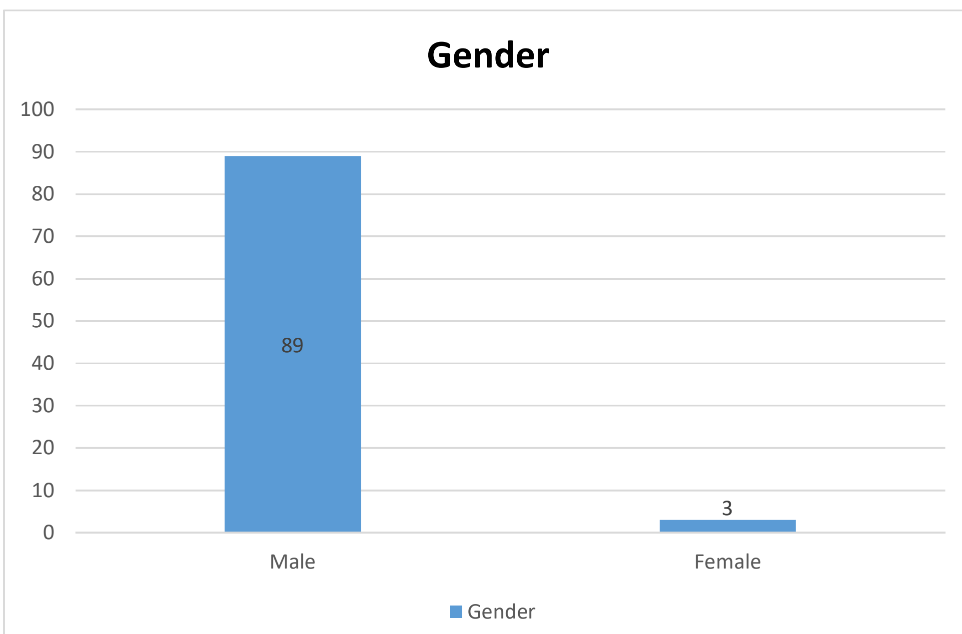

Figure 9: Showing the gender distribution among study participants

Table 5: Shows the distribution of history of alcohol Consumption among study participants

		Frequency	Percentage
ALCOHOL CONSUMPTION	Yes	72	78.3
	No	20	21.7
	Total	92	100.0

In the present study, out of 92 patients, 78.3% (n= 72) of the patients had a history of alcohol consumption.

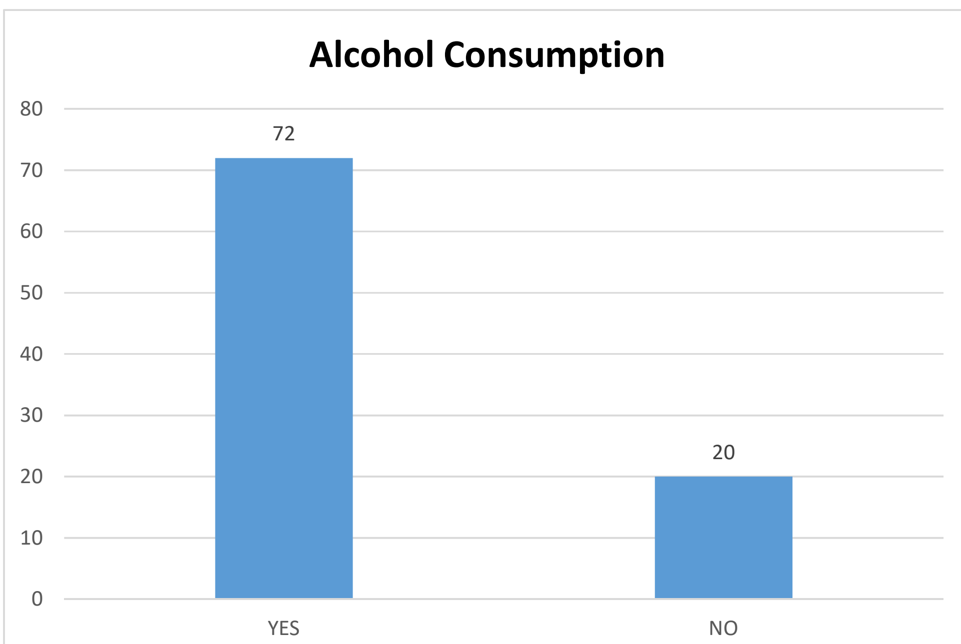

Figure 10: Showing the distribution of presence of history of alcohol Consumption among study participants

Table 6: Showing the distribution of presence of diabetes mellitus among study participants

		Frequency	Percentage
DIABETES MELLITUS	Yes	29	31.5
	No	63	68.5
	Total	92	100.0

Out of 92 patients in our study, 31.3% (n= 29) patients had history of Diabetes Mellitus.

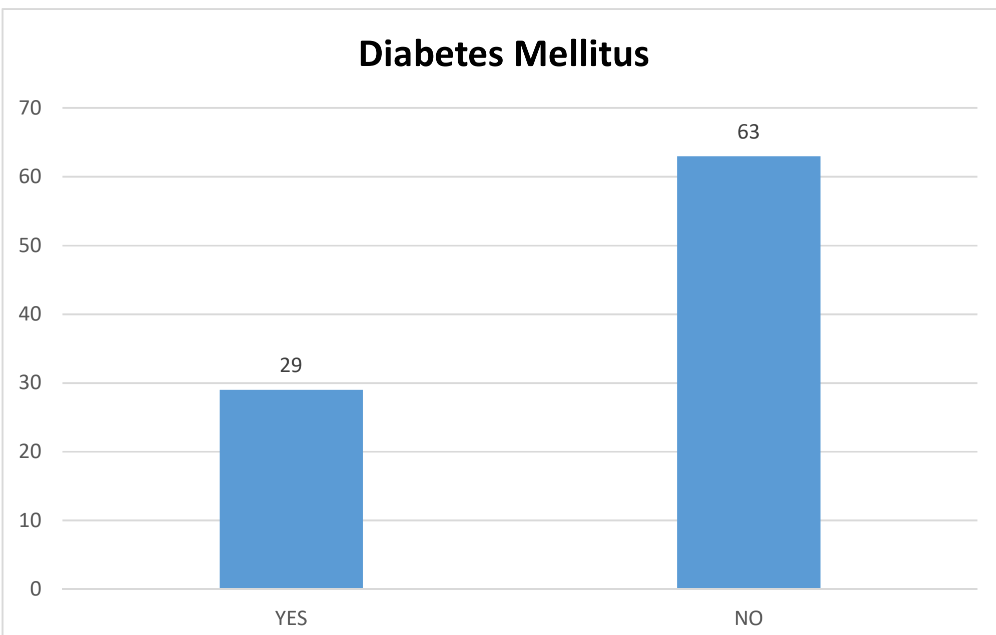

Figure 11: Showing the distribution of presence of diabetes mellitus among study participants

Table 7: Showing the distribution of presence of hypertension among study participants

		Frequency	Percentage
HYPERTENSION	Yes	13	14.1
	No	79	85.9
	Total	92	100.0

Among the study participants, 14.1% (n= 13) were Hypertensive and 85.9% (n= 79) were Non Hypertensive.

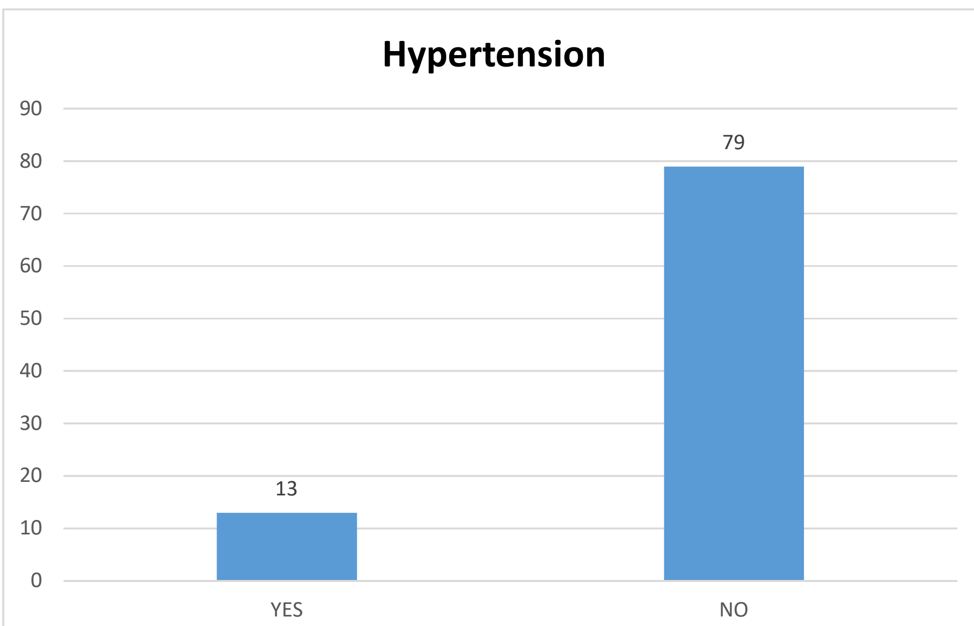

Figure 12: Showing the distribution of presence of hypertension among study participants

Table 8: Showing the distribution of presenting symptom of yellowish discoloration of eyes (jaundice) among study participants

		Frequency	Percentage
JAUNDICE	Yes	61	66.3
	No	31	33.7
	Total	92	100.0

In this study, 66.6% (n= 61) of the study participants had yellowish discoloration of eyes and remaining 33.7% (n= 31) did not have yellowish discoloration.

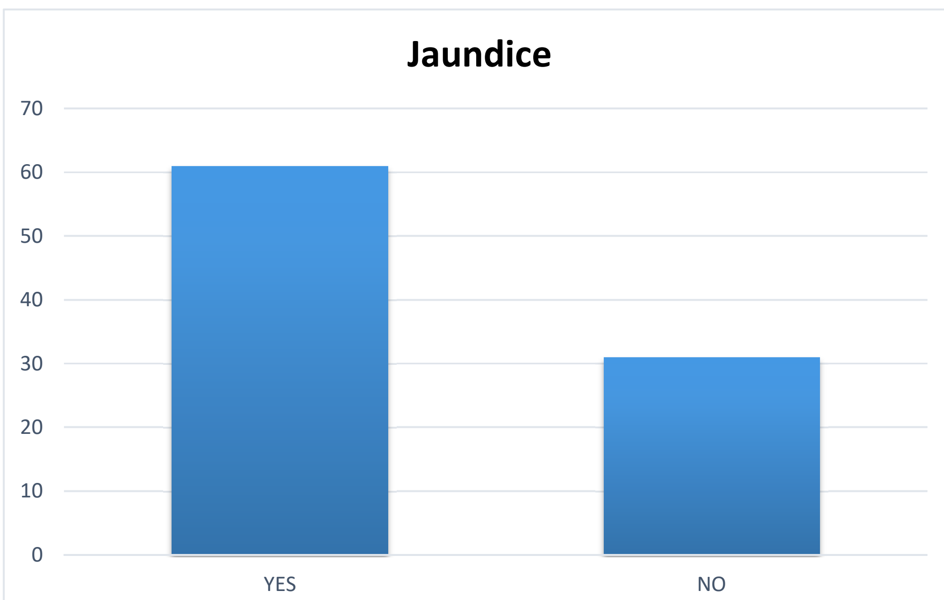

Figure 13: Showing the distribution of presence of yellowish discoloration of eyes (jaundice) among participants

Table 9: Showing the distribution of presence of abdominal distension among study participants

		Frequency	Percentage
ABDOMINAL DISTENSION	Yes	58	63.0
	No	34	37.0
	Total	92	100.0

In this study, 58 out of 92 patients presented with abdominal distension. Thus, abdominal distention was seen in 63% of the patients.

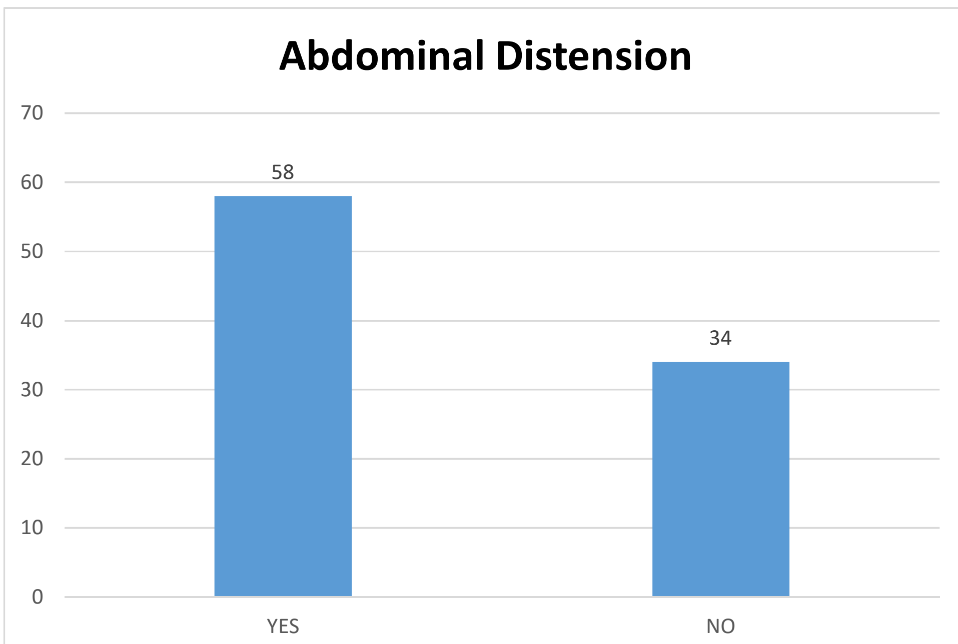

Figure 14: Showing the distribution of presence of abdominal distension among study participants

Table 10: Showing the distribution of presence of pedal edema among study participants

		Frequency	Percentage
PEDAL EDEMA	Yes	58	63.0
	No	34	37.0
	Total	92	100.0

In this study, 58 out of 92 patients presented pedal edema. Thus, pedal edema was seen in 63% of the patients.

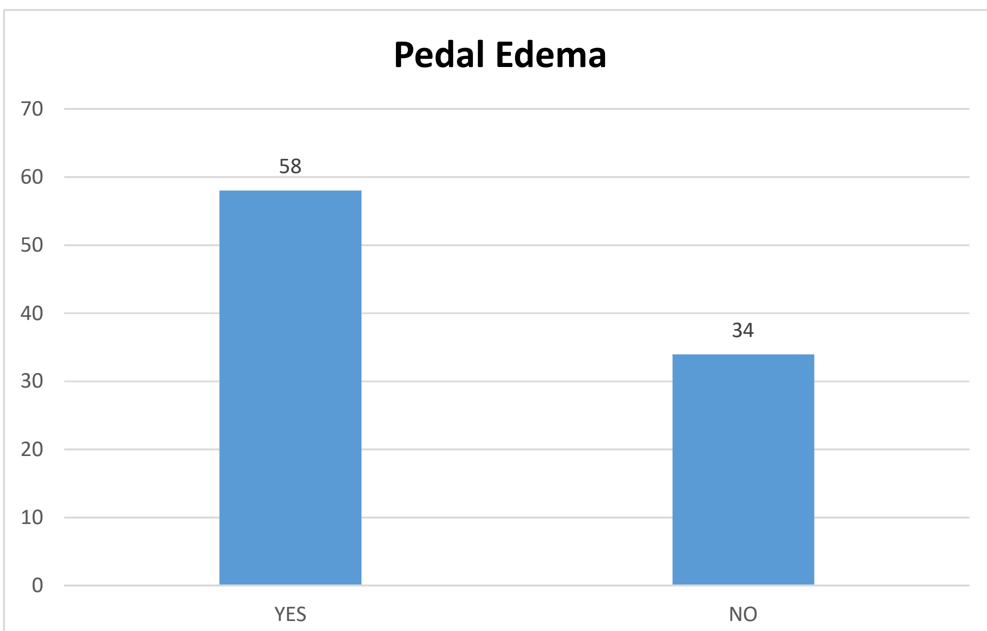

Figure 15: Showing the distribution of presence of pedal edema among study participants

Table 11: Showing the distribution of presence of hematemesis or melena among study participants

		Frequency	Percentage
HEMATEMESIS OR MALENA	Yes	28	30.4
	No	64	69.6
	Total	92	100.0

Among the study participants, 30.4% (n= 28) patients presented with hematemesis or melena. 69.6% (n= 64) patients did not have history of upper GI bleed.

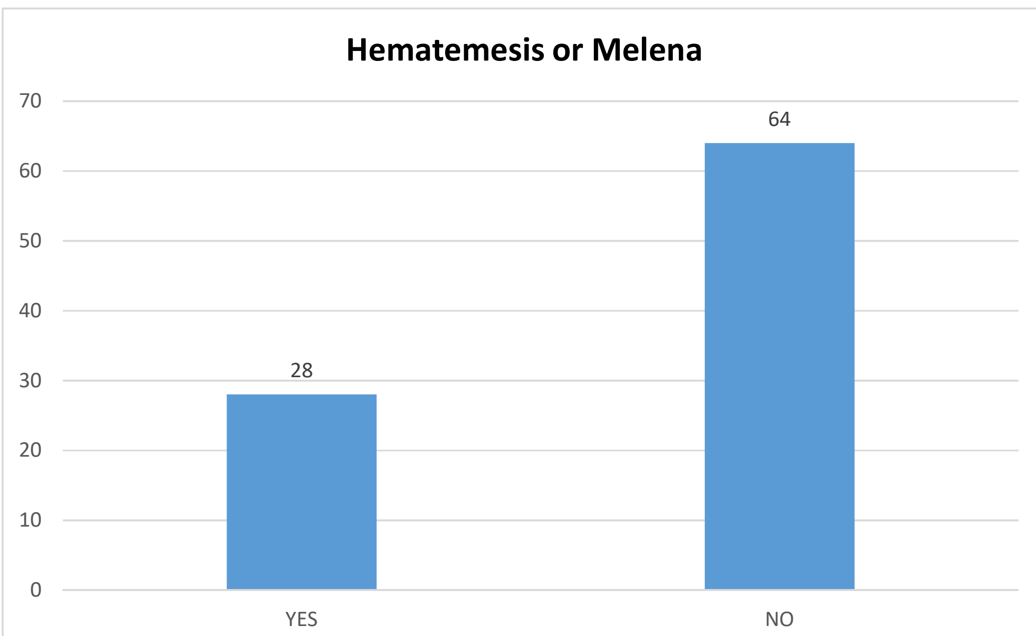

Figure 16: Showing the distribution of presence of hematemesis or melena among study participants

Table 12: Showing the distribution of presence of abdominal pain among study participants

		Frequency	Percentage
ABDOMINAL PAIN	Yes	26	28.3
	No	66	71.7
	Total	92	100.0

In this study, 28.3% (n= 26) of the study participants complained of abdominal pain and remaining 71.1% (n= 66) did not have similar complaints.

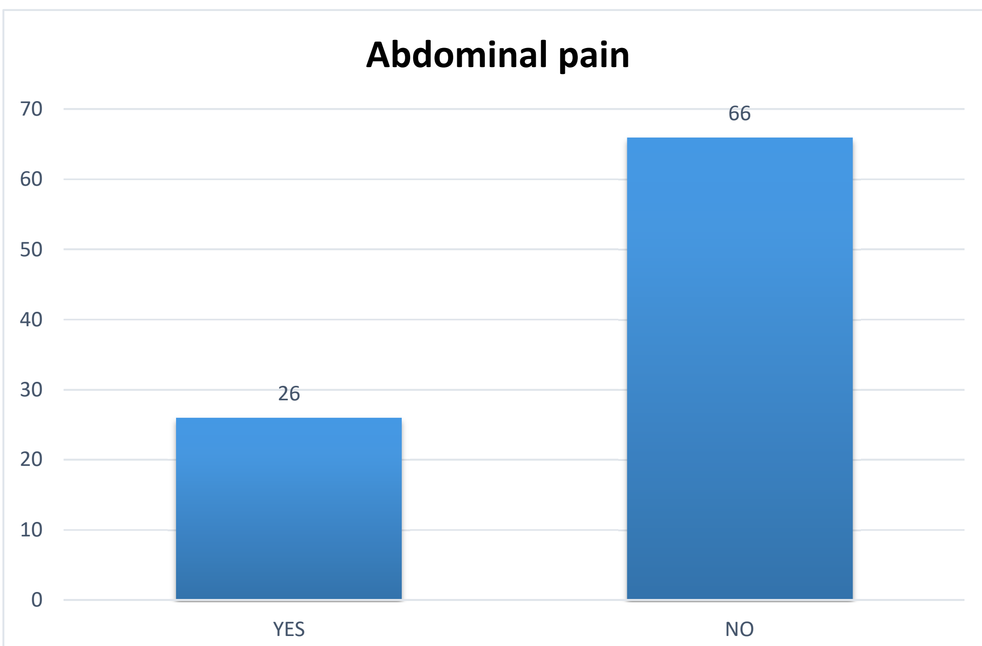

Figure 17: Showing the distribution of presence of abdominal pain among participants

Table 13: Showing the distribution of presence of altered sensorium among study participants

		Frequency	Percentage
ALTERED SENSORIUM	Yes	26	28.3
	No	66	71.7
	Total	92	100.0

Out of 92 study participants, 28.3% of the patients (n= 26) had altered sensorium and 71.7% (n= 66) of the patients had normal sensorium.

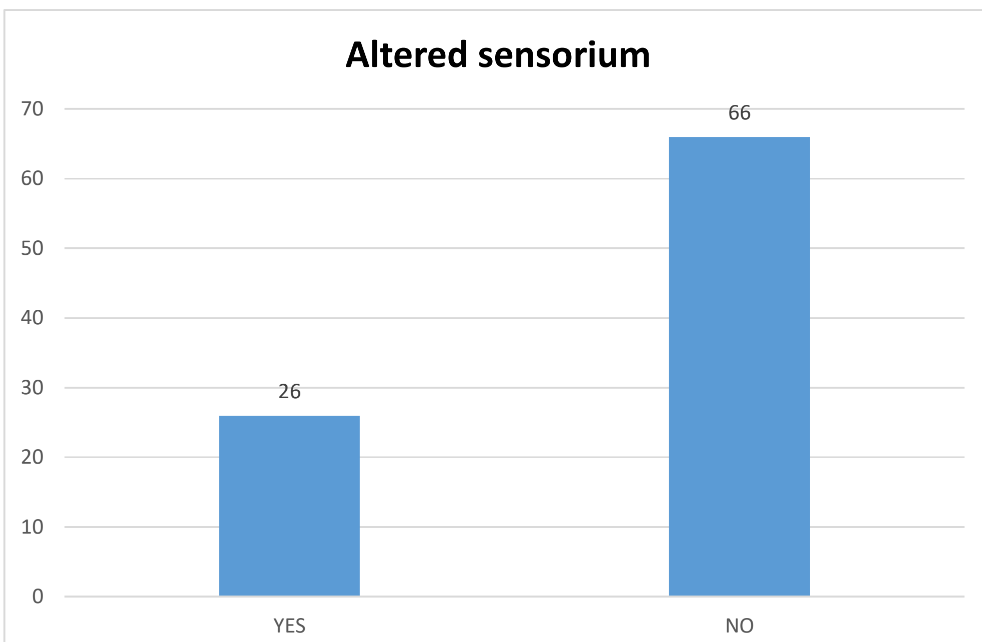

Figure 18: Showing the distribution of presence of altered sensorium among study participants

Table 14: Showing the distribution of presence of fever among study participants

		Frequency	Percentage
FEVER	Yes	13	14.1
	No	79	85.9
	Total	92	100.0

Among the study participants, the fever was present in 14.1% (n= 13) of the participants and rest 85.9% (n= 79) were afebrile.

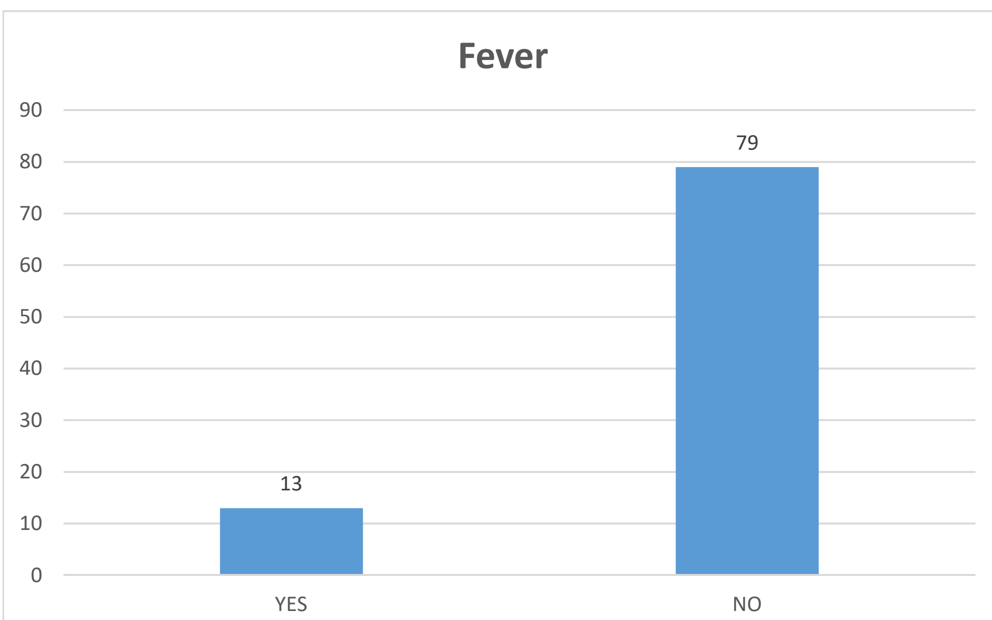

Figure 19: Showing the distribution of presence of fever among study participants

Table 15: Showing the distribution of presence of decreased urine output among study participants

		Frequency	Percentage
DECREASED URINE OUTPUT	Yes	11	12.0
	No	81	88.0
	Total	92	100.0

In our study, 12% (n= 11) of the study participants presented with decreased urine output. And remaining 88% (n= 81) did not complain of decreased urine output.

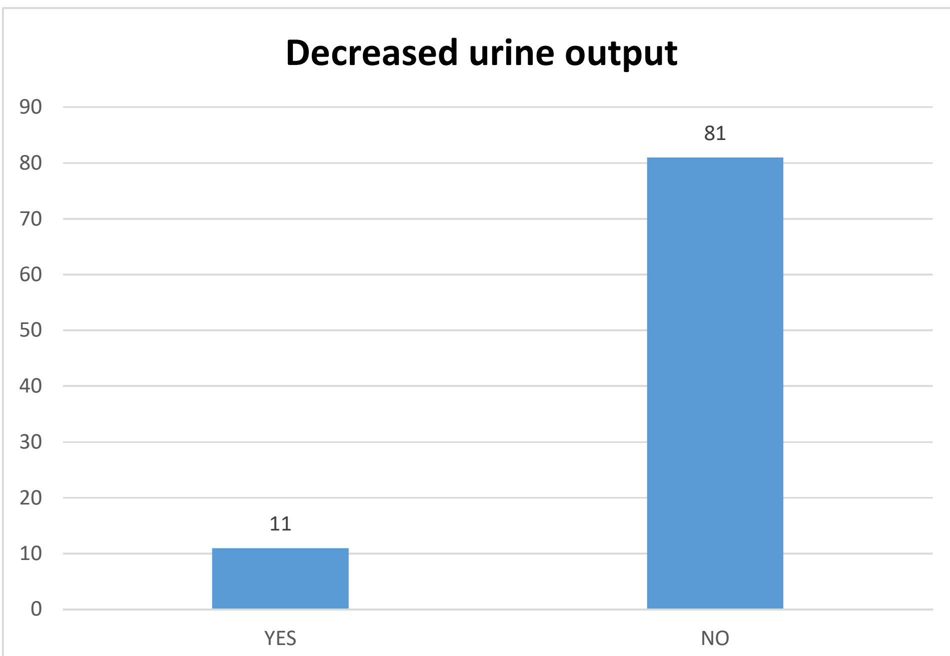

Figure 20: Showing the distribution of presence of decreased urine output among study participants

TABLES DEMONTRATING DISTRIBUTION OF PHYSICAL SIGNS PRESENT IN ENROLLED PATIENTS

Table 16: Showing the distribution of presence of ascites among study participants

		Frequency	Percentage
ASCITES GRADING	1	26	28.2
	2	41	44.6
	3	25	27.2
	Total	92	100

Among the 92 study participants, Grade 1 ascites was present in 28.2% (n= 26) of the patients, Grade 2 ascites was present in 44.6% (n= 41) and Grade 3 ascites was present in 27.2% (n= 25) of the study participants.

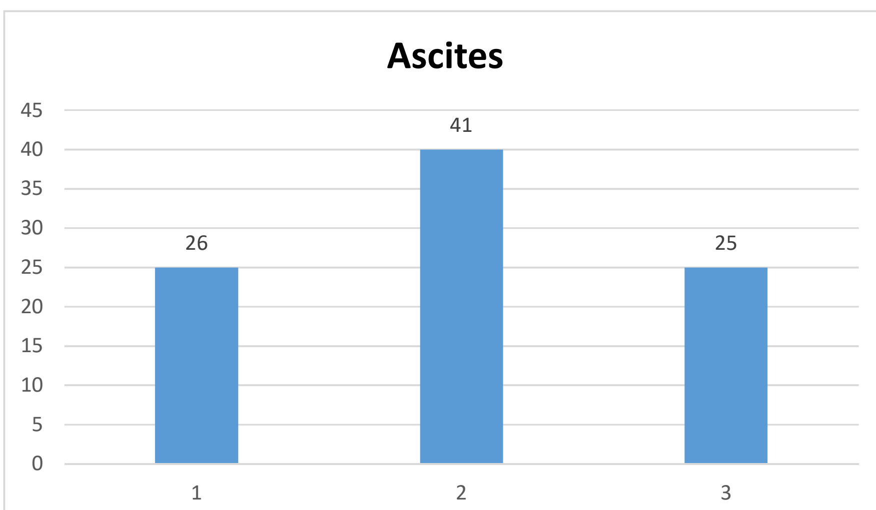

Figure 21: Showing the distribution of presence of ascites among study participants

Table 17: Showing the distribution of presence of anemia among study participants

		Frequency	Percentage
ANEMIA	Yes	67	72.8
	No	25	27.2
	Total	92	100.0

In this study, 72.8% (n= 67) of the study participants had anemia and remaining 27.2% (n= 25) did not have anemia.

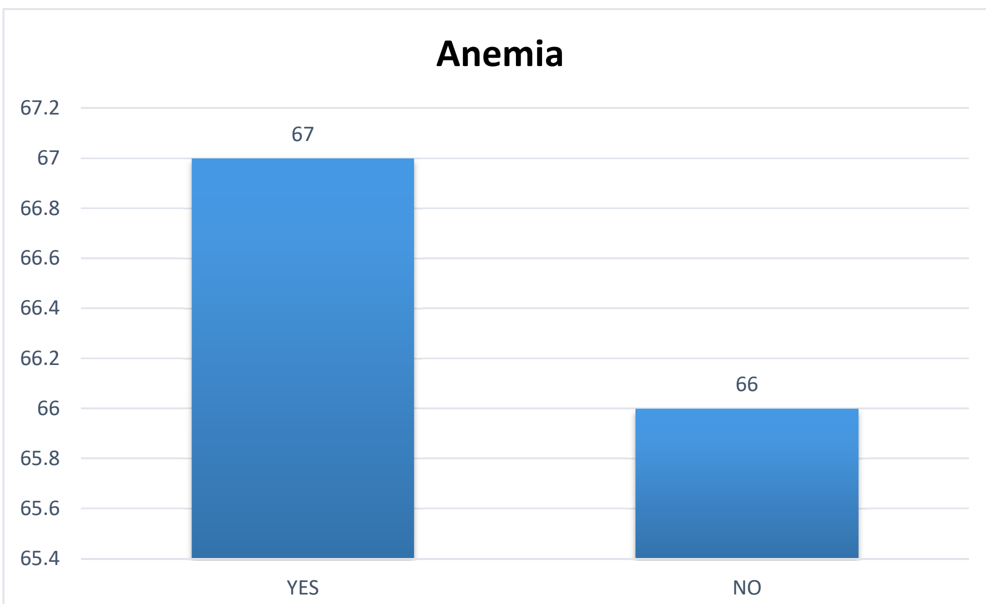

Figure 22: Showing the distribution of presence of anemia among participants

Table 18: Showing the distribution of presence of jaundice among study participants

		Frequency	Percentage
JAUNDICE	Yes	61	66.3
	No	31	33.7
	Total	92	100.0

In this study, 66.6% (n= 61) of the study participants had jaundice and remaining 33.7% (n= 31) did not have jaundice.

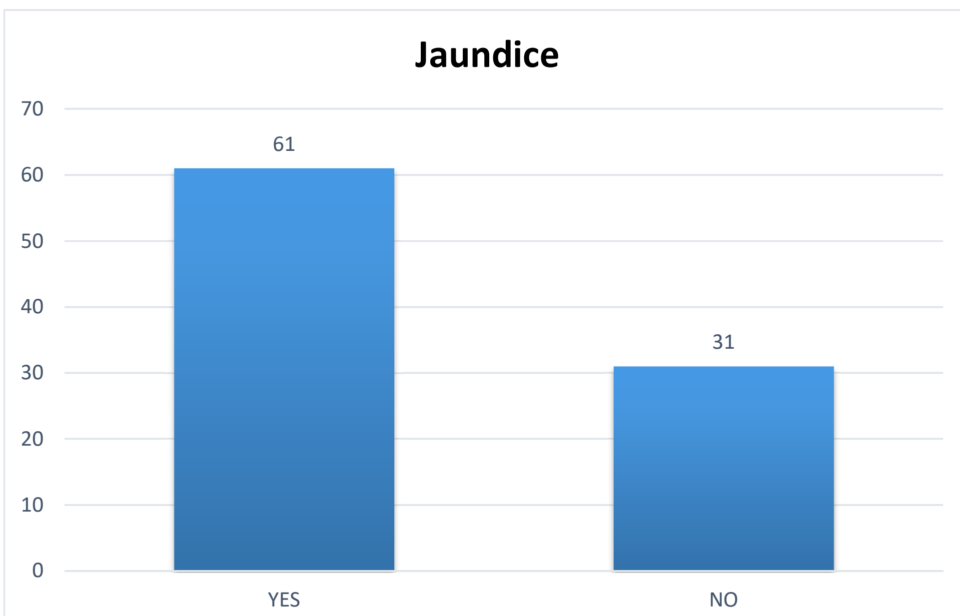

Figure 23: Showing the distribution of presence of jaundice among participants

Table 19: Showing the distribution of Stages of hepatic encephalopathy among study participants

	Stage of HE	Frequency	Percentage
HEPATIC ENCEPHALOPATHY	0	56	60.8
	1	16	17.4
	2	18	19.6
	3	2	2.2
	Total	92	100.0

Among the 92 study participants, Grade 0 HE i.e. normal sensorium was present in 60.8% of the patients, Grade 1 HE was present in 17.4% of the patients, Grade 2 HE was present in 19.6% of the study participants and Grade 3 HE was present in 2.2% of the patients.

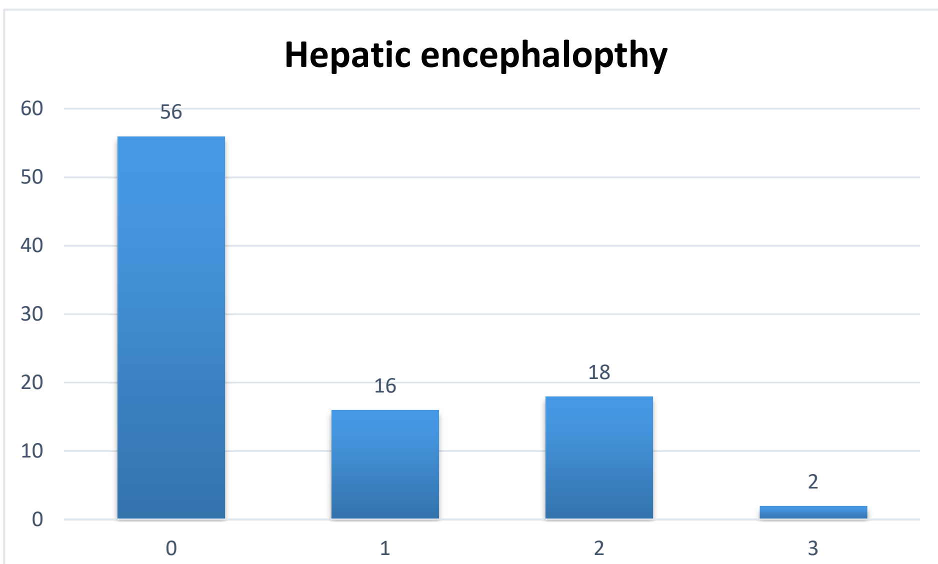

Figure 24: Showing the distribution of presence of hepatic encephalopathy among study participants

Table 20: Showing the distribution of CTP class among study participants

		Frequency	Percentage
CTP CLASS	Class A	3	3.3
	Class B	31	33.7
	Class C	58	63.0
	Total	92	100.0

According to CTP class, 63% were with class C, 33.7% with Class B and 3.3% with Class A liver disease.

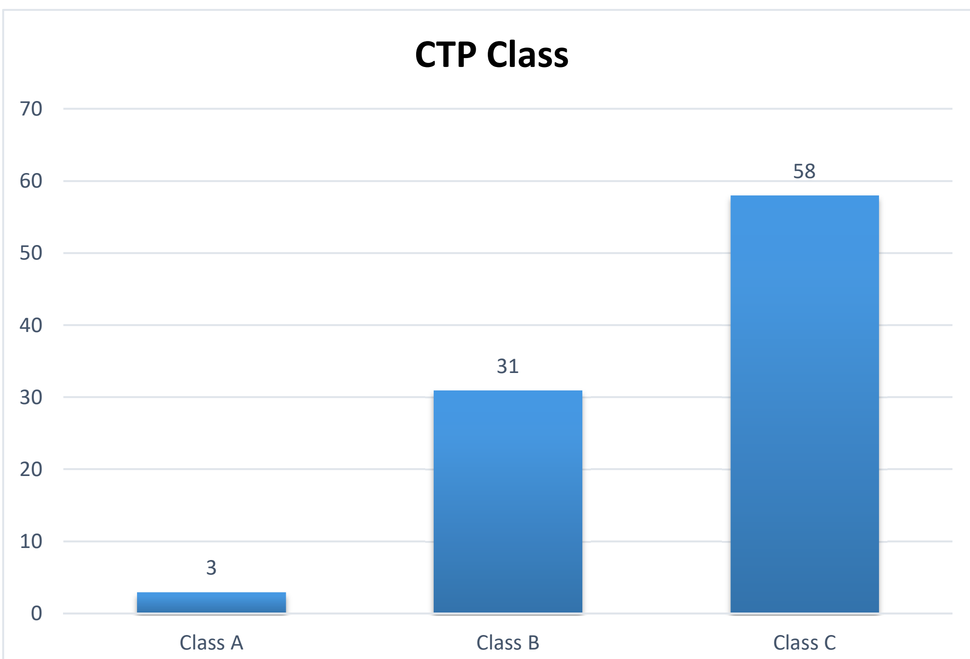

Figure 25: Showing the distribution of CTP class among study participants

Table 21: Showing mean level of LFT parameters and it's correlation with CTP class among study participants

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
Total Bilirubin	0.55	.05	4.55	6.64	10.16	7.59	0.01*
SGOT	18	7	69	57	105	144	0.234
SGPT	21	3	36	31	49	72	0.498
Total proteins	6.1	.9	6.2	1.0	6.1	1.1	0.900
Sr. albumin	3.8	.7	2.9	.7	2.5	.5	0.01*
AG Ratio	1.30	.69	.91	.32	.87	.88	0.611

The mean value of Total bilirubin in CTP class A was 0.55±0.05, mean value in CTP class B was 4.55±6.64 and in CTP class C was 10.16±7.59 (p value= 0.01). This was statistically significant. The value of SGOT was higher than SGPT in CTP class B and C. The mean value of serum albumin was 3.8±0.7 in CTP class A, 2.9±0.7 in CTP class B and 2.5±0.5 in CTP class C. (p value= 0.01)

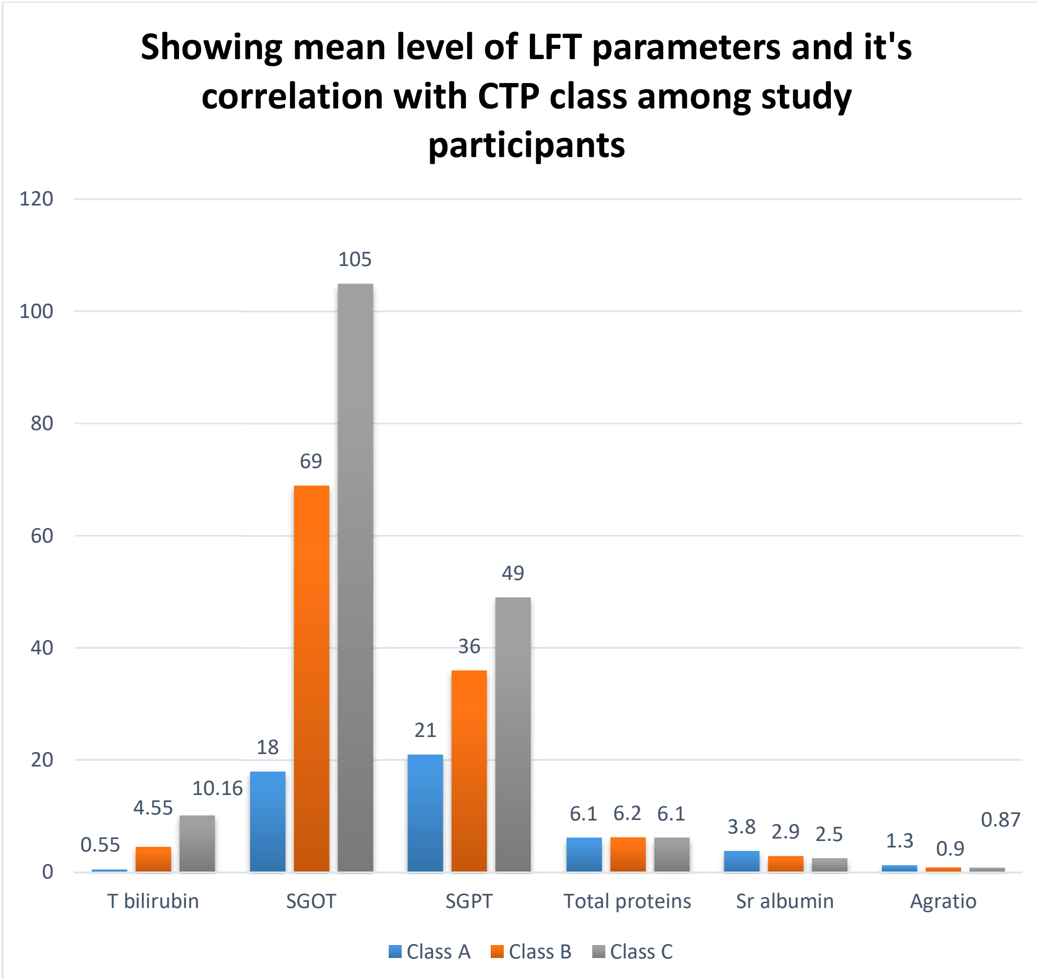

Figure 26: Showing mean level of LFT parameters and its correlation with CTP class among study participants

Table 22: Showing mean level of PT / INR parameters and it's correlation with CTP class among study participants

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
PT	12.1	1.9	16.7	3.4	27.0	15.1	0.01*
INR	.923	.311	1.400	.269	2.295	1.534	0.01*

In CTP class A, mean value of PT is 12.1±1.9, in CTP class B is 16.7±3.4 and in CTP class C is 27±15.1 (p= 0.01). In CTP class A mean value of INR is 0.923, in CTP class B is 1.4 and in CTP class C is 2.295. (p= 0.01)

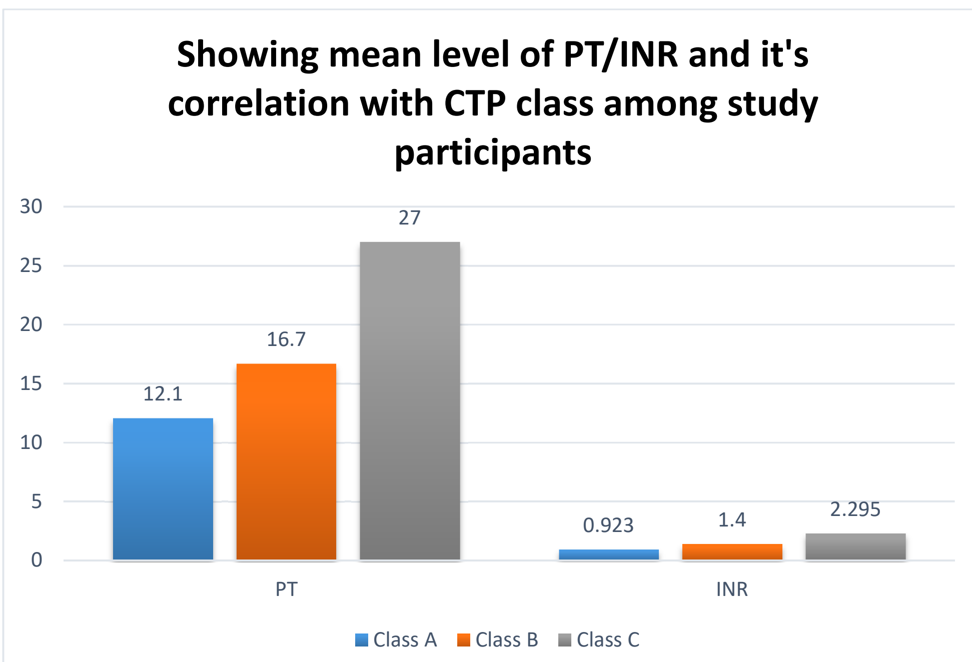

Figure 27: Showing mean level of PT / INR parameters and it's correlation with CTP class among study participants

Table 23: Showing mean level of CBC parameters and it's correlation with CTP class among study participants

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
Hemoglobin	11.5	2.8	9.8	3.6	9.1	1.8	0.189
WBC	8433.3	3362.0	8206.8	4147.3	10612.0	6442.3	0.160
Neutrophils	71	8	72	13	74	12	0.730
Lymphocytes	21	7	21	15	16	11	0.112
Monocytes	6	4	6	4	7	3	0.416
Eosinophils	2	1	1	2	3	6	0.294
Basophils	0	0	0	2	0	0	0.384
Platelet count	142667	22942	134516	83274	111552	84278	0.416

The mean value of hemoglobin in CTP class A was 11.5±2.8, in CTP class B was 9.8±3.6 and in CTP class C was 9.1±1.8. The mean value of platelet count in CTP class A was 142667±22942, in CTP class B was 134516±83274 and in CTP class C was 111552±84278.

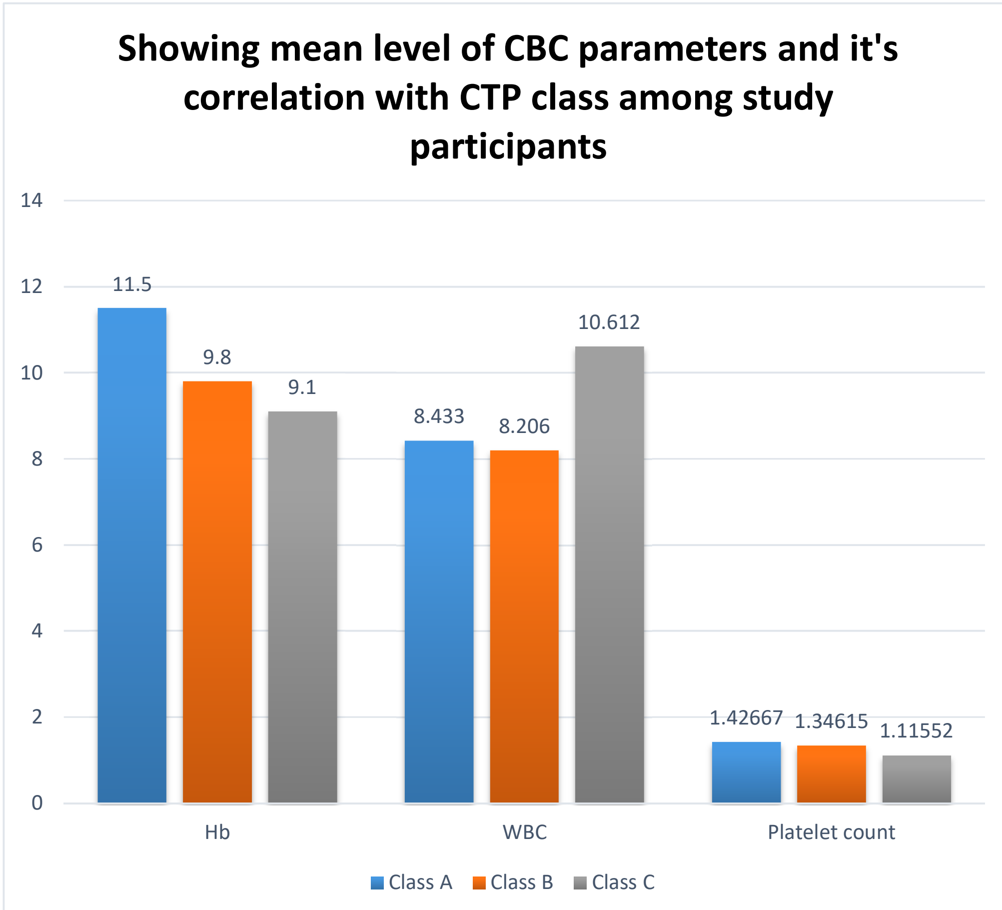

Figure 28: Showing mean level of CBC parameters and it's correlation with CTP class among study participants

Table 24: Showing mean of parameters RFT and it's correlation with CTP class among study participants

The mean value of creatinine in CTP class A was 2.64±2.86, In CTP class B was 7.49±3.61 and in CTP class C was 1.31±0.7. The mean value of sodium in CTP class A was 136±7, in CTP class B was 133±5 and in CTP class C was 127±17.

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
Serum Creatinine	2.64	2.86	7.49	3.61	1.31	.70	0.419
Blood Urea	59.0	42.2	40.8	32.9	47.1	43.1	0.654
Sodium	136	7	133	5	127	17	0.12
Potassium	5.40	1.06	4.06	.64	4.04	.90	0.02*
Chloride	102	6	99	6	95	8	0.081

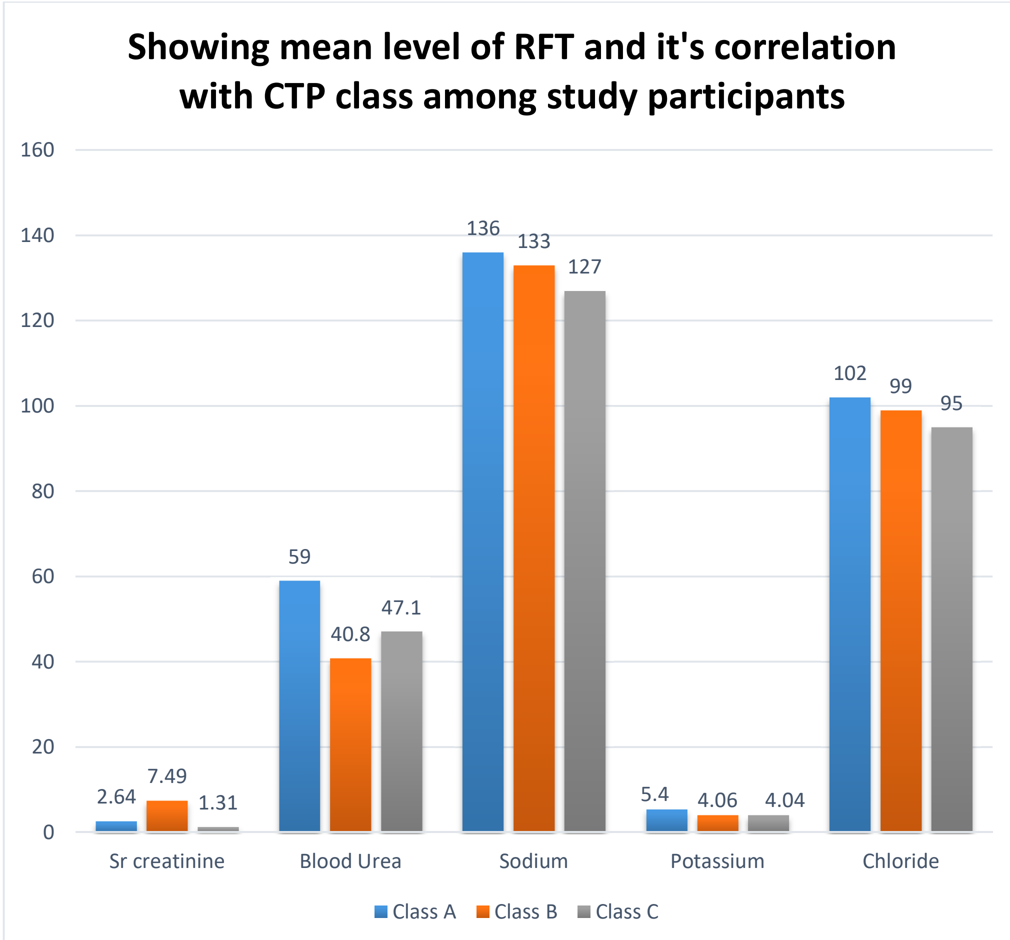

Figure 19: Showing mean of parameters RFT and it's correlation with CTP class among study participants

On correlation of the blood parameters with CTP class, we found that significant mean difference was seen in PT, INR, total bilirubin, serum albumin and potassium levels. Patients with CTP class C had significantly higher mean PT, INR, and total protein levels than classes B and A. Similarly, individuals with cirrhosis in CTP class C had significantly lower mean levels of blood albumin and potassium than patients in CTP classes A and B. ($p<0.05$)

Table 25: Comparison of the mean of 2D- ECHO parameters with severity of liver disease using CTP class

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
LVEF	55.0	5.0	57.1	3.1	56.6	3.2	0.515
E/A ratio	.80	.10	.97	.30	.97	.31	0.638
Deceleration Time	228	63	217	53	220	57	0.921
e/e	8.7	2.1	9.7	2.7	9.7	2.6	0.803
E/e	6.7	1.1	7.7	1.8	7.3	2.1	0.557

The patients in class C of CTP class had normal LVEF on 2D- ECHO at rest. However, this was not statistically significant.

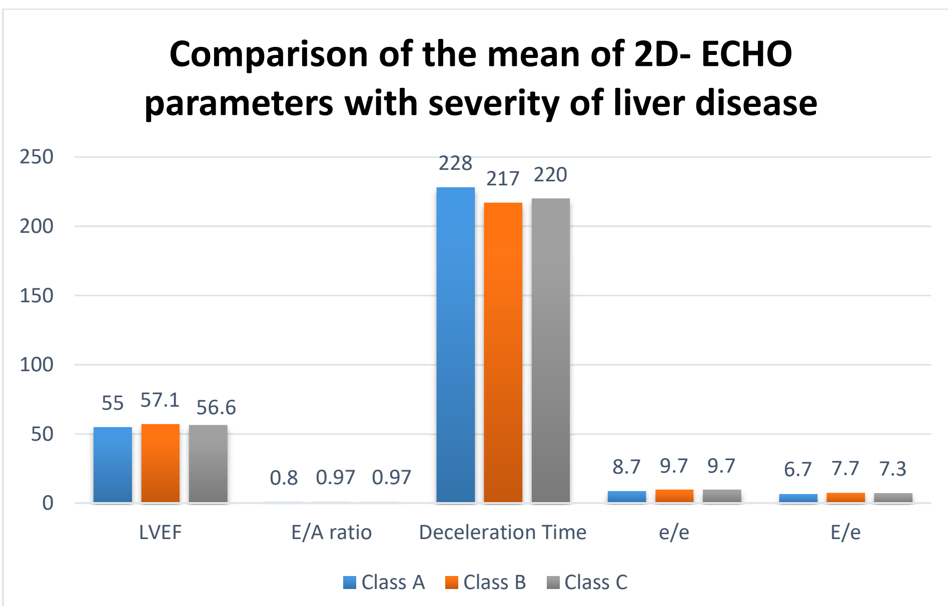

Figure 20: Comparison of the mean of 2D- ECHO parameters with severity of liver disease

Table 26: Showing the distribution of presence of DDF grade among study participants

		Frequency	Percent
DDF GRADE	0	32	34.8
	1	47	51.1
	2	12	13.0
	3	1	1.1
	Total	92	100.0

The DDF grade of 1 was present in 51.1% of patients, 34.8% with grade 0, 13% with grade 2 and 1.1% with grade 3.

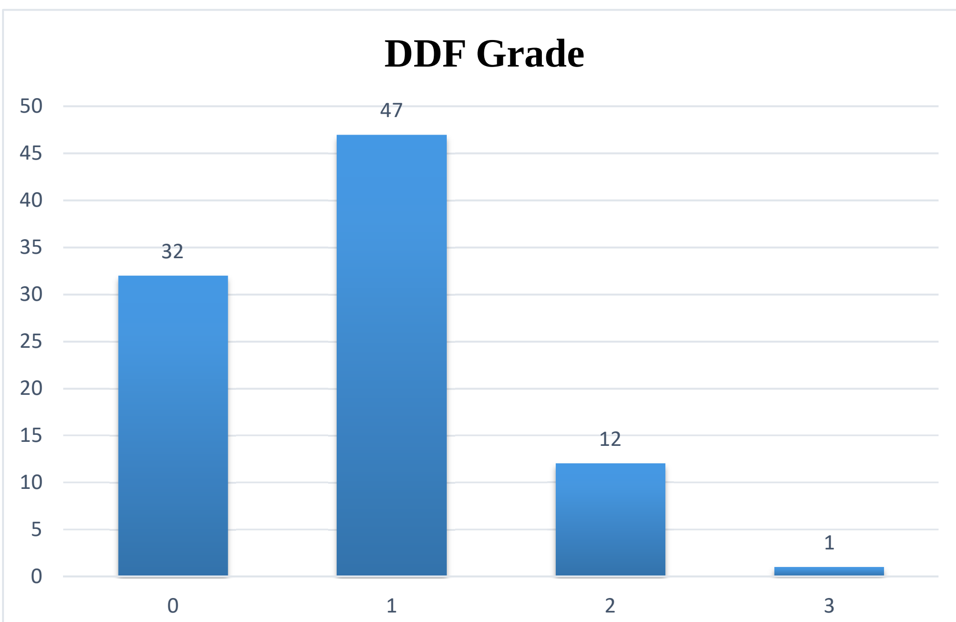

Figure 31: Showing the distribution of presence of DDF grade among study participants

Table 27: Comparison of the DDF grade with CTP class among study participants

		CTP Class						Chi-square (p-value)
		Class A		Class B		Class C		
		Count	N %	Count	N %	Count	N %	
DDF GRADE	0	1	33.3%	11	35.5%	20	34.5%	2.678 (0.848)
	1	2	66.7%	14	45.2%	31	53.4%	
	2	0	0.0%	6	19.4%	6	10.3%	
	3	0	0.0%	0	0.0%	1	1.7%	

On assessment of DDF grade with the CTP grade, we discovered that liver disease in CTP class C had a higher incidence than in CTP class A or CTP class B, although this finding was not statistically significant.

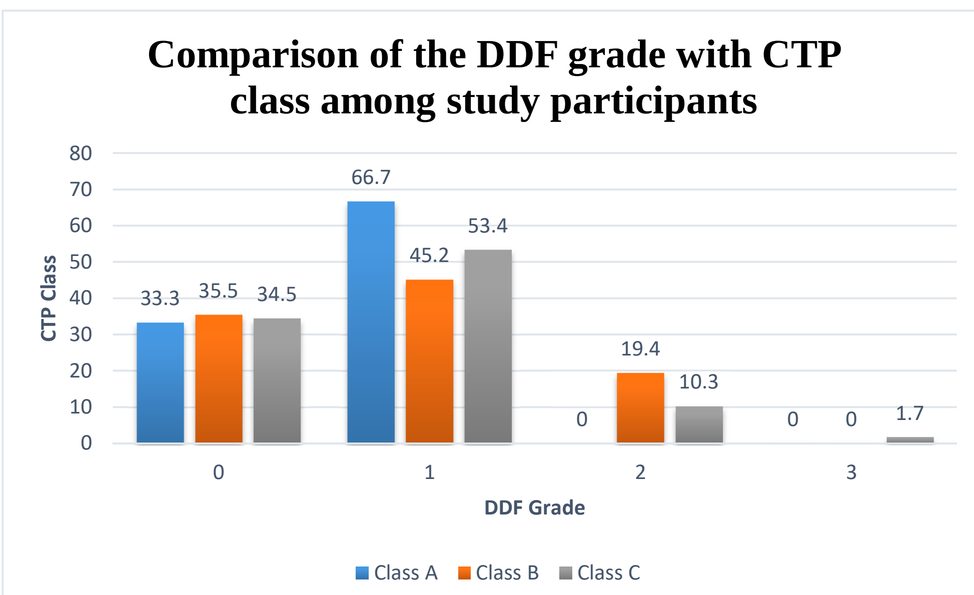

Figure 32: Comparison of the DDF grade with CTP class among study participants

Table 28: Showing the correlation of mean level of NT-proBNP with CTP class among study participants

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
NT pro BNP	241	229	1879	3132	2352	6398	0.01*

The mean value of NT-proBNP in CTP class A was 241±229, in CTP class B was 1879±3132 and in CTP class C was 2352±6398. When compared to patients with CTP Class A and CTP Class B disease, patients with CTP Class C disease had a higher value of NT-proBNP. The results were statistically significant. (p<0.01)

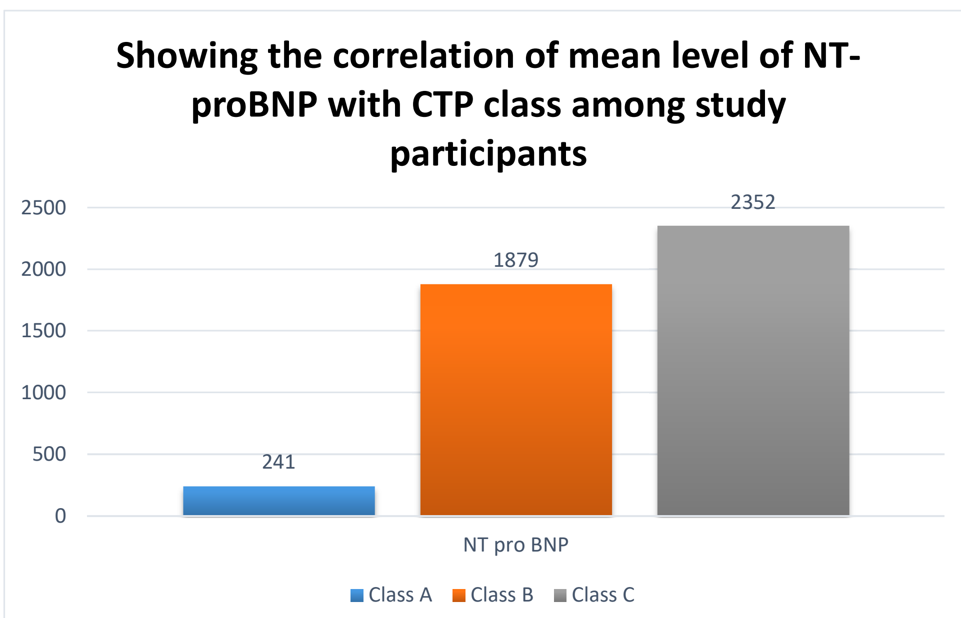

Figure 33: Showing the correlation of mean level of NT-proBNP with CTP class among study participants

Table 29: Comparison of the presence of low voltage QRS complexes and prolonged QT interval with CTP class

		CTP Class						Chi-square (p-value)
		Class A		Class B		Class C		
		Count	N %	Count	N %	Count	N %	
Prolonged QT	No	3	100.0%	24	77.4%	40	69.0%	1.887 (0.389)
	Yes	0	0.0%	7	22.6%	18	31.0%	
Low voltage QRS	No	3	100.0%	27	87.1%	42	72.4%	3.421 (0.181)
	Yes	0	0.0%	4	12.9%	16	27.6%	

When compared to patients with CTP Class A and CTP Class B disease, patients with CTP Class C disease had a greater incidence of low voltage QRS complexes and QT interval prolongation on the ECG. The results, however, were not statistically significant.

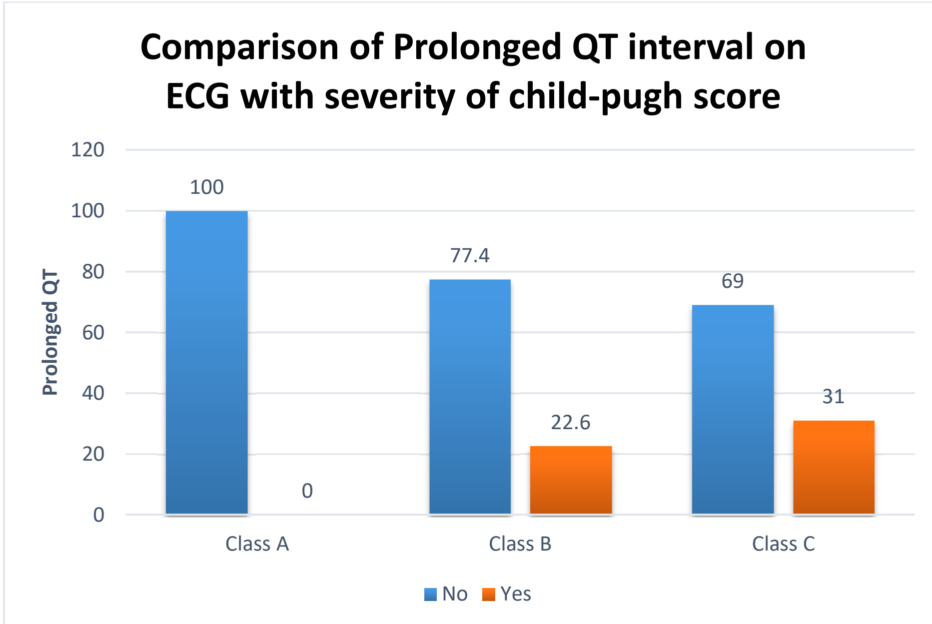

Figure 34: Comparison of Prolonged QT interval on ECG with severity of Child-Pugh score

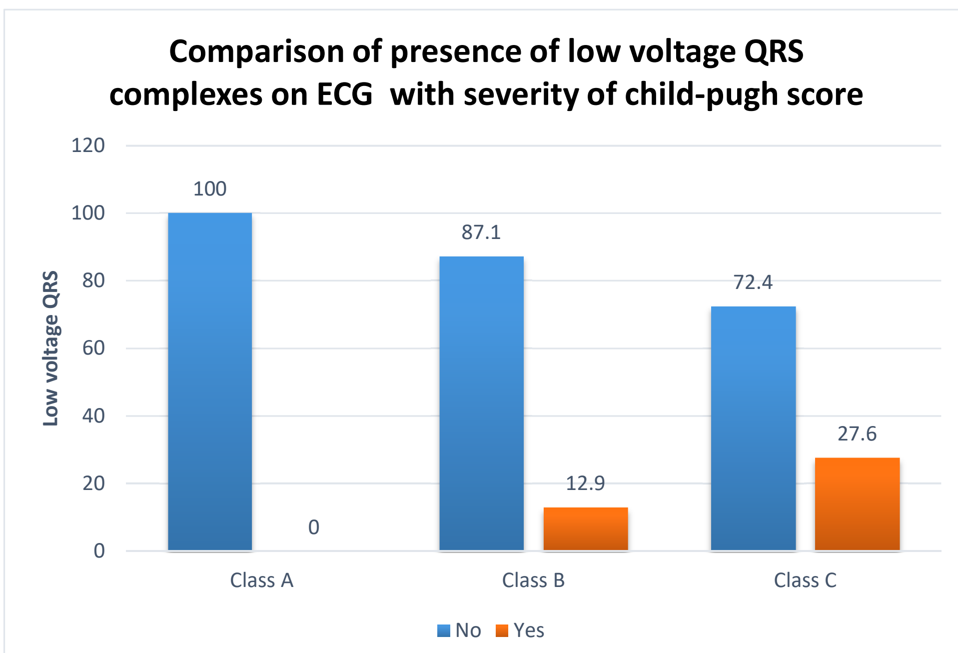

Figure 35: Comparison of presence of low voltage QRS complexes on ECG with severity of Child-Pugh score

Table 30: Comparison of parameters on ultrasonography of liver and spleen with CTP class among patients

	CTP Class						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
Liver size (cm)	11.1	1.7	16.2	3.6	16.1	3.6	0.06
Spleen size (cm)	12.1	2.7	13.2	2.1	14.6	2.3	**0.01***
Portal vein diameter (cm)	1.1	0.2	1.7	2.1	1.2	0.2	0.266

When compared to individuals in CTP Classes A and B, patients in CTP Class C had much greater spleen size. It was statistically significant. (p= 0.01)

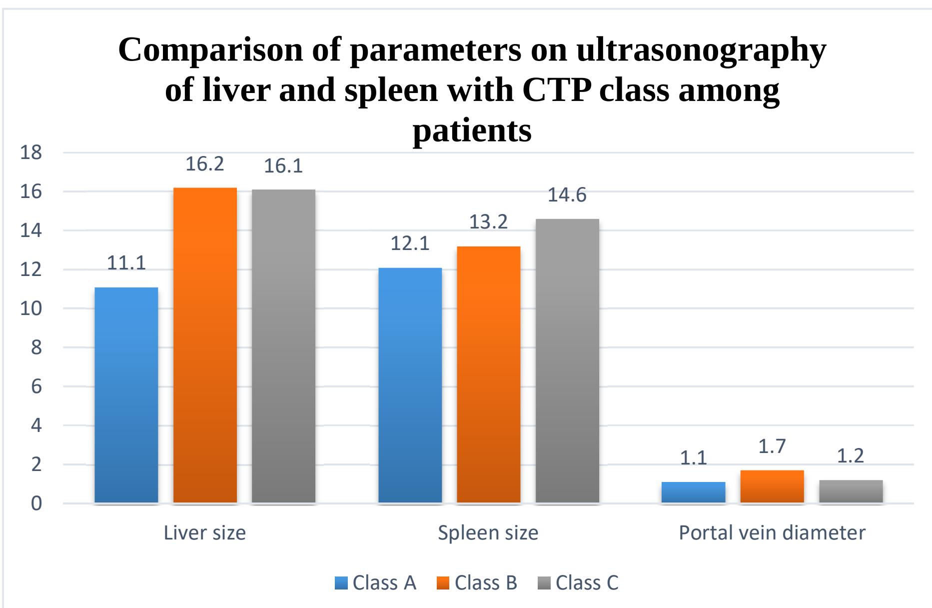

Figure 36: Comparison of parameters on ultrasonography of liver and spleen with CTP class among patients

Table 31: Comparison of echo texture of liver on ultrasound with the severity of chronic liver disease

		CTP Class						Chi-square (p-value)
		Class A		Class B		Class C		
		Count	N %	Count	N %	Count	N %	
ECHO TEXTURE OF LIVER	Altered	0	0.0%	7	22.6%	5	8.6%	37.880 **(0.01)***
	Coarse	1	33.3%	18	58.1%	45	77.6%	
	Increased	1	33.3%	6	19.4%	7	12.1%	
	Irregular	0	0.0%	0	0.0%	1	1.7%	
	Normal	1	33.3%	0	0.0%	0	0.0%	

In present study, majority of the patients with CTP class C showed abnormal echo texture compared to the class A. This difference was statistically significant. ($p= 0.01$)

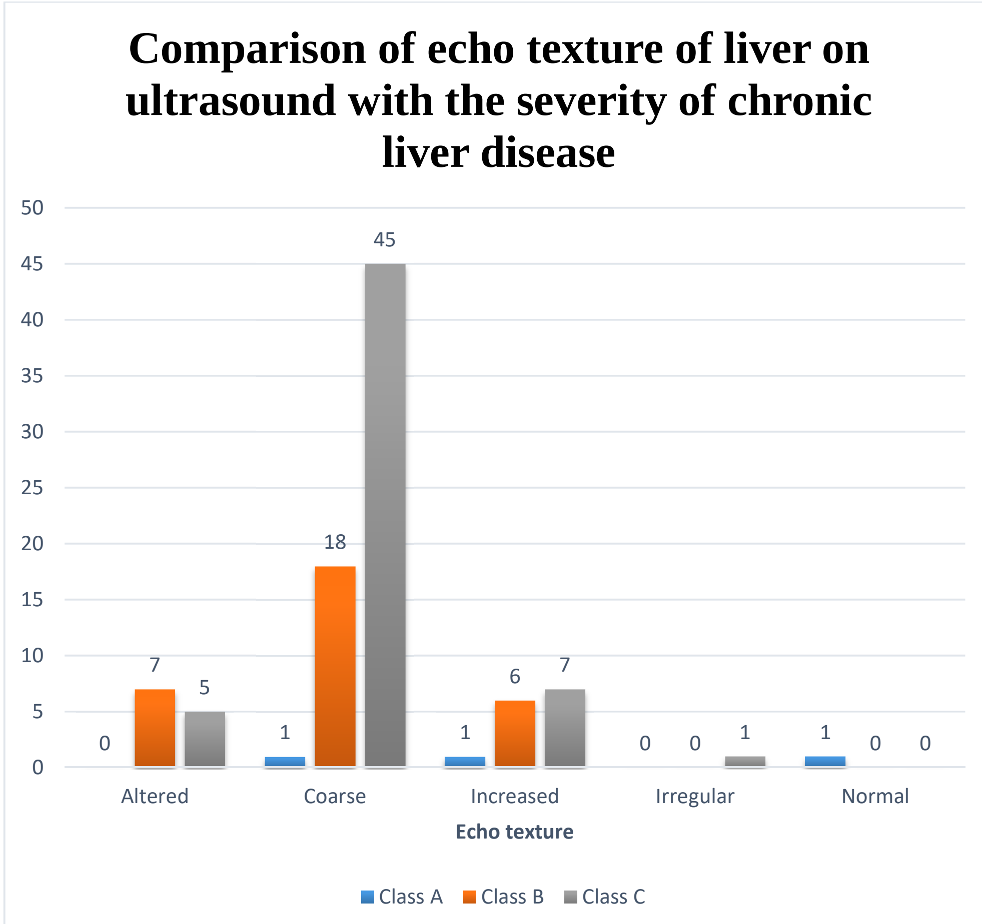

Figure 37: Comparison of the echo texture of liver on ultrasound with the severity of chronic liver disease

Table 32: Comparison of MELD score with the CTP class among patients.

	"CTP Class"						p-value
	Class A		Class B		Class C		
	Mean	SD	Mean	SD	Mean	SD	
MELD	8.38	11.29	13.33	12.23	23.86	6.60	0.01*

When compared to study participants in Child-Pugh class A and Child-Pugh B, the study participants with CTP class C had a considerably higher MELD score on evaluation. ($p<0.05$)

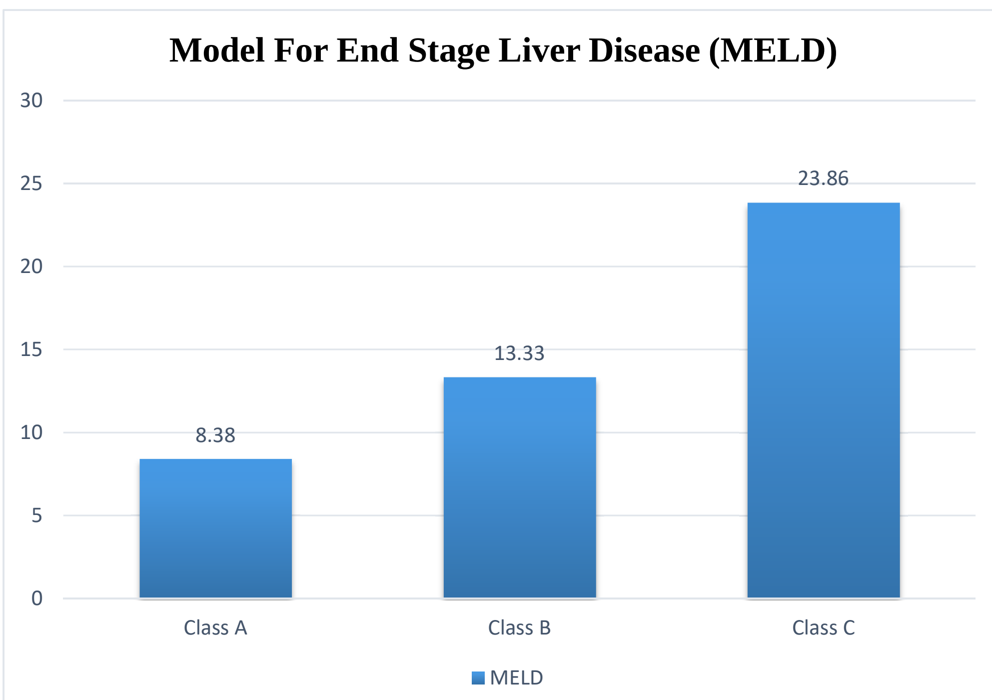

Figure 38: Comparison of MELD score with CTP class among patients

Table 33: Pearson's correlation of MELD and Child-Pugh score with NT pro BNP and echo findings among study participants

Pearson's correlation		NT pro BNP	LVEF	E/A ratio	Deceleration time	e/e	E/e
MELD	r	.196	-.134	-.082	.025	-.086	-.006
	p-value	.060	.204	.436	.814	.413	.957
CHILD-PUGH SCORE	r	.204	-.109	.011	.076	-.123	.113
	p-value	.02*	.01*	.918	.474	.242	.284

The current study's assessment of correlation indicated a substantial positive association between NT-proBNP and Child-Pugh scores and a significant negative correlation between Child-Pugh scores and LVEF.

DISCUSSION

Cirrhotic cardiomyopathy is 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 absence of known cardiac disease.”[1] Chronic liver disease (CLD) causes significant morbidity and mortality worldwide. Several etiologic factors lead to a similar clinicopathologic syndromes in CLD, although clinical course and progression rates may differ. Study aimed to assess the utility of NT-proBNP levels, 2D-ECHO and ECG to rule out cardiovascular dysfunction, this can lead to early diagnosis and treatment of the same.

Demographics and symptoms:

A total of 92 patients who met the inclusion criteria were enrolled in the study, after obtaining informed consent. The mean age of the included patients was 51.5±10.75 years. Among the included patients, males outnumbered females by 96.7% and 3.3%, respectively.

In a study by Mishra D et al., the mean age of the study participants with cirrhosis was found to be 46.35yrs with male preponderance. This was similar to present study where 97.5% were male participants.[47] Another study reported by Mukherjee P et al., documented the median age of 46-45yrs with male predominance.[48] In an another study by Mihailovici AR et al., the median age of the study participants was found to be 55.2yrs with male preponderance. Above findings were similar to the present study.[49]

Among the study participants, 78.3% of the patients had history of alcohol consumption, 31.3% of the patients had diabetes mellitus, 14.1% had hypertension.

Among the study participants, abdominal distension and pedal edema were seen in 63% of the patients, hematemesis or malena was present in 30.4%, altered sensorium in 28.3%, and abdominal pain was seen in 28.3%, fever was present in 14.1%, decreased urine output in 12% of the patients. On examination, grade 2 and grade 3 ascites was present in 43.5, 27.2% of the study participants respectively, jaundice was present in 66.3% of the study participants, anemia was observed in 72.8% and 39.2% had hepatic encephalopathy.

In study by Mukherjee P et al., it was documented that, the presence of diabetes mellitus in 11.7% of the patients presented with diagnosis.[48] The presence of ascites, pedal edema, hematemesis, reduced urine output, altered sensorium in severe cases were documented in various studies.[45,48,50]

Blood and other investigations:

On correlation of the blood parameters with CTP class, we found that significant mean difference was seen in PT, INR, total bilirubin, serum albumin and potassium levels. CTP class C had significantly higher mean PT, INR, and total protein levels than classes B and A. Similarly, individuals with cirrhosis in CTP class C had significantly lower mean levels of blood albumin and potassium than patients in CTP classes A and B. ($p<0.05$)

Although a prothrombotic shift of the hemostatic balance in patients with liver cirrhosis has been demonstrated, little is known about the relationship between liver function tests and the coagulation profile, with the exception of a single study by Gatt et al.,[51] which reported an increasing trend of prothrombin time with an increasing

INR. Liver function tests are still routinely used in clinical practice as indicators of increased bleeding risk in patients with liver cirrhosis.[50–53] Zermatten MG et al., also documented that the increase in total bilirubin is associated with an increasing prothrombotic profile.[54]

According to CTP class, 63% were with class C, 33.7% with Class B and 3.3% with class A liver disease.

The grade 1 DDF was present in 51.1% of patients, 34.8% with grade 0, 13% with grade 2 and 1.1% with grade 3. On correlation of DDF grade with the CTP grade, we found higher DDF grade was found to be more common with class C of CTP scoring system versus class B and class A of Child-Pugh scoring system, however, this was not statistically significant. When compared to the study participants with class B and class A Child-Pugh Scores, patients with class C Child-Pugh Score had a considerably higher MELD score. ($p<0.05$) The results of the current study's analysis of correlation revealed a substantial positive relationship between NT pro-BNP and Child-Pugh scores and a significant negative relationship between LVEF and Child-Pugh score.

Licata A et al., documented that left atrial volume (LAV) (61.8±26.3 vs 43.5±14.1 ml; $p=0.001$), and left ventricular ejection fraction (62.7±6.9 vs. 65.5±4%; $p=0.05$) were also altered in cirrhotic patients that in controls. Patients with F2-F3 esophageal varices as compared to F0/F1, showed higher e' velocity (0.91±0.23 vs 0.66±0.19 m/s, $p<0.001$), and accordingly a higher E/A ratio”(1.21±0.46 vs 0.89±0.33 m/s, $p=0.006$).[42]

Mihailovici A et al., documented that Cirrhotic patients' left atrial size, left ventricular wall thickness, diastolic function and LV ejection fraction were all substantially different from controls.[49] In a similar research, it was also shown that

51.3% of the patients had diastolic dysfunction on ECHO. Study even showed that cirrhotic individuals have both biochemical (higher levels of NT-proBNP) and echocardiographic (increased LA volume) evidence of subclinical cardiac dysfunction, which is directly proportional to the severity of the liver illness.[49] Some studies also documented that, the ratio of early to late left ventricular diastolic filling (E/A), which is often employed in medical practice to estimate diastolic function, is susceptible to error and is dependent on the preload. There may be a pseudo-normalization of mitral inflow in the context of abnormal LV relaxation and high left atrial pressure, disguising the presence of diastolic dysfunction. Because it is less impacted by changes in ventricular filling, TDI may help to ease some of these issues.[55–57]

Cardiac function appears to decline with advancement of cirrhosis and has an impact on prognosis. Patients with stable cirrhosis, on the other hand, show minimal advancement in cardiac dysfunction over a 2-year period, with only a minor influence on survival. The findings advocate for vigilant cardiac monitoring in advanced cirrhosis. [44] In cirrhosis, LVDD develops together with other alterations in cardiac function and structure and leads to circulatory dysfunction which suggests that patients with cirrhosis leads to primarily left ventricular diastolic dysfunction (LVDD) with normal systolic function at rest. Tissue Doppler imaging and standard 2D-echocardiography are both real-time, non-invasive, quick imaging technologies and good accuracy for identifying cardiovascular anomalies, suggestive of cirrhotic cardiomyopathy.[3]

Among the study participants, there is significant higher mean level of NTpro-BNP among the CTP class C study participants compared to the CTP class A and CTP class B.

In a study by Mihailovici A et al., documented the plasma levels of NT-proBNP in cirrhotic patients were substantially greater than in healthy participants. Study participants with the class C of Child-Pugh score had significantly greater levels of NT-proBNP than those in classes B and A.

Licata A et al., documented the higher levels of NT pro-BNP (365.2±365.2 vs 70.8±70.6 pg/ml; with $p<0.001$) among cases compared to control. According to the study's findings, the progression of chronic liver disease was correlated with an increase in NT-pro-BNP plasma concentrations.[42]

When compared to study participants with class A of CTP scoring system and class B of CTP scoring system disease, study participants with class C of CTP scoring system have a greater incidence of low voltage QRS complexes and the prolonged QT interval on the ECG. However, this finding was statistically significant. Also, on 2D-ECHO the changes were seen however it wasn’t statistically significant.

In a study similar to the present study by Toma L et al., the amplitude of the QRS complex were lower in decompensated CLD patients compared to patients with compensated CLD disease. They found an accentuated slowing of the T wave in patients with cirrhosis. These results correlated with serum levels of cholesterol, ammonia and albumin. The study showed that advanced liver disease was associated with prolonged QT intervals.[45]

In present study, majority of the patients with CTP class C showed abnormal echo texture compared to the class A. This was statistically significant. ($p=0.01$) Those in Class C of CTP scoring system had significantly larger spleen over patients in Class A and Class B of CTP scoring system.

In a study by Roy CK et al., it was found that pulmonary arterial systolic pressure (PASP), E wave transmitral /early diastolic mitral annular velocity (E/e ratio), Left atrial diameter (LAD), CTP, MELD score and natriuretic peptide levels were all substantially higher (p 0.05) in patients with LVDD. When compared to Grade 1 LVDD and those without LVDD, Grade 2 and Grade 3 LVDD were linked to ascites and higher plasma renin activity, suggesting a clear link between circulatory dysfunction and LVDD. Heart rate (HR) and Systolic function were all within normal limits. In 3 study groups, survival did not change based on the severity of LVDD (p = 0.739).[3]

In study by Wiese S et al., found changes in systolic function and diastolic function of the patients with the severity of cirrhosis. The prognosis may be impacted by cardiac dysfunction, which appears to worsen in correlation with the development of cirrhosis. Myocardial structural abnormalities and left atrial enlargement appear to be of particular significance. A hypodynamic cardiac condition also appears to have a detrimental effect on survival in AD patients. But generally speaking, over a period of time, people with stable cirrhosis have modest advancement in cardiac dysfunction. [44]

The present study documented cardiac dysfunction in cirrhosis of liver using ECG, 2D-ECHO and NT-proBNP. These findings were correlated with CHILD-PUGH score, it was found that cardiac dysfunction was more significant in patients in class C Child-Pugh score.

SUMMARY

The present cross-sectional study was conducted in the Department of General Medicine, KLES Dr. Prabhakar Kore Hospital, Belagavi to evaluate cardiac dysfunction in patients of CLD using the investigations ECG, 2D- ECHO and NT-proBNP and correlating the severity of CLD using Child Pugh score. A total of 92 adult patients with were included in the study. Ethical approval and informed consent were obtained prior to the study.

Patients' demographics and detailed history of patients were recorded. Blood was analyzed for CBC, LFT, RFT, PT/INR and NT-proBNP, ECG, USG abdomen and 2D-ECHO were done. To correlate the cardiac dysfunction with the severity of the CLD, Child Pugh score was also calculated. The data was analyzed using SPSS v21 operating on windows 10.

Patients belonged to the age group of 28 to 78 years having a mean age of 55.50 ± 15.63 years. Majority of the study population comprised of males (96.7%). In our study, 31.3% of the patients had diabetes mellitus, 14.1% had hypertension and 78.3% of the patients had history of alcohol consumption. On presentation to the hospital, 63% of the study participants had abdominal distention and pedal edema, 30.4% had hematemesis or melena, 28.3% were in altered sensorium and few of them had abdominal pain, fever and decreased urine output. On examination, grade 2 and grade 3 ascites was present in 43.5, 27.2% of the study participants respectively, jaundice was present in 66.3%, anemia was observed in 72.8% and 39.2% had hepatic encephalopathy.

In our study, patients were further categorized into Class A, B, C based on Child Pugh score (CTP) to grade the severity of CLD. According to CTP class, 63% were in class C, 33.7% in Class B and 3.3% in class A. On assessment of MELD score, it was significantly higher among the patients with CTP class C. ($p<0.05$)

On comparison of the blood parameters with CTP class, there was significant elevation of mean levels of total bilirubin, PT/INR and total protein in CTP class C participants. Similarly, individuals with cirrhosis in CTP class C had significantly lower mean levels of blood albumin and potassium. ($p<0.05$)

On 2D- ECHO, the incidence of grade 1 DDF was seen in 51.1% of the study participants. There was non-significant higher incidence of grade 3 DDF (1.1%) in CTP class C participants. There was a significant negative correlation between Child Pugh scores and LVEF.

On ECG, there was statistically non-significant higher incidence of low voltage QRS complexes and the prolonged QT interval among the study participants with CTP Class C.

Significant increase in NT-proBNP levels were observed in study participants with Child-Pugh class C as compared to those in classes B and A. ($p<0.01$)

The current study's analysis of correlation showed a substantial positive association between NT-proBNP and Child Pugh scores and a significant negative correlation between Child Pugh scores and LVEF.

STRENGTH AND LIMITATION

The present study found a significant cardiac dysfunction in patients with cirrhosis of liver, assessed by simple bed side investigations like ECG, 2D–ECHO and NT-proBNP. This will help us in early detection of cardiac dysfunction in patients with cirrhosis of liver.

However, this study was entitled to some limitations which include the study being a single centric study with small sample size. The study did not include follow-up of the patients' outcomes. Hence, it is recommended to conduct a larger sample size based multicentric study with follow-up of patients to strengthen the present findings of the study.

CONCLUSION

The present study found significant cardiac dysfunction in patients with cirrhosis of liver, assessed by NT-proBNP, ECG and 2D- ECHO.

This association between cardiac dysfunction and cirrhosis was mainly observed in patients with Child Pugh Class C.

Cirrhotic cardiomyopathy (CCM) is usually underdiagnosed by the treating physician and is often overlooked. Simple bed side investigations can help us in early diagnosis and management of CCM.

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ANNEXURE 1

INFORMED CONSENT FORM

Dear Mr. /Mrs. /Dr. ______________________________, you are kindly requested to enroll yourself in a research study tilted, "A STUDY OF CARDIAC DYSFUNCTION IN CIRRHOSIS OF LIVER USING ECG, 2D-ECHO AND NT-proBNP AND ITS CORRELATION WITH CHILD PUGH SCORE**"** being conducted by __________________, a post graduate student in M.D. General Medicine and the study will be carried out under the direct supervision and guidance of ______________________________, Professor, Department of General Medicine, Jawaharlal Nehru Medical College, Belgaum.

You have been requested to participate in this as you fit into the laid out criteria for a study 'subject'/ participant.

Your participation in study is voluntary. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge. Your decision whether or not to participate in the study will not affect your treatment in any form. If you decide to participate you are free to withdraw at any time.

<u>TITLE OF THE STUDY</u>:

"A STUDY OF CARDIAC DYSFUNCTION IN CIRRHOSIS OF LIVER USING ECG, 2D-ECHO AND NT-proBNP AND ITS CORRELATION WITH CHILD PUGH SCORE"

<u>PURPOSE OF THE STUDY</u>: To evaluate cardiac dysfunction in patients with Chronic Liver disease using 2D-ECHO, ECG and NT-proBNP levels and to correlate it with CHILD PUGH SCORE.

<u>PROCEDURES INVOLVED</u>: If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail and investigated accordingly.

Then you will be subjected to a few blood investigations, namely Liver function tests, Platelet count, Serum Blood urea nitrogen, Serum Creatinine, PT/INR, ECG, ECHO, NT-proBNP levels.

<u>RISKS AND BENEFITS</u>: There are no potential risks involved in this study.

<u>BENEFITS OF TAKING PART IN THIS RESEARCH</u>: By taking part in this study, prognosis and risk of development of cardiovascular dysfunction in chronic liver disease can be detected with the help of non-invasive markers like ECG and ECHO.

<u>VOLUNTARY PARTICIPATION / WITHDRAWAL FROM THE STUDY</u>: Taking part in the study is voluntary. You may choose not to enroll yourself in this study and may choose to leave the study anytime in between.

<u>ALTERNATIVES</u>: Your decision regarding participation in study will not change present or future health care services offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. You would simply be excluded from the study if you wish to, and all your details shall be kept confidential and you will get the routine line of management.

<u>PRIVACY AND CONFIDENTIALITY</u>: All data collected or disclosed by you during the course of participation of study, will be kept fully confidential. If however during the course it becomes necessary for the progress of the course to disclose the identity, it would be done so only after your informed & written consent. The only people to know that you are a research subject are members of the research team. No information about you will be disclosed to other without your written permission except:

In emergency to protect your rights AND welfare.

If required by law.

<u>AUTHORIZATION TO PUBLISH RESULT</u>: The results of the study may be used to publish an article. When the results of research published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information obtained in connection with this study and that can be identified with you will remain confidential.

<u>FINANCIAL INCENTIVES FOR PARTICIPATION</u>: No additional costs shall be incurred upon you for the purpose of this study. It is purely being done with the idea of research and all the cost of study will be borne by the investigator.

<u>COMPENSATION</u>: In the event that you become injured as a result of taking part in this study, treatment will be offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, or you will be given information about where to receive medical care. However, no reimbursement, compensation or free medical care will be given.

In case of the queries during study or in future you may contact following persons,

1. **Dr. Harsha Hegde,** Chairperson, JNMC, IEC & Scientist D, ICMR, National Institute of Traditional Medicine, Belagavi- 9480422500

CONSENT FORM

I, voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me, this consent form and have had all the questions answered.

……..…………………………….. …..………………………………

Name of the Participant Signature of the participant

or Left-Hand Thumb impression

…………………………………… .…………………………………

Name of Investigator Signature of investigator

or Left-Hand Thumb impression

…………………………………. …………………………………..

Name of Witness Signature of Witness

or Left-Hand Thumb impression

Date:

Place:

ANNEXURE -II

PROFORMA

A STUDY OF CARDIAC DYSFUNCTION IN CIRRHOSIS OF LIVER USING ECG, 2D-ECHO AND NT-proBNP AND ITS CORRELATION WITH CHILD PUGH SCORE- A ONE YEAR CROSS-SECTIONAL STUDY IN KLE'S DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI.

NAME:

AGE/SEX:

IP NO.:

ADDRESS:

OCCUPATION:

COMPLAINTS AT PRESENTATION:

Past history:

Family history:

Personal history:

Treatment history:-

PHYSICAL EXAMINATION:

GENERAL CONDITION:

- PALLOR
- ICTERUS
- LYMPHADENOPATHY
- CYANOSIS
- CLUBBING
- EDEMA
-

VITALS:

- TEMPERATURE:
- PULSE:
- RESPIRATORY RATE:
- BLOOD PRESSURE:

SIGNS OF HEPATOCELLULAR FAILURE	**SIGNS OF HEPATIC ENCEPHALOPATHY**
LOSS OF AXILLARY HAIR	ASTERIXIs
LEUCONYCHIA	CONSTRUCTIONAL APRAXIA
DUPYTREN’S CONTRACTURE	
GYNECOMASTIA	
SPIDER NAEVI	
ASCITES	
TESTICULAR ATROPHY	

SYSTEMIC EXAMINATION:

C.V.S.:

R. S.:

P.A.:

C.N.S.:

INVESTIGATIONS

BLOOD PICTURE	**LIVER FUNCTION TEST**
HB -	T.BILIRUBIN-
WBC –	D. BILIRUBIN-
Platelet count-	SGOT -
Neutrophils -	SGPT -
Lymphocytes -	Sr. Albumin
Monocytes -	A/ G Ratio
Eosinophils -	**RENAL FUNCTION TEST**
Basophils –	Serum Creatinine –
COAGULATION PROFILE	Blood Urea -
PT -	Sodium-
INR –	Potassium-
	Chloride -
VIRALS-	

USG ABDOMEN

LIVER SIZE

ECHOTEXTURE

SPLEEN SIZE

PORTAL VEIN DIAMETER

COLLATERALS (IF ANY)

NTproBNP

ECG

a) Prolonged QT interval

b) low voltage QRS complexes

ECHO

a) **SYSTOLIC DYSFUNCTION**

Ejection fraction (EF) –

b) **DIASTOLIC DYSFUNCTION**

Mitral Valve Inflow Pattern**- E/A RATIO**	
Deceleration Time (**DT)** –	
Tissue Doppler at Mitral Valve Annulus (**e/e')**	
E/e'	
Left Atrial Pressure (**LAP)**	
Left Ventricular End Diastolic Pressure **(LVEDP)**	
Pulmonary Vein Velocity	

EARLY [E] & ATRIAL [A] WAVEFORMS

- E = Peak early mitral inflow velocity (Early diastolic filling)
- A = Peak mitral inflow velocity (late diastolic atrial kick)

e' = Early Mitral Valve Annular diastolic velocity

ANNEXURE III – KEY TO MASTER CHART

HB	Hemoglobin
WBC	White Blood Cells
INR	International Normalised Ratio
SGOT	Serum Glutamic Oxaloacetic Acid Transaminases
SGPT	Serum Glutamic-Pyruvic Transaminases
LVEF	Left Ventricular Ejection Fraction
DDF	Diastolic Dysfunction
MELD	Model For End Stage Liver Disease
CTP	Child Tourette Pugh Score
E	Peak Early Mitral Inflow Velocity (Early Diastolic Filling)
A	Peak Mitral Inflow Velocity (Late Diastolic Atrial Kick)
E’	Early Mitral Valve Annular Diastolic Velocity
DT	Deceleration Time

ANNEXURE IV – MASTER CHART

SL NO	AGE	SEX	IP NO	ABDOMINAL DISTENSION, PEDAL EDEMA	FEVER	HEMATEMESIS OR MALENA	DECREASED URINEOUPUT	ALTERED SENSORIUM	ABDOMINAL PAIN	OTHERS	PAST HISTORY	ALCOHOLIC	SMOKER	DIABETES	HYPERTENSION	ASCITES	HEPATIC ENCEPHALOPATHY	HB	WBC	NEUTROPHILS	LYMPHOCYTES	MONOCYTES	EOSINOPHILS	BASOPHILS	PLATELET COUNT	PT	INR	T. BILIRUBIN	SGOT	SGPT	TOTAL PROTEINS	SR. ALBUMIN	AG RATIO	SR CREATININE	BL UREA	SODIUM	POTASSIUM	CHLORIDE	LIVER SIZE	ECHOTEXTURE	SPLEEN SIZE	PORTAL VEIN DIAMETER	COLLATERALS	NT PRO BNP	PROLONGED QT	LOW VOLTAGE QRS	LVEF	E/A RATIO	DECELERATION TIME	e/e'	E/e'	DDF GRADE	MELD	CHILD PUGH POINT	CTP CLASS
1	55	M	1085313	Y	N	N	N	N	N		CLD	Y	N	Y	N	2	0	7.5	13600	76	12	10	2	0	138000	30.3	2.59	7.21	46	12	5.6	2.5	0.8	1.15	20	130	3.56	93	14.8	COARSE	14.2	1	N	4297	N	N	55	0.8	272	8	5	1	25.89336284	12	C
2	69	M	1096085	N	N	N	Y	N	N		NO	Y	Y	Y	Y	1	0	11.7	6800	64	23	10	3	0	132000	11.1	0.95	0.61	14	20	6.8	4.3	1.7	5.94	50	128	6.18	95	13	INCREASED	9	0.9	N	480	N	N	55	0.9	156	11	8	0	21.03803157	5	A
3	47	M	1116443	Y	Y	N	N	N	N	SEIZURE	NO	Y	N	N	N	2	2	11.2	19800	83	8	7	0	0	83000	35	2.94	8.59	145	106	6.6	2.2	0.5	1.8	164	127	5.83	93	10.5	COARSE	10	1.2	N	4119	N	N	55	0.7	252	9	7.2	1	32.26256919	13	C
4	46	M	1116946	Y	N	N	N	N	N	JAUNDICE	CLD	Y	Y	N	N	3	0	5.5	10900	76	13	7	4	0	159000	21.4	1.77	1.69	38	24	5.1	1.7	0.5	1.49	34	139	3.76	111	11.7	COARSE	14.1	1.2	Y	668	Y	N	55	1.5	140	12	6	0	18.62473236	10	C
5	37	M	1116176	N	N	Y	N	Y	N		NO	Y	Y	N	N	1	2	10.4	9800	85	8	7	1	0	44000	13.6	1.12	3.73	157	38	7.9	3.5	0.8	0.52	22	132	3.14	96	16	COARSE	9.5	1.2	Y	484	Y	N	60	0.9	240	12	10	0	6.417228105	9	B
6	51	M	1085725	Y	N	N	N	Y	N	JAUNDICE	CLD	Y	N	N	N	2	1	6.5	5300	89	5	5	1	0	42000	35.9	2.97	19.37	66	27	5.8	2.9	1	1.69	78	129	4.11	97	11.8	COARSE	14.1	1.2	Y	8481	N	N	55	0.8	242	9	7	1	34.8464285	12	C
7	71	M	1085711	Y	N	N	Y	Y	N		DIABETIC NEPHROPATHY	Y	N	Y	Y	2	3	14.2	6400	54	34	10	2	0	116000	13.6	1.12	1.9	20	26	7.0	3.1	0.8	3.01	90	136	4.85	98	12	COARSE	14	0.9	N	1406	Y	N	60	0.9	140	11	10	0	20.67105567	9	B
8	61	M	1085965	Y	N	N	Y	Y	N		EPILEPSY	N	N	Y	N	3	1	9.6	14800	81	11	8	0	0	283000	13.1	1.08	0.2	14	10	4.3	1.6	0.6	1.54	63	129	2.19	93	12	COARSE	10.5	1.3	Y	2846	Y	Y	60	1.1	168	15	7.4	0	5.340446066	10	C
9	72	M	1085861	N	N	Y	N	N	N	JAUNDICE	NASH,IHD	N	N	Y	Y	3	0	4.5	6300	76	17	1	0	0	114000	16.2	1.34	1.05	24	18	5.7	3.3	1.4	1	30	129	4.44	96	12	COARSE	13	1.2	N	135	N	N	60	1.1	210	13	5.4	0	9.892326533	8	B
10	58	M	1109315	Y	N	N	Y	N	N			Y	Y	N	N	2	1	11.9	6700	48	23	7	22	0	108000	19.7	1.63	3.21	80	42	6.6	2.2	0.5	2.66	29	132	4.63	100	14.8	COARSE	14.2	1	N	4572	N	N	60	0.6	270	8	5	1	25.6731815	11	C
11	54	M	1116392	Y	N	N	N	N	N			Y	N	N	N	2	2	9.1	7400	85	10	5	0	0	66000	19.8	1.64	14.58	215	43	6.8	3.2	0.9	1	22	136	3.3	108	14	COARSE	16	1.3	Y	366	Y	N	55	0.7	290	7	5	1	22.09967782	10	C
12	39	M	1116251	Y	N	N	N	N	N		CLD	Y	Y	N	N	2	0	9.7	10300	65	4	0	1	0	161000	24.1	1.99	9.94	88	47	5.6	2.5	0.8	0.81	17	132	5.12	102	15.1	COARSE	14.9	1.2	Y	308	N	Y	60	0.8	284	9	6	1	20.80153117	11	C
13	46	M	1117531	Y	N	N	N	N	N			Y	Y	Y	N	1	0	11.4	4700	93	5	2	0		24000	29.3	2.42	6.29	105	40	7.2	2.4	0.5	1.26	27	139	3.84	107	19	COARSE	13	1.2	N	862	Y	N	55	1.4	234	13	6	0	25.49120867	11	C
14	55	M	1117517	Y	N	N	Y	N	N			Y	Y	N	Y	2	0	12.2	24600	84	7	8	1	0	107000	16.9	1.4	6.38	78	39	6.3	2.6	0.7	4.29	157	134	4.36	100	16.5	COARSE	15.5	1.3	N	2385	Y	N	50	0.7	248	7	5	1	31.14012875	10	C
15	62	M	1117370	Y	N	N	Y	Y	Y			Y	Y	N	N	3	2	10.8	6700	81	8	1	2	0	168000	23.2	1.92	26.98	93	29	7.2	2.4	0.5	1.24	28	135	2.73	104	14	COARSE	12	1.1	N	1080	Y	Y	60	0.7	270	9	6	1	28.25012053	13	C
16	40	M	1117613	N	Y	N	N	N	Y		CLD	Y	Y	N	N	1	0	10.6	5000	46	46	5	3	0	107000	16.8	1.39	3.3	46	19	3.6	1.7	0.9	0.77	10	145	3.37	113	16	ALTERED	14	1.2	Y	235	Y	N	55	1.2	168	5	9	2	12.12996817	9	B
17	77	M	1117353	Y	N	N	N	N	N			Y	N	Y	N	1	0	7	3400	57	34	5	2	0	58000	25.4	2.1	0.98	25	11	6.0	1.7	0.4	1.3	27	133	3.92	106	20	COARSE	14	1.2	N	2646	Y	Y	55	0.8	252	8	7	1	17.17415815	8	B
18	53	M	1117506	Y	N	N	Y	N	N		NAFLD	N	N	Y	N	3	0	7.6	5300	36	37	8	19	0	108000	23.0	1.9	1.62	51	23	6.6	2.2	0.5	1.53	15	133	4.35	96	18	COARSE	14	1.3	N	232	Y	Y	60	1.4	152	11	9	0	19.51214673	10	C
19	53	M	1115419	Y	N	N	N	N	N	JAUNDICE		Y	Y	N	N	1	0	11.5	8700	84	5	10	1	0	87000	44.6	3.69	25.52	102	70	5.3	2.2	0.7	1.47	66	126	2.78	89	19.2	COARSE	14.6	0.8	N	122	N	N	55	1	144	12	6	0	36.98514592	11	C
20	48	M	1114533	Y	N	N	N	N	Y			Y	Y	N	N	2	0	5.8	15400	81	9	0	0	0	168000	22.3	1.84	7.4	35	28	4.4	2.1	0.9	1.31	97	129	4.07	98	11.8	COARSE	14.1	1.2	Y	657	Y	Y	60	0.8	244	9	7	1	23.40912868	11	C
21	46	M	1117348	Y	N	Y	N	N	Y		CLD	Y	N	Y	N	1	1	7.8	4500	71	18	10	1	0	36000	31.2	2.58	3.93	85	28	5.9	2.2	0.6	2.53	35	16	4.74	91	20	COARSE	16	1.3	Y	35000	Y	N	50	1.3	230	11	7	0	31.10175728	12	C
22	56	M	1117299	Y	Y	Y	N	N	N	COUGH		Y	N	Y	N	3	0	9.8	13500	63	29	7	1	0	62000	21.8	1.8	7.06	41	20	4.8	2.8	1.4	1.39	47	127	4.65	90	19	COARSE	16	1.3	N	718	N	N	60	1.4	152	12	9	0	23.55244998	11	C
23	46	M	1116429	N	N	N	N	N	Y		ALD	Y	Y	N	N	3	0	10.3	24500	81	12	7	0	0	54000	36.7	3.03	4.58	39	19	4.6	2.3	1	1	40	124	4.65	90	20.1	COARSE	17.3	1.4	N	418	N	N	55	0.7	262	7	6.4	1	24.59792374	13	C
24	58	M	1125691	N	N	N	N	Y	Y	LOOSE STOOLS	NAFLD	N	N	Y	N	1	2	10.2	10800	91	6	3	0	0	64000	20.3	1.68	4.16	96	31	7.4	3.3	0.8	202	128	127	4.03	93	14	ALTERED	12	1.1	N	9672	N	N	55	0.6	290	9	7	1	68.42905998	9	B
25	63	M	1125605	N	N	N	N	N	Y		CLD	Y	Y	N	N	3	1	8.3	6400	74	12	10	4	0	32000	20.3	1.68	7.7	75	46	5.5	3.1	1.3	2.5	166	126	3.38	94	12.3	COARSE	17.8	1.1	Y	398	Y	N	55	0.7	280	9.2	6	1	28.72520587	11	C
26	67	M	1120977	Y	N	N	N	N	N	DYSPNEA	CLD	Y	Y	Y	N	2	0	6.5	3600	82	8	9	1	0	55000	23.8	1.97	5.26	32	22	6.3	2.8	0.8	1.47	100	125	4.4	91	10	COARSE	14	1.3	Y	799	N	Y	60	1	166	13	7	0	23.98623232	10	C
27	47	M	1120442	Y	N	N	N	N	N			Y	Y	Y	N	3	0	13.3	6600	79	11	10	0	0	152000	14.6	1.21	0.77	32	16	7.0	2	0.4	1.51	84	135	4.36	96	15	coarse	12	1.2	y	1308	Y	N	60	0.8	244	8.8	7.2	1	11.52087863	9	B
28	58	M	1121064	Y	N	N	N	N	N		NAFLD	N	N	Y	N	1	0	9.8	5700	65	27	4	4	0	82000	15.9	1.31	2.35	14	19	6.7	2.5	0.6	0.69	32	129	4.04	93	16.3	ALTERED	12	1.1	N	9672	N	N	60	1.4	156	14	6	0	9.132914475	8	B
29	46	M	1116429	N	N	N	N	Y	N	WEAKNESS		Y	Y	Y	N	1	2	9.8	13500	63	29	7	1	0	62000	21.8	1.8	4.58	39	19	4.6	2.3	1	1.35	84	122	5.64	96	20.1	COARSE	17.3	1.4	Y	35000	N	N	55	1.4	190	7	11	2	21.63723397	11	C
30	78	M	1118545	Y	N	N	N	N	Y		NAFLD	N	N	Y	Y	2	0	8.2	27900	89	4	7	0	0	97000	28.6	2.36	1.52	20	41	6.3	2.6	0.7	1.61	50	132	4.05	103	16.8	ALTERED	10	1.2	N	1140	N	Y	55	1.3	180	7	11	2	22.18729646	10	C
31	48	M	1119309	Y	N	N	Y	N	N		ALD	Y	Y	N	N	2	0	8.3	11400	86	4	9	1	0	140000	24.9	2.11	14.01	136	33	6.5	3	6	1.23	34	116	3.12	78	15	ALTERED	18	1.4	N	1222	N	N	60	1.3	240	12	7.4	0	26.75236657	10	C
32	44	M	1120835	N	Y	N	N	Y	Y			Y	N	N	N	3	1	9.3	18600	84	10	6	0	0	81000	28.3	2.34	3.5	80	39	4.2	1.7	1	1.61	75	132	3.67	100	12	ALTERED	13	1.1	N	369	Y	N	55	1.4	220	13	15	0	25.24469572	14	C
33	66	M	120799	N	N	Y	N	N	N		HYPOTHYROIDISM	N	N	Y	Y	1	0	8.7	12300	80	13	6	1	0	127000	14.3	1.22	0.54	15	19	5.1	3	0.5	0.85	105	141	5.84	106	10	NORMAL	14.1	1	Y	219	N	N	50	0.8	262	7	6	1	4.772639838	6	A
34	59	F	1121277	N	N	Y	N	N	N	SYNCOPE	EHVPO	N	N	N	N	1	1	7.7	13600	87	10	3	0	0	199000	19.4	1.6	0.6	33	21	4.4	2.1	0.9	0.65	75	139	4.76	106	15	ALTERED	12	1.4	N	492	N	Y	60	1.3	156	14	6	0	5.640527274	8	B
35	45	M	1120806	N	N	Y	Y	Y	N		ALCHOLIC HEPATITIS	Y	Y	N	N	3	2	10.3	20800	90	5	4	1	0	90000	24.5	2.08	9.45	95	80	6.2	2.4	0.5	3.34	221	112	7.87	88	16	COARSE	15	1.2	Y	2872	N	N	55	1.2	160	7	10	2	34.66359705	13	C
36	47	M	1119048	N	N	N	N	Y	N	WEAKENESS OF UPPERLIMBS P>L	CLD	Y	Y	N	N	2	2	9.6	9800	54	33	10	30	0	107000	28.1	2.32	4.56	59	42	5.4	2.4	0.8	0.71	28	141	3.84	108	15	COARSE	16	1.3	Y	209	Y	Y	55	0.7	268	8	6	1	18.31339986	13	C
37	38	M	1106638	Y	N	Y	N	Y	Y		ALD	Y	N	N	N	3	2	10.2	5500	86	8	6	0	0	101000	18.2	1.5	22.57	59	48	4.7	2.1	0.8	2.15	68	130	3.42	97	20.1	IRREGULAR	17.8	1.4	N	486	N	N	55	0.9	250	9.8	8	1	30.07756632	12	C
38	48	M	1108374	Y	N	N	N	N	Y		CLD	Y	N	N	N	2	0	14.9	8510	63	32	4	1	0	150000	16.5	1.36	0.2	24	22	5.3	2.8	1.1	0.8	20	135	3.6	106	10	COARSE	10	1.2	N	278	N	N	60	1	210	12	7.6	0	1.654669492	7	B
39	44	M	1108481	N	Y	N	Y	Y	Y	LOOSE STOOLS		Y	Y	Y	N	1	2	8.7	6400	70	16	10	4	0	65000	26.6	2.2	12.26	140	30	7.8	2.6	0.5	1.14	19	129	4.06	93	17	COARSE	13	1.3	N	370	N	N	55	0.6	258	8.2	7.4	1	25.98863561	11	C
40	60	M	1108135	Y	Y	N	Y	N	Y			Y	Y	N	N	2	1	7.7	6200	68	14	10	8	0	52000	28.0	2.31	6.74	40	17	5.9	3.6	1.6	1.62	76	124	3.85	90	17	COARSE	17	1.4	N	2011	N	N	55	0.82	30	9.2	6.8	1	27.63645726	11	C
41	28	M	1117318	N	N	N	N	N	Y			Y	Y	N	N	1	0	10.8	21600	84	7	8	1	0	485000	27.2	2.25	29.71	146	30	5.9	2.6	0.8	0.59	12	131	2.8	98	17	COARSE	14	1.2	N	471	N	N	60	1.3	190	14	7	0	23.2827816	10	C
42	29	M	1117308	Y	N	Y	N	Y	Y			Y	N	N	N	2	1	15.1	20000	81	9	10	0	0	316000	13.1	1.08	0.52	10	12	7.8	3.7	0.9	0.76	26	126	5.08	93	13	COARSE	10	1.2	Y	568	N	N	60	1.4	220	14	8	0	2.193760956	7	B
43	49	M	1117067	Y	N	Y	N	N	Y		CLD	Y	N	Y	N	3	1	7.2	6800	78	11	8	3	0	156000	19.0	1.57	1.42	21	11	4.1	1.8	0.8	0.75	10	130	3.05	95	12	COARSE	10	1.4	N	842	Y	N	55	0.6	262	7.7	6.6	1	10.05441252	10	C
44	44	M	1117631	Y	N	N	N	Y	N	JAUNDICE		Y	N	N	N	3	2	10.9	10300	83	9	7	1	0	129000	26.6	2.2	29.54	120	34	7.2	2.4	0.5	0.63	10	137	2.94	102	15	COARSE	17	1.2	Y	759	Y	N	60	0.76	290	9	7	1	23.63716042	13	C
45	36	M	1106660	Y	N	Y	N	N	N		CLD	Y	N	N	N	2	0	6.1	4870	75	21	3	1	0	127000	24.1	1.99	4.3	46	182	6.1	2.3	0.6	0.7	19	135	3.95	102	14.4	COARSE	17	0.9	N	510	N	Y	60	1.1	166	14	6.8	0	16.23729363	11	C
46	39	M	1108126	Y	N	N	N	Y	N			N	N	Y	Y	2	0	6.7	8000	65	28	5	2	0	28000	30.6	2.53	10.96	78	24	4.2	2.1	1	0.81	33	121	3.7	101	21	COARSE	17.6	1.4	Y	384	N	N	55	1.1	202	12	7.4	0	23.85972973	12	C
47	58	M	1126800	Y	N	N	N	Y	Y			Y	Y	N	Y	2	1	14.1	11000	68	21	1	10	0	154000	41.7	3.45	22.32	978	158	2.6	2.3	7	0.95	27	125	5.15	91	16	COARSE	15	1.4	Y	248	N	N	55	0.6	272	9.2	6.8	1	31.54764108	13	C
48	52	M	1126795	N	Y	N	N	N	N			Y	Y	Y	Y	2	0	5.7	2000	50	38	10	2	0	29000	16.5	1.36	1.59	64	26	6.2	3.5	1.3	0.47	12	133	3.25	99	17	COARSE	11	1	N	301	N	N	60	0.6	280	8.8	7	1	4.401177066	7	B
49	38	M	1127940	Y	N	Y	N	N	N			Y	Y	N	N	2	0	8.3	7800	72	17	10	1	0	193000	17.2	1.46	1.12	33	13	6.3	1.4	0.3	0.43	10	134	3.89	100	13	COARSE	14	1.6	N	271	N	N	60	0.8	245	9	7	1	3.020076902	8	B
50	55	M	1126416	N	N	N	N	Y	Y			Y	N	N	N	1	3	6.3	7700	70	16	10	4	0	216000	15.7	1.34	1.41	122	22	5.5	2.2	0.66	0.73	26	138	3.69	104	14	COARSE	10	1.5	N	750	N	Y	55	1.2	180	7.5	11	2	7.994886947	9	B
51	46	M	1127055	N	N	Y	N	N	N	WEAKNESS, JAUNDICE		Y	N	N	N	1	0	7.6	8800	74	12	9	5	0	65000	35.3	2.92	20.63	61	21	5.9	2.2	0.6	0.73	17	115	3.27	84	12	COARSE	9	1.4	N	210	N	N	55	1	202	14	9	0	26.861056	11	C
55	58	M	1125691	Y	N	N	N	N	Y		NAFLD	N	N	Y	N	2	0	10.2	10800	91	6	3	0	0	0	20.4	1.69	4.16	96	31	5.5	3.3	1.5	2.2	128	127	4.03	93	12	COARSE	15	1.3	N	9672	Y	N	55	1.3	150	6	11	2	25.24094364	9	B
56	38	M	1125600	Y	Y	N	N	Y	N			Y	Y	N	N	3	2	12.1	22500	88	6	5	1	0	311000	26	2.2	22.23	170	29	6.4	2.5	0.6	0.44	19	104	3.51	64	19	COARSE	15.2	1.2	N	222	N	N	50	1.95	135	4	16	3	19.1273922	13	C
57	40	M	1125300	Y	N	Y	N	N	N		CLD	Y	N	Y	N	2	1	7.8	3300	74	15	10	1	0	70000	25.7	2.18	10.84	139	22	7.3	2.1	0.4	1.18	30	127	3.42	80	14	COARSE	14.2	1.3	N	308	N	N	50	1.2	160	7	10	2	25.75107052	12	C
58	48	M	1122951	N	Y	Y	N	N	N			Y	N	N	Y	2	1	8.4	16700	86	6	8	0	0	44000	30.7	2.6	6.82	35	13	7.1	3.1	0.8	1.19	84	125	5.01	94	16	COARSE	16.7	1.8	Y	951	N	Y	55	0.6	260	8.8	6.8	1	26.05353034	12	C
59	60	M	1114397	Y	N	Y	N	N	N	N	CLD	Y	N	N	N	3	0	8.2	7300	59	58	10	17	0	59000	19.0	1.62	7.6	38	22	6.3	2.8	0.8	1.27	53	125	4.9	96	22.8	COARSE	16.2	0.9	N	2011	N	Y	60	1.1	166	14	6	0	21.78696514	10	C
60	66	M	1113695	N	N	N	N	Y	N		CLD	Y	N	N	N	2	2	9.2	5900	70	76	7	0	0	70000	11.7	1.15	2.15	77	21	6.2	3.4	1.2	1.76	54	133	3.57	102	19.8	INCREASED	15.9	1.4	Y	206	N	N	55	0.6	288	6	5	1	16.29885545	9	B
61	68	M	1114446	N	Y	N	N	N	N	COUGH	CLD	Y	Y	N	N	1	0	12.9	14400	65	23	10	0	0	90000	21.0	1.79	13.26	111	56	6.6	3.3	1	0.75	32	137	3.8	101	22	COARSE	12.6	1.3	N	443	N	N	55	0.7	256	9.6	7.4	1	19.96806015	9	B
62	50	M	1110202	N	N	N	N	N	N	JAUNDICE	CLD	Y	N	N	N	1	0	10.5	12400	77	12	10	0	0	220000	21.9	1.86	14.94	121	37	6.9	2.6	0.6	0.98	27	133	4.5	99	18	INCREASED	13.2	1.3	Y	351	Y	N	60	1.3	160	12	6	0	23.40839637	10	C
63	49	M	1111331	N	N	N	N	N	N	JAUNDICE	AYURVEDIC	Y	N	N	N	1	0	11.8	8000	74	14	0	2	0	242000	17.0	1.1	27.78	254	54	6.1	2.9	0.9	0.57	18	129	3.14	92	21	COARSE	16.3	1.3	Y	571	N	Y	55	0.6	284	7	6.2	1	14.68391181	8	B
64	45	M	1110546	Y	N	Y	N	N	N		CLD	Y	N	N	N	3	0	6.2	21900	71	18	10	1	0	113000	23.2	1.97	11.64	249	140	5.4	2.4	0.8	1.15	56	132	4.46	100	20	COARSE	16.4	0.9	Y	148	N	Y	60	0.7	284	7.4	5	1	24.63930899	12	C
65	58	F	1113927	Y	N	Y	N	N	N	APPETITE LESS	CLD	N	N	N	Y	2	0	8.8	9500	75	14	9	0	0	93000	22.8	1.94	5.35	84	40	6.7	2.5	0.6	1.21	39	114	4.11	81	23.8	COARSE	15.2	1.4	Y	826	N	N	60	0.8	274	9	7	1	22.0157673	11	C
66	39	M	1113052	N	N	Y	N	Y	N		CLD	Y	N	N	N	1	0	6.1	7500	70	20	2	8	0	100000	16.4	1.4	21.68	59	108	6.6	2.7	0.7	0.93	18	123	5.23	94	17.5	INCREASED	13	0.9	N	308	Y	N	55	1.2	144	13	8	0	21.13274254	9	B

67	43	M	1112142	N	N	Y	N	N	N	JAUNDICE	CLD	Y	N	N	N	1	0	705	6000	83	15	2	0	0	98000	16.4	1.4	16.8	108	59	5.9	2.6	0.8	1.23	18	126	5.23	94	17	INCREASED	12.5	1.2	N	754	N	N	60	1.4	182	6	10	2	22.84442701	9	B
68	45	M	1114337	Y	N	N	N	N	N	JAUNDICE		Y	N	N	N	2	0	11	15500	81	12	1	0	0	151000	21.0	1.79	9.89	100	87	6.3	1.8	0.4	1.2	28	130	3.3	94	14.9	COARSE	16.2	1.8	Y	241	N	N	60	1	150	12	7	0	23.35759369	11	C
69	48	M	1109389	Y	N	N	N	N	N	JAUNDICE		Y	N	N	N	3	0	9.2	5400	71	11	8	2	0	42000	32.0	2.71	14.5	63	21	6.1	4	1.9	2.27	29	127	3.2	83	12.9	COARSE	15.9	1.2	Y	440	N	Y	60	0.6	250	8	7	1	35.5493999	11	C
70	52	M	1110256	N	N	Y	N	N	N	JAUNDICE		Y	N	N	N	2	0	9.5	15400	77	12	10	1	0	220000	22.0	1.8	12.2	141	54	6.9	2.6	0.6	0.98	19.5	132	4.58	99	26.4	INCREASED	13	1.3	Y	2314	Y	Y	55	0.8	290	9.6	7.4	1	22.2752988	11	C
71	56	M	1112424	Y	N	Y	N	N	N		CLD, HCC, HCV	Y	N	N	N	3	0	6.3	2500	53	30	8	1	0	71000	11.7	1.46	1.18	51	44	6.5	3.1	0.9	0.64	23	138	3.8	105	12	INCREASED	16.3	1.7	N	28	N	N	60	0.7	262	9.2	6.8	1	7.023165092	8	B
72	66	M	1113435	Y	N	N	N	N	N	JAUNDICE	CLD	Y	N	N	N	2	0	9.6	7400	70	18	1	3	0	59000	25.0	2.16	7.72	94	55	8.1	2.7	0.5	1.07	26	136	3.2	99	11	COARSE	13.2	1	N	892	N	N	60	0.8	264	8.4	5	1	23.42832382	11	C
73	60	M	1113468	N	N	N	N	N	N	WEAKNESS	CLD	Y	N	N	N	3	0	6.2	2400	49	31	10	5	0	27000	24.8	2.1	3.84	78	62	5.3	2.8	1.1	1.1	46	127	3.9	78	13	INCREASED	10	0.8	N	1256	N	N	55	0.7	284	8	6	1	20.73770238	11	C
74	48	M	1116732	N	N	N	N	N	N	EPISTAXIS	HBV	N	N	N	N	1	0	7.2	7100	72	13	10	5	0	56000	130.0	13.1	19.5	49	20	6.8	3.2	0.9	0.7	21	132	4.8	97	12.9	INCREASED	15.9	1.2	Y	130	N	N	60	1.2	160	13	8	0	43.05804483	10	C
75	42	M	1114287	Y	Y	N	N	N	Y	JAUNDICE	CLD	Y	N	N	N	2	2	8.5	7700	67	22	2	1	0	46000	26.0	2.24	4.94	82	29	7.2	2.7	0.6	0.92	12	138	4.61	96	12	COARSE	10	0.9	N	420	Y	Y	55	1.2	182	6	10	2	20.7026088	12	C
76	71	M	1114222	N	N	Y	N	N	Y			N	N	Y	N	1	0	7.2	9600	82	13	5	0	0	123000	16.5	1.4	0.96	36	19	4.6	2.3	1	0.47	32	139	3.97	105	10.3	COARSE	13.2	1.4	N	117	N	N	55	1.2	154	12	8	0	2.818615742	7	B
77	64	M	1114923	Y	N	Y	N	N	N		ABD VENOUS THROMBOSIS	N	N	N	N	2	0	14.2	6200	70	26	3	2	0	169000	10.8	0.6	0.51	26	24	6.4	4	1.7	1.13	22	140	4.19	104	10.2	COARSE	13.1	1.3	N	23	N	N	60	0.7	267	8	6.2	1	-0.666866727	6	A
78	42	M	1114962	Y	N	N	N	N	Y		ALD	Y	N	N	N	2	1	8.6	14600	53	37	8	0	0	132000	25.0	2.3	4.8	29	14	6.3	2.8	0.8	0.9	14	132	4.5	97	18	INCREASED	15.5	0.9	N	459	N	N	50	0.7	276	7	5	1	20.67965036	11	C
79	60	M	1115666	Y	N	N	N	N	Y		CLD	N	N	Y	N	3	0	9	12800	43	47	9	0	0	120000	27.5	2.27	4.72	29	14	6.4	2.7	0.8	0.87	16	128	4.66	98	17	COARSE	15.3	0.9	N	795	N	N	60	0.68	254	9.2	6.6	1	20.14463353	12	C
80	38	M	1118111	Y	N	N	N	N	N			Y	N	N	N	3	2	15.3	8300	50	42	7	1	0	289000	11.0	0.91	0.95	53	33	7.3	4.4	1.5	1.12	45	145	3.97	107	16	COARSE	16.3	13	N	10	N	N	50	1	164	13.2	7	0	6.264387254	8	B
81	57	M	1114052	Y	N	Y	N	N	N		CLD	Y	N	N	N	2	0	3.7	6300	85	12	3	2	0	79000	17.7	1.46	0.5	18	19	5.4	2.4	0.8	1.08	50	139	4.1	107	14	COARSE	18.8	1.3	Y	659	N	N	55	0.6	274	8.8	7.4	1	8.784908926	8	B
82	42	M	1113425	Y	N	N	N	N	Y		CLD	Y	N	N	N	2	0	9.3	5400	61	26	13	5	0	71000	23.5	1.94	2.64	48	19	6.9	2.3	0.5	0.63	19	135	3.8	106	14.9	INCREASED	16.2	1.7	Y	786	N	Y	55	1.3	182	13	7	0	13.09997033	10	C
83	49	F	1116476	Y	N	N	N	Y	N			N	N	Y	N	2	1	8	9400	86	7	1	0	0	26000	22.4	1.85	2.93	37	17	7.4	3.5	0.9	1.86	33	133	3.9	102	18	COARSE	13.2	1.2	Y	1958	N	N	60	0.6	265	7.9	5.8	1	23.32250548	10	C
84	69	M	1116781	Y	N	N	N	N	N		HCV	N	N	Y	Y	2	2	10	11100	61	32	6	1	0	302000	23.7	1.96	0.47	15	11	7.2	3.6	1	0.57	21	134	4.06	100	14	COARSE	12	1.2	N	1202	N	N	50	0.7	292	8.6	5.4	1	5.733514678	8	B
85	48	M	1117878	N	N	Y	N	Y	N			Y	N	N	N	3	1	11.6	4100	82	8	10	0	0	31000	13.3	1.1	15.8	615	522	5.4	2.7	1	1	68	146	3.36	106	14	INCREASED	16	1.4	N	639	N	N	60	1.2	160	14	7	0	17.93031171	12	C
86	45	M	1116644	Y	Y	N	N	N	N	LOOSE STOOLS	ALD	Y	Y	Y	N	3	0	9.9	7300	67	22	0	3	0	57000	24.3	2.01	3.43	57	59	6.3	2.8	0.8	0.61	45	129	4.12	96	16.5	COARSE	18	1.5	N	22	Y	N	55	0.75	252	9.2	7.5	1	14.17777096	11	C
87	31	M	1118205	Y	N	N	N	N	Y			Y	Y	N	Y	2	0	17	9900	83	7	9	1	0	170000	13.0	1.077	9.1	45	48	6.0	3.4	1.3	0.71	19	128	3.91	92	21	INCREASED	13	1.4	N	1300	N	N	60	1.4	170	7	10	2	12.33045435	9	B
88	58	M	1113951	Y	N	Y	N	N	N			Y	N	Y	N	2	0	10.5	5400	75	18	9	2	0	88000	19.4	1.6	3.16	49	26	7.0	2.9	0.7	0.67	11	133	3.9	96	23	INCREASED	14.3	1.6	Y	9672	N	N	60	0.6	280	9	6	1	12.21063266	9	B
89	41	M	1112176	Y	N	N	N	N	N	JAUNDICE		Y	N	N	N	3	0	10.6	9200	76	11	8	0	0	303000	18.4	1.52	17.3	128	53	7.2	2.7	0.6	0.49	12	134	4.13	99	23.4	COARSE	14.3	1.6	Y	4382	N	N	55	0.7	292	7	6	1	15.06846799	11	C
90	63	M	1117934	Y	N	N	N	Y	N		CLD	Y	Y	N	N	2	2	8	3800	65	19	13	6	10	45000	19.4	1.6	5.5	96	66	6.1	3.6	1.4	0.86	44	131	5.17	100	20	COARSE	13.5	1.5	N	398	N	N	60	1.1	150	14	9	0	16.69461349	9	B
91	50	M	1113701	N	Y	Y	N	N	N		CLD	Y	Y	N	N	2	0	8	6800	81	8	1	0	0	150000	14.5	1.2	2	48	22	5.1	1.9	0.6	0.81	10	131	3.47	96	20	ALTERED	13.5	1.5	N	3343	N	N	55	0.8	251	8.9	7.2	1	9.075497537	9	B
92	46	M	1112705	Y	N	N	N	N	Y			Y	N	N	N	1	0	15.2	5800	81	8	1	0	0	150000	14.2	1.17	7.31	160	53	7.0	2.9	0.7	2.12	71	127	3.02	82	20	ALTERED	13.5	1.5	N	893	N	N	55	0.7	260	9	6	1	22.8988337	8	B