**BY**

**REGISTRATION NO: BG0117003**

# Dissertation

**Submitted to**

**KAHER, Belagavi, Karnataka**

**In partial fulfillment**

**of the requirements for the degree of**

**M .D.**

**IN**

**GENERAL MEDICINE**

**J. N. MEDICAL COLLEGE**

**BELAGAVI- 590010. KARNATAKA**

**APRIL 2020**

**" CORRELATION OF SERUM PROLACTIN LEVEL WITH CHILD PUGH SCORING SYSTEM IN CIRRHOSIS OF LIVER " - A ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL**

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I hereby declare that this dissertation entitled **"CORRELATION OF SERUM PROLACTIN LEVEL WITH CHILD PUGH SCORING SYSTEM IN CIRRHOSIS OF LIVER" - A ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL"** is a bonafide and genuine research work carried out by me in the Department of General Medicine, Jawaharlal Nehru Medical College, Nehru Nagar, Belagavi-590010.

**Date**:

**Place**: Belagavi

**REGISTRATION NO:**

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Sub: Acceptance Letter

Sir/Madam,

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| ACTH | Adrenocorticotrophic Hormone |
| ALD | Alcoholic Liver Disease |
| ALP | Alkaline Phosphatase |
| CLD | Chronic Liver Disease |
| CT | Computerised Tomography |
| CTP | Child Turcotte Pugh |
| EEG | Electroencephalography |
| ELISA | Enzyme Linked Immunosorbent Assay |
| EVL | Endoscopic Variceal Ligation |
| FSH | Follicle Stimulating Hormone |
| GH | Growth Hormone |
| GnRH | Gonadotrophin Releasing Hormone |
| HBsAg | Hepatitis B Antigen |
| HCV | Hepatitis C Virus |
| HCC | Hepatocellular carcinoma |
| H.E | Hepatic Encephalopathy |
| HPS | Hepatopulmonary syndrome |
| HRS | Hepatorenal syndrome |
| ICU | Intensive Care Unit |
| Igf-1 | Insulin Like Growth Factor 1 |
| INR | International Normalised Ratio |
| LH | Luteinizing Hormone |
| MRI | Magnetic Resonance Imaging |
| NAFLD | Non Alcoholic Fatty Liver Disease |
| NASH | Non Alcoholic Steatohepatitis |
| NPV | Negative Predictive value |

| | |
|---|---|
| OPD | Outpatient Department |
| PPV | Positive Predictive Value |
| RAAS | Renin Angiotensin Aldosterone System |
| SGOT | Serum glutamic oxaloacetic transaminase |
| SGPT | Serum glutamic pyruvic transaminase |
| SPSS | Statistical Package for the Social Sciences |
| TRH | Thyrotrophin Releasing Hormone |
| TSH | Thyroid Stimulating Hormone |
| TIPSS | Transjugular intrahepatic portosystemic shunt |
| USG | Ultrasonography |
| WHO | World Health Organization |

# ABSTRACT

**OBJECTIVES:** To correlate the serum prolactin levels with CHILD PUGH score in cirrhosis of liver.

**MATERIALS & METHODS:**

This study was a cross sectional study, conducted in the department of general medicine, DR.Prabhakar Kore hospital, KLE University, Belgaum. The study included 100 adults, aged above 18 years, with chronic liver disease. The data collection for the study was done between 1st January 2018 to 31st December 2018 for one year . All the patients were subjected to CBC, LFT, RFT, USG Abdomen, Upper Gastrointestinal Endoscopy. Serum prolactin assay was done for each patient. CHILD-PUGH score was calculated and compared with the prolactin levels.

**RESULTS:** 102 patients were included in our study based on clinical, biochemical and sonography findings of cirrhosis of liver. The average age in our study was 49.46 ± 12.15 years with most of the patients (57.84%) in the age group off 41-60 years. In the present study, 93% of the patients with cirrhosis were males . Alcohol was the most common etiology for cirrhosis, i.e. 78.43 %. 33 subjects (29.41%) had prolactin values above 40 ng/ml. The observations in our study showed that majority of the subjects, 59 (57.84%) were categorized as Child Pugh class C. 35 subjects (34.31%) fitted into Child Pugh class B and the rest belonged to Child Pugh class A.

Prolactin was found to have a highly significant positive correlation with both Child Pugh score and hepatic encephalopathy in our study(p value <0.0001). Similarly, bilirubin, albumin, ascites also had significant positive correlation with prolactin level.

**CONCLUSIONS:** We were able to come to the conclusion that prolactin could serve as a valuable indicator of severity of liver disease. Hence, a single parameter like prolactin, which has a significant association with the severity of cirrhosis of liver, can be considered for application in future clinical practice.

**KEY WORDS**: PROLACTIN, CIRRHOSIS OF LIVER, CHILD PUGH SCORE

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# INTRODUCTION

## INTRODUCTION

Cirrhosis is a common hepatological disorder observed in clinical practice that is associated with a range of distinctive clinical manifestations. [1,2]

"Cirr"means yellowish tan colour in Greek therefore describing the yellow colour that is typical of the nodules in cirrhotic liver. In the present era of modern medicine, cirrhosis of liver has been studied in depth. [3,4]

Liver cirrhosis is associated with various hormonal disturbances including pituitary hormones and sex hormones. Prolactin is normally secreted in a pulsatile pattern with a nocturnal elevation. In cirrhotic patients, prolactin levels are seen to be elevated throughout the day, thus signifying a loss of its normal circadian rhythm[1,11].

Elevated prolactin values were also seen to be coexisting with presence of hepatic encephalopathy. These patients also showed an exaggerated tendency to develop severe hepatic disease. [13,5]

While evaluating patients with gynecomastia in patients with cirrhosis, it was detected that many of these patients had hyperprolactinemia.[16]

Entry of amino acids across the blood brain barrier is affected, along with their metabolism. Elevation in the serum concentration of false neurotransmitters, namely octopamine and phenylethanolamine, is noted. These proteins inhibit dopamine release, thus resulting in elevated prolactin levels. [1,3,5]

CHILD-PUGH score is the common scoring system which is currently being employed in hospital to estimate the severity of liver cirrhosis. This score utilizes 5 components, namely total bilirubin, prothrombin time, degree of ascites, grade of hepatic encephalopathy and serum

albumin concentration. It is a reliable indicator of possibility of complications in the near future. Common complications include portal hypertension and spontaneous bacterial peritonitis. The higher the score, more are the chances that patient will develop upper gastrointestinal bleeding and altered sensorium. It can also be used to prognosticate liver cirrhosis and decide whether patient can be taken up for liver transplantation. [5,14,10,40]

Similar studies have been done in smaller subject groups. Thus, we have conducted a study in our population with 102 subjects to establish a stronger link between the prolactin levels with the components of CHILD PUGH scoring system.

High prolactin levels have been linked with greater derangement of components of Child Pugh score, greater mortality and greater complications of chronic liver disease. [1,2]

Hence, the use of a single biomarker such as prolactin, whose levels give us an idea about the severity of the disease and the possibility of complications, is a very vital indicator in EARLY INTERVENTION in such cases.

# OBJECTIVE

## OBJECTIVE

To correlate the serum prolactin levels with the CHILD-PUGH score in patients of cirrhosis of liver and thus, assess the severity of cirrhosis of liver.

# REVIEW OF LITERATURE

## REVIEW OF LITERATURE

Cirrhosis of the liver is linked with several endocrine disturbances. One such hormone is prolactin.[1,2]

### DEFINITION

Cirrhosis is defined by the presence of the following three components on histopathology: altered echotexture of liver, regenerative nodules and bridging fibrosis. [19]

### EPIDEMIOLOGY

Chronic liver disease can affect any individual, regardless of age, sex, race or geographical boundary. According to WHO, 59 % of the total mortality in the global population is caused due to chronic diseases. [22,23]

Liver disease is stated to be one of the most common causes of death especially in the developed countries of the world. While alcoholic liver disease is the most common cause of cirrhosis in Asian countries, Non Alcoholic Steatohepatitis (NASH) is slowly replacing other etiologies of liver cirrhosis in many parts of the world. [22]

### LIVER ANATOMY – IN HEALTH

Liver is the biggest organ in the body and its weight can average around 1 to 1.5 kilograms.

The right anatomical lobe is six times greater in size than the left. [25]

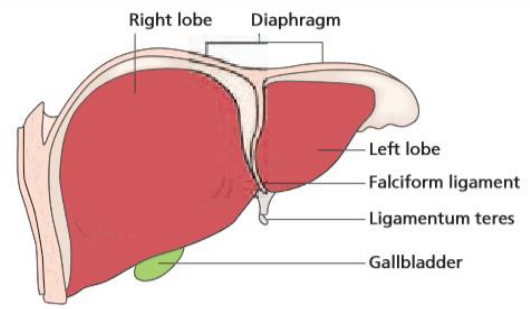



**Figure A- Anterior view of liver**

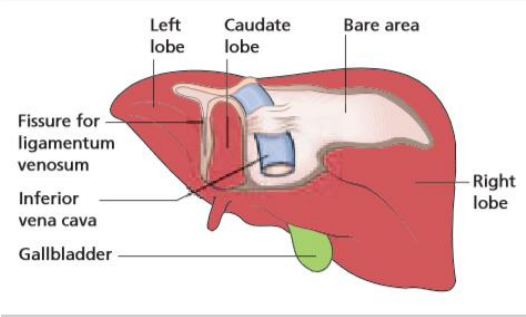



**Figure B- Posterior view of liver**

The right and the left hepatic lobes are of almost equal size and are divided by the Cantlie line. It is a plane which goes through the bed for the gallbladder and the notch for the inferior vena cava.[26,27]

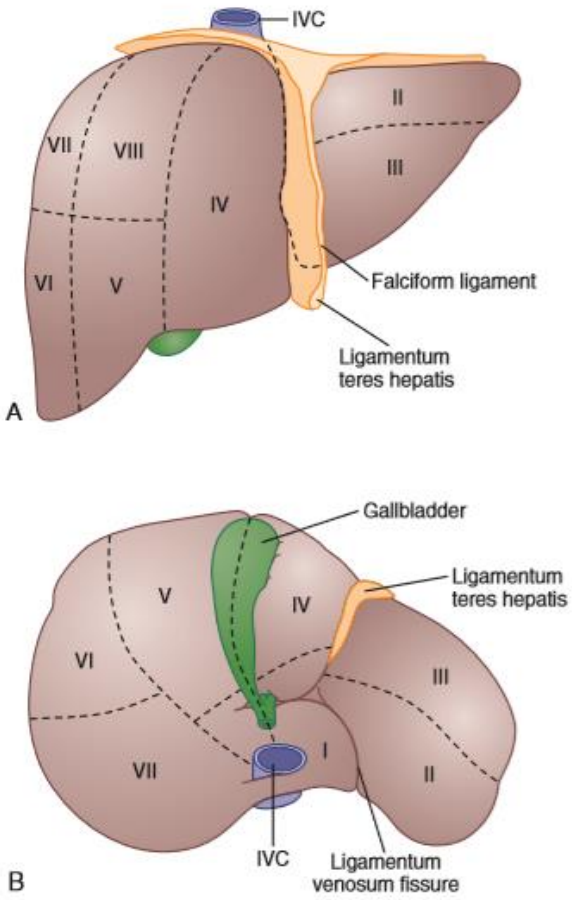



**Figure C- Segmental anatomy of liver based on Couinaud terminology**

The liver is also functionally separated into right and left lobes, based on arterial blood supply, portal venous blood supply, biliary drainage, and hepatic venous drainage. The most commonly accepted system used to divide the liver is based on the distribution of portal vein and bile duct. The liver is divided into 8 segments based on this system.[27,28]

The liver has dual blood supply. The superior mesenteric vein and splenic vein join to form the portal vein, which divides into the right and left branches. The celiac trunk gives rise to the hepatic artery. About three quarters of the liver's blood supply is provided by the portal vein and the rest by the hepatic artery. [29,30]

There are small veins accompanying the ligamentum teres, which function by connecting the portal vein with the veins around the umbilicus. These veins become prominent in portal hypertension and are then called 'caput medusae'. [34]

Another group of lymphatics goes along with the inferior vena cava to go into the thoracic cavity and terminate at the intrathoracic part of inferior vena cava.[31]

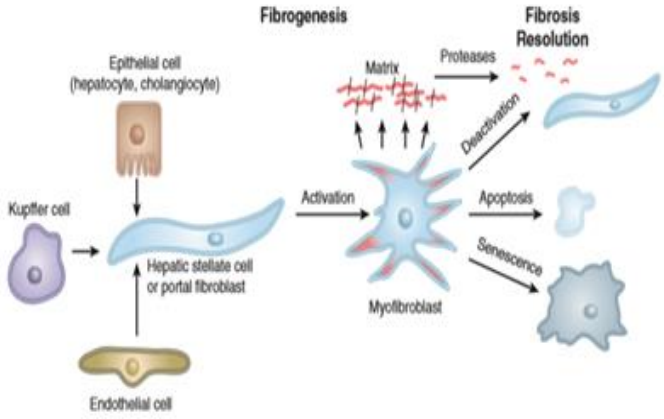
The liver is fully enclosed with peritoneum, excluding three sites. These include the bare area of liver where it comes in contact with the diaphragm, this area lies to the right of the inferior vena cava fossa. The other areas are the fossae for the inferior vena cava and gallbladder. There are two factors which work to ensure that the liver stays in its position. One is the peritoneal ligamentous attachment and the other is the tone of the abdominal muscles which provide the right amount of intraabdominal pressure.[31,32]

**PATHOGENESIS OF CIRRHOSIS**

Various chronic liver diseases finally result in the pathology of liver cirrhosis. Whatever the cause of cirrhosis, there are a few criteria required to diagnose the pathology-these include degeneration and death of hepatocytes, replacement of liver parenchyma by fibrosis and regenerative nodules, and loss of liver function[32,34].

All the liver cells are involved in the pathogenesis of liver cirrhosis, both parenchymal and non parenchymal cells. The hepatic sinusoids are lined by three different non parenchymal cells: liver sinusoidal endothelial cells, Kupffer cells, and hepatic stellate cells. [36]

The cell most commonly implicated in the formation of cirrhosis is stellate cell. The stellate cell is activated into a myofibroblast by the action of inflammatory cytokines and this process leads to collagen deposition, which is the main component of cirrhosis of liver .[33]




Schematic overview of the pathogenesis of fibrosis and reversal of fibrosis in cirrhosis. Epithelial cell injury in combination with cytokine release by Kupffer cells and paracrine molecule release by sinusoidal endothelial cells leads to activation of hepatic stellate cells (or portal fibroblasts) into myofibroblasts. Reversal of fibrosis results from myofibroblast deactivation, apoptosis, or senescence. Matrix proteases can also achieve fibrosis resolution (see text for details).

**Figure D – Pathogenesis of cirrhosis**

They are also called Ito cells and the main function is to store Vitamin A and other retinoids.

Kupffer Cells are reticuloendothelial cells and they are activated during inflammatory crisis[34] .

Hepatocytes also play a significant role in the pathogenesis of cirrhosis. Injured hepatocytes release free radicals and accelerate the fibrogenic actions of myofibroblasts. In short, various cells take part in the process of fibrogenesis and cirrhosis but the stellate cell, with its immense capacity to produce collagenous matrix, is the most important. [35,59,60]

## ETIOLOGY

Chronic liver disease (CLD) encompasses a range of liver disorders where the inflammation and necrosis have been progressing for over atleast 6 months.[57,58]

**Table I-Common causes of cirrhosis[32]**

| | |
|---|---|
| Viral | Hepatitis B Virus<br>Hepatitis C Virus<br>Hepatitis D Virus |
| Autoimmune | Autoimmune hepatitis Primary Biliary Cirrhosis<br>Primary Sclerosing Cholangitis |
| Toxic | Alcohol<br>Arsenic |
| Metabolic | α1-Antitrypsin deficiency<br>Galactosemia<br>Glycogen storage disease<br>Hemochromatosis<br>Nonalcoholic fatty liver disease<br>Wilson disease |
| Biliary | Atresia<br>Stone<br>Tumor |
| Vascular | Budd-Chiari syndrome<br>Cardiac fibrosis |

| | |
|---|---|
| Genetic | Cystic Fibrosis<br>Lysosomal acid lipase deficiency |
| Iatrogenic | Biliary injury<br>Drugs: high-dose vitamin A, methotrexate |

**ALCOHOL INDUCED LIVER DISEASE**

This entity deserves a special mention as it contributes to more than half of all the mortalities due to cirrhosis. Initial response to alcohol is fatty liver, and if alcohol intake is continued, there is progress into alcoholic hepatitis and liver cirrhosis. Once the patient develops liver cirrhosis, it is irreversible and prognosis is poor in view of increased susceptibility to coagulopathy and encephalopathy. The quantity of alcohol consumption, female gender, concurrent HCV infection, genetic susceptibility and presence of fatty liver are risk factors for developing alcohol induced liver injury. Pentoxifylline or glucocorticoids can be used depending on the discriminant function. These patients are not ideal transplant candidates due to the increased surgical risks. [32]

**CLINICAL FEATURES**

**Symptoms** —During the initial stages of the disease, patient may be asymptomatic. Gradually, they develop symptoms of fatigue, loss of appetite, nausea, vomiting. Jaundice is a common symptom which brings the patient to the hospital. Other complaints encountered commonly are ascites, pedal edema, hematemesis, melena. Ascites, though commonly explained by portal hypertension, can also happen in its absence. Once patient develops ascites, spontaneous bacterial peritonitis should be expected and appropriate diagnostic and therapeutic steps should be taken, especially if patient develops abdominal pain or fever in the presence of ascites. Hematemesis and melena are because of variceal bleeding seen in portal hypertension. Low

platelets and coagulopathy further worsen the intensity. Patients may also come with altered sensorium due to hepatic encephalopathy although this happens in later stages of the disease. Early stages of hepatic encephalopathy may manifest as only alteration of sleep cycle with patients sleeping more in the daytime and less at night. Few patients develop hepatopulmonary syndrome (HPS) characterized by difficulty in breathing in the sitting position. Hepatorenal syndrome (HRS) is a diagnosis of exclusion which should be suspected if patients complain of decreased urine output.[20,21]

**Signs**: Icterus, loss of pubic and axillary hair, abdominal distension, pedal edema, gynecomastia, parotid enlargement, caput medusa, flapping tremors, Dupuytren's contracture, leuconychia, palmar erythema, testicular atrophy are the signs that should be looked for. Alcoholic liver disease typically has parotid enlargement. Gynecomastia, loss of axillary hair, testicular atrophy are due to the hyperestrogenemia seen in these patients.[20,47,48]

## NATURAL HISTORY OF DISEASE

Cirrhosis may be classified broadly as compensated or decompensated. Decompensated cirrhosis is regarded as the occurrence of one or more of variceal hemorrhage, ascites, encephalopathy, jaundice, or hepatocellular carcinoma. Most deaths in patients with cirrhosis occur due to hepatic decompensation; however, in the compensated stages, the most common cause of death is cardiovascular disease, followed by stroke, malignancy, and renal disease[32]. Complications of portal hypertension, hepatocellular carcinoma (HCC), and sepsis are the usual causes of mortality in patients with decompensated cirrhosis.[44]

## DIAGNOSIS

Laboratory tests —

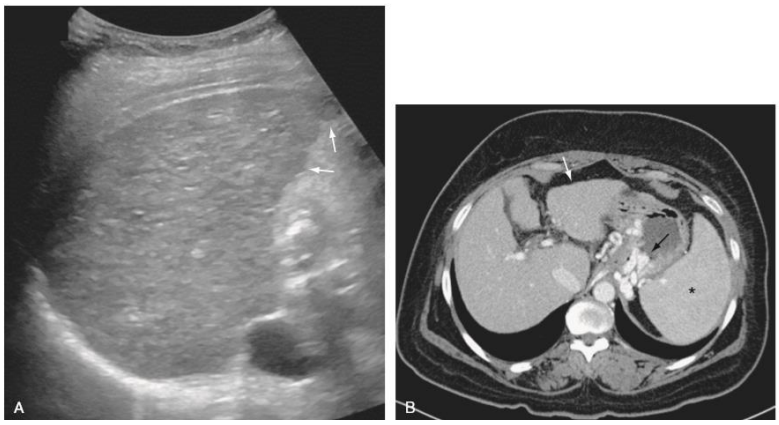


**Figure E-i) USG showing heterogenous parenchyma with nodularity**

**ii) CT scan showing nodular left lobe of liver**

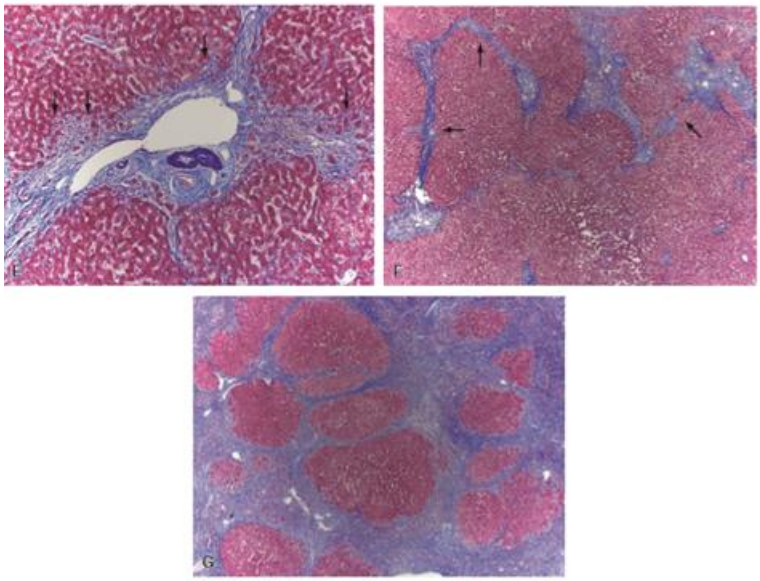


**Figure F- Periportal fibrosis – Histology**

Biochemical tests done in liver disease are hepatic enzymes (SGOT, SGPT, ALP, GGT), total and direct bilirubin, serum albumin, serum globulin and total proteins, along with prothrombin time. Serum albumin and prothrombin time are indicators of synthetic function of liver.

Alcoholic hepatitis patients may have raised SGOT as compared to SGPT. The opposite is seen

in viral hepatitis. Complete blood counts may show anemia and thrombocytopenia mostly due to hypersplenism. Upper gastrointestinal endoscopic screening is advisable to check for esophageal varices. Hepatic venous pressure gradient may also be measured if varices are present. Ultrasound of the abdomen may show ascites, altered echotexture of liver, splenomegaly. and portosystemic collaterals. Ascitic fluid tapping should be done and fluid analysed for total count, differential count, fluid protein, albumin. If the number of neutrophils in the ascitic fluid is more than 250 cells/ cu mm, a diagnosis of spontaneous bacterial peritonitis is made.[53] The serum ascitic albumin gradient also is helpful. When it is greater than 1.1, portal hypertension is the most likely cause of the ascites.[39,40]

The diagnostic sensitivity of either biopsy or sonography is less than 90% (ultrasound, 87%; liver biopsy, 62%), but it has been proposed that ultrasound be done before liver biopsy is performed.[38,45]

Elastography – Increasing scarring of the liver is associated with increasing "stiffness" of the tissue. This is one of the methods that have been developed to assess liver stiffness.

**CHILD PUGH SCORE**

Child Turcotte Pugh score was initially formulated by Child and Turcotte to assess the preoperative and perioperative complications that could arise in portal hypertension patients undergoing shunt surgery for esophageal varix bleeding. Previously, Child–Pugh score included ascites, hepatic encephalopathy (HE), nutritional status, total bilirubin, and albumin. Pugh et al included PT(INR) and excluded nutritional status. Serum albumin is an indicator of the synthetic function of the liver and its levels are reduced in chronic liver disease.[50,51,52] Hypoalbuminemia can also be seen in other conditions like protein losing enteropathies and nephrotic syndrome.

Raised prothrombin time in liver disease is an effect of the altered synthesis of the coagulation factors namely factors II, VII, IX and X.[55] Raised bilirubin, especially direct bilirubin is an indicator of liver disease. There is no direct correlation between serum bilirubin and severity of liver disease.[56] But, its value has been found to be significant in a few conditions like viral hepatitis, where the higher the bilirubin, the higher the degree of hepatocellular damage.[41]

CRITERIA FOR CHILD-TURCOTTE CLASSIFICATION

| Group designation | A | B | C |
|---|---|---|---|
| Serum bilirubin[a] (mg·%) | Below 2.0 | 2.0–3.0 | Over 3.0 |
| Serum albumin (gm·%) | Over 3.5 | 3.0–3.5 | Under 3.0 |
| Ascites | None | Easily controlled | Poorly controlled |
| Neurological disorder | None | Minimal | Advanced "coma" |
| Nutrition | Excellent | Good | Poor, "wasting" |

**Table II- Original Child – Turcotte classification**

The following table of modified Child Pugh Classification was used in our study.

| Factor | Points | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| Serum bilirubin (mg/dL) | <2.0 | 2.0-3.0 | >3.0 |
| Serum albumin (g/dL) | >3.5 | 3.0-3.5 | <3.0 |
| Prothrombin time | | | |
| Seconds prolonged | <4 | 4-6 | >6 |
| INR | <1.7 | 1.7-2.3 | >2.3 |
| Ascites | None | Easily controlled | Poorly controlled |
| Hepatic encephalopathy | None | Minimal | Advanced |

**Table III-Modified Child- Pugh classification**

**Management of Hepatic encephalopathy**: Hepatic encephalopathy is treated using osmotic laxatives like lactulose which alter the gut pH along with helping to sterilize the gut. This helps to convert ammonia to ammonium which is excreted through feces thus ensuring that ammonia does not reach the brain. Patients who have had hepatic encephalopathy must be put on antibiotics usually norfloxacin to prevent infections which may further precipitate hepatic encephalopathy.[64] In addition to infections, other factors which precipitate hepatic encephalopathy have to be prevented. These include electrolyte abnormalities, use of sedatives and dehydration.[63] Anything that increases the portosystemic shunt can lead to hepatic encephalopathy, hence even treatment modalities like TIPPS should be cautiously undertaken.[6,62]

**Management of Portal Hypertension**: Primary prophylaxis of variceal bleeding, management of acute bleeding and prevention of rebleeding are the main objectives. For preventing variceal bleeding, it is necessary to screen all known patients of cirrhosis by upper gastrointestinal endoscopy. Once esophageal varices are identified, they are either considered for medical line of management or endoscopic variceal ligation (EVL) if varices are larger than 5 mm. Non specific beta blockers like propranolol and nadolol are preferred. Once they undergo variceal ligation, they are subjected to repeat endoscopies every one to two years. Patients with an acute bleeding episode are first managed to stabilize their vitals by maintaining their airways and circulation. Adequate amount of packed RBCs are transfused. They are started on drugs like somatostatin, terlipressin or vasopressin. They help to prevent gastrointestinal bleeding by causing splanchnic vasoconstriction. These patients may require fresh frozen plasma or platelets as PT(INR) and platelet counts are often deranged in liver disease patients. Once vitals are managed, gold standard of therapy is EVL or sclerotherapy. Ligation is done from distal to proximal. EVL has fewer complications than sclerotherapy. Even though its use in practice has not been advocated

recently, the Sengstaken Blakemore (SB) tube can be used to arrest severe, acute bleeds especially when the site of bleeding cannot be identified in a timely manner.[42,45]

## ASCITES

Ascites is defined as fluid in the peritoneal cavity. The commonest cause is liver disease. Mechanisms which lead to fluid accumulation are many, including hypoalbuminemia, fluid retention due to increased RAAS activation, lymphatic obstruction. Mild ascites may not be detected clinically. Shifting dullness may be demonstrated in clinically significant ascites and tense ascites may show presence of fluid thrill. The initial management includes fluid and salt restriction and use of diuretics. Commonly used diuretics are spironolactone and furosemide. A maximum of 160 mg of furosemide and 400 mg of spironolactone can be given. Contraindications are hepatic encephalopathy and renal dysfunction. Those who do not respond to these maximal doses are classified as refractory ascites. Treatment for this entity is complicated. Large volume paracentesis, i.e, removal of more than 4 litres of peritoneal fluid can be attempted. But this carries a risk of complications, primarily Type 1 hepatorenal syndrome. If undertaken, 10 grams of albumin should be transfused for every litre of peritoneal fluid removed.[46]

## SERUM PROLACTIN AND LIVER DISEASE

Prolactin is synthesized in the lactotropes of the anterior pituitary gland. The main function of prolactin is to induce and maintain lactation. Hyperprolactinemia can be seen in pituitary adenomas, pregnancy, lactation, chronic kidney disease, hypothyroidism, cirrhosis of liver. Certain drugs like atypical antipsychotics and metoclopramide block the dopamine receptors and

cause raised prolactin levels. Normal adult serum prolactin levels are about 10–25 μg/L(ng/ml) in women and 10–20 μg/L(ng/ml) in men. Prolactin secretion is pulsatile, with the highest secretory peaks occurring during rapid eye movement sleep. Peak serum prolactin levels (up to 30 μg/L) occur between 4:00 and 6:00 a.m.[72]

Circulating oestrogens are elevated in liver cirrhosis due to an increased peripheral aromatization of testosterone via androstenedione and to a lesser extent through a decreased elimination by the liver. These oestrogens stimulate prolactin release by interfering with the dopamine secretion from the hypothalamus, and through a direct effect on the anterior pituitary.

Decompensated liver function leads to a change in the type of amino acids entering the central nervous system. Circulating concentrations of aromatic amino acids have been found to increase leading to an increase in the synthesis of false neurotransmitters such as octopamine and phenylethanolamine. These false neurotransmitters may inhibit the dopamine release contributing to hyperprolactinemia.[69,70]

**RELEVANT STUDIES**

Pravin Prabhu et al, conducted a study on 100 patients of liver cirrhosis in Madurai medical college in 2017-2018 to correlate the serum prolactin level with the CHILD-PUGH score to assess the severity of cirrhosis of liver. The mean prolactin value was 56ng/ml in patients with gross ascites ; and in patients with grade 3 or 4 oesophageal varices it was around 55 ng/ml and 58 ng/ml respectively. Mean prolactin value was observed to be 8.0, 26 and 56 ng/ml in Child Pugh Class A ,B and C respectively and it was found to be positively correlating with the severity of the disease. In patients with and without encephalopathy, mean prolactin value was found to be 56ng/ml and 8ng/ml, respectively. Thus, prolactin level and presence of hepatic

encephalopathy were seen to have a positive correlation. Also, there was a direct relation between the clinico-biochemical severity of the disease and morbidity. Thus, prolactin levels were found to indicate the severity of disease. Normal circadian rhythm of prolactin secretion is found to be altered in liver disease. Dopamine levels are difficult to measure, therefore prolactin levels were assayed and this was considered as an indirect measure of dopamine levels in blood. Increasing prolactin levels were seen to have a rising trend as the Child-Pugh score increased, thus endorsing the routine use of prolactin levels as a marker in hepatic cirrhosis. They concluded that prolactin levels were significantly correlating with liver disease intensity and may even help to foresee the complications that could arise in these patients. Thus, with further research, analyzing the prolactin level in chronic liver disease patients may ideally help to prevent these complications. [71]

In another study by Balakrishnan et al, (2017) 60 patients of liver cirrhosis were studied. Patients with chest wall radiation or trauma, history of chronic renal failure, patients with history of pituitary or thalamic disease and those on certain medications known to alter serum prolactin levels were excluded. 44 (73%) patients were found to have alcoholic cirrhosis, 5 (9%) were hepatitis B positive and 3 (5%) were hepatitis C positive. The complications of cirrhosis observed in the study were ascites in 53 (88.3%) patients, portal hypertension in 50 (83.3%), oesophageal varices (including portal gastropathy) in 39 (65%) with upper GI bleed in 22 (36.7%) patients, hepatic encephalopathy (grades 1-4) in 15 (25%) patients, spontaneous bacterial peritonitis in 5 (8.33%) patients and hepatorenal syndrome in 3 (5%) patients. 60 patients were divided into three Child Pugh Score Classes – A (score of 5-7), B (score of 7-9) and C (score 10-15). 6 (10%) patients were categorized as Class A, 24 (40%) patients were Class

B and 30 (50%) belonged to Class C. 44 (73.33%) of them had serum prolactin levels elevated above 19 ng/ml. The greatest prolactin level found was 60 ng/ml. Values greater than 35 ng/ml were seen in patients of Class C, Child Pugh, while normal serum prolactin levels were seen in all patients except one in those patients with Class A Child Pugh. In the 44 patients with elevated serum prolactin in our study; it was seen that all the patients with a serum prolactin level above 35 ng/ml were Child Pugh Class C. Thus, they concluded that serum prolactin levels can be instrumental as a useful prognostic indicator in patients with cirrhosis of the liver and that the serum prolactin level correlated well with the disease severity and the presence of complications.[1]

K. Sridharan et al,(2016) conducted a preliminary cross sectional study to compare the serum prolactin levels in patients with liver disease and normal adults. The study was conducted in Uttar Pradesh and included 70 patients with liver disease. There were 25 acute viral hepatitis patients, 15 of these had symptoms and signs of hepatic encephalopathy. Of the 35 patients with liver cirrhosis, 20 had hepatic encephalopathy features. 19 were Hepatitis B positive (13 with viral hepatitis and 6 with cirrhosis liver). 12 of these were Child Pugh A and 8 were Child Pugh B. Prolactin was observed to be increased in a patient with cirrhosis of liver regardless of presence of encephalopathy. But, among the patients with viral hepatitis, a noteworthy increase was observed only in patients with hepatic encephalopathy. Of 35 study participants with cirrhosis, 15 expired. A cut-off value of 50 ng/ml of serum prolactin was observed to predict the mortality. In patients with viral hepatitis and hepatic encephalopathy, 1 out of 4 with prolactin value of <50 ng/ml died while among those without any such features ($n$ = 21), 9 died ($P < 0.05$).

They opined that serum prolactin has a significant association with the severity of liver disease and it predicts mortality.[2]

R. Metwally et al, (2017) investigated 50 patients in a hospital in Egypt to assess the usefulness of prolactin as a biological marker in severity of liver cirrhosis. In their study, there was a statistically substantial correlation of prolactin with severity of cirrhosis and encephalopathy grading. There was a statistically major correlation with severity of cirrhosis and degree of ascites, prolactin level, albumin level, bilirubin level, prothrombin time and Child Pugh score. There was no major correlation with severity of cirrhosis and portal vein diameter, creatinine level, Sex or age. There were statistically very important differences found in the serum prolactin level and sex, statistically highly important differences were found in the serum prolactin level and hepatic encephalopathy grades and statistically major differences in the serum prolactin level and Child grades. As compared to no encephalopathy, grade 3 and grade 4 encephalopathy had higher levels of prolactin. Prolactin levels were higher in Child Pugh C as compared to Child Pugh B and Child Pugh A . By using Roc curve for serum prolactin level as a predictor for moderate and severe liver cirrhosis, it is found that at the cutoff point 18.8 ng/ml, the sensitivity is 67.74%, the specificity is 78.95, the positive predictive value (PPV) is 84%, and the negative predictive value ( NPV) is 60%. They came to the conclusion that prolactin levels showed positive correlation with the severity of liver disease, particularly in patients who had complications of liver cirrhosis like ascites and hepatic encephalopathy. Hence, raised prolactin could be used as a negative prognostic indicator of liver disease.[3]

C. Ress (2014) conducted a study on serum prolactin to assess the severity of liver disease in Austria. 35 patients belonged to Child Pugh A, 98 patients were classified as Child Pugh B, 45 patients were categorized as Child Pugh class C. Prolactin levels progressively became elevated as the Child Pugh class became more severe ($p<0.01$). Prolactin levels were also found to be higher in female gender than in male gender. Most of the patients had alcoholic liver disease(62 patients), NASH(32 patients), viral hepatitis patients (55 patients), autoimmune disorders (25 patients). They came to a consensus that hyperprolactinemia in CLD patients has to be evaluated as it is not commonly expected in patients without comorbidities or patients not on drugs altering prolactin levels.[4]

Daniel Seehofer et al, (2002) studied the pituitary hormone levels before transplant and postoperatively. ACTH, cortisol, FSH, GH, IGF-1, LH, estradiol, prolactin and testosterone levels were determined prior to and post liver transplantation. Prolactin values were normal before and after transplantation but there was a notable decrease in prolactin level in female patients three months after liver transplantation. No distinctions between patients classified as Child B and C were noted. After stimulation with TRH, prolactin values in male patients were significantly higher before liver transplantation than afterwards. Female patients had greater prolactin values post stimulation with TRH than in male patients. No significant changes of prolactin response to TRH stimulation were found in female patients after transplantation but results were not significantly different from the female control group. In this article, a successive global pituitary function test and a long term follow up of the gonadal axis after liver transplantation for chronic alcoholic and non--alcoholic liver disease were explained for the first time. In comparison to other studies, it was observed that endocrine changes in chronic liver

failure are indeed dependent on the grade of liver cirrhosis than on the underlying etiology. Various factors may lead to endocrine dysfunction in chronic liver disease. Progressive destruction of liver parenchyma can lead to impaired hormone synthesis. The portocaval shunt can cause hormonal disturbances by decreased catabolism of hormones like estrogen and also by decreased breakdown of metabolites that occur in liver failure. This was perceived to be the cause of hepatic encephalopathy. No correlation could be found between the degree of pituitary dysfunction and grade of hepatic encephalopathy. Pituitary hormones almost normalized after the patient underwent transplant. They also concluded that peripheral endocrine parameters could be normalized by liver transplantation.[10]

Vellisaris et al, (2008) conducted a study with an objective to investigate the pituitary hormone and circadian rhythms of melatonin. Out of the 26 patients with liver cirrhosis included in the study, 13 patients were admitted in the hospital for other causes and were taken as controls. Child Pugh score was estimated in all patients to assess the severity of liver disease. EEG, MRI, detailed neurological system examination were undertaken in all these patients. In addition, pituitary hormone levels, melatonin levels and routine biochemical blood investigations were also done. In the Brain MRI, basal ganglia structural changes were looked for. It was observed that pituitary hormone and melatonin diurnal rhythms were changed in liver cirrhosis patients even though they did not develop clinical encephalopathy yet. But, basal cortisol levels were detected to be low and this also incidentally correlated with the EEG and MRI Brain findings. Melatonin was the only hormone whose values correlated with the degree of liver cirrhosis. Physical examination did not show any asterixis or tone abnormalities in the cirrhosis patients. 2 patients had presence of ascites, 14 had splenomegaly and 8 had esophageal varices on

endoscopy. Prolactin levels did not show noteable differences during the daytime in the control group. On the other hand, prolactin levels were found to be lower in the afternoon compared to morning and night levels. Melatonin levels were higher in the morning as compared to the afternoon and evening values. Brain MRI showed abnormalities in basal ganglia in18 of the 26 cirrhotic patients. EEG showed mild disturbances in 7 individuals, moderate changes in 3 individuals and severe changes in 1 individual of the cirrhotic group. There was no significant correlation of prolactin or TSH levels with the Child-Pugh score. They found a correlation between cortisol levels and Child Pugh score and between melatonin levels and Child Pugh score. They came to the conclusion that circadian hormone variations happen early in cirrhosis and could be correlated with disease severity. These disturbances could be an early sign of incipient clinical hepatic encephalopathy.[17]

Zietz et al,(2001) aimed to study the anterior pituitary function and its correlation to the Child Pugh score in males with virus related and alcohol related cirrhosis of liver. It was a case control study where 52 male cirrhotics were matched with 50 controls. 26 patients belonged to CTP class A, 16 belonged to CTP class B and 10 belonged to CTP class C. 57.6 % of CTP A, 31.1 % of CTP B and 20% of CTP C had normal cortisol response to CRH stimulation test. Levels of IGF 1 were lesser in cirrhotics. Prolactin levels were higher in liver cirrhosis group, especially in CTP C group. LH levels were found to be elevated in CTP class A and CTP class B. FSH levels were same in all classes. Differences of basal prolactin to prolactin after TRH stimulation were almost similar in both groups.

In 7.7% of CTP class A patients, 18.7% of CTP Class B patients, 40% of CTP Class C patients and 8% of controls, prolactin increased more than three times after TRH stimulation. This confirms the relationship between hypothalamic dysfunction and severity of liver disease.

Prolactin is basically released in response to the stimulus of stress and is inhibited by dopamine. This study opined that CTP score is helpful to determine the status of endocrine axes in cirrhosis.[7]

Morgan et al, (1978) attempted to study the relationship between serum prolactin level in liver disease and gynecomastia. 150 liver cirrhosis patients were taken out of which 78 had alcohol liver disease and 72 were non alcohol related. The non-alcoholic group consisted of 24 Primary biliary cirrhosis patients, 18 HBsAg negative hepatitis patients, 14 cryptogenic cirrhosis patients, 4 haemochromatosis patients , 3 HBsAg positive liver disease patients, and 13 were due to other causes. The average serum prolactin in the control was 183 mU/I and did not differ much between males (178 mU/l) and females (190 mU/l). None of the patients in this trial were taking drugs known to interfere with the prolactin level. 18 of the 150 patients had elevated prolactin levels. There was no difference in the prolactin levels between the alcoholic(13%) and nonalcoholic groups(11%). Similarly, prolactin levels in male and female groups were also similar. 72 patients in the non alcoholic liver disease group were further seen to have precirrhotic (19) disease and cirrhotic disease(53). Prolactin levels were seen to be almost similar in precirrhotics(5%) and cirrhotics (13%). 78 patients with alcohol liver disease were further seen to have fatty change (23), alcoholic hepatitis (19) and cirrhosis(36). 19 out of 84 patients were found to have gynecomastia. The incidence of gynaecomastia in the alcoholics (14) was similar to that in the non alcoholics (5). There was no direct correlation between serum prolactin and presence of gynecomastia. They decided that the exact etiology of the hyperprolactinaemia in these patients and its clinical consequences needed further research.[16]

Gonzales et al, (2007) proposed to study the male gonadal function, prolactin levels and lactotroph population in an experimental model of cirrhosis. Adult male rats were subjected to carbon tetrachloride to induce cirrhosis. 8 cirrhotic rats were put into the case group and 20 rats were put into the control group. Prolactin, LH and FSH were assayed. No important variation in mean proportion of lactotrophs was found. Mean prolactin level was 20.37ng/ml in the case group, whereas it was 19.31ng/ml in the control group. Estradiol levels were 19.5ng/ml in the case group and 14.6ng/ml in the control group. Testosterone levels were 122ng/dl and 138ng/dl in the case and control group, respectively. LH levels in controls was found to be 1.53 ng/ml in the case group and 1.58 ng/ml in the control group. FSH levels were 18.27 ng/ml in the case group and 19.11 ng/ml in the control group. Thus, they came to the conclusion that hyperprolactinemia and hyperestrogenemia associated with cirrhosis do not equate to lactotroph hyperplasia and they suggested that a hypothalamic disorder could be the cause for hypogonadism in these animals.[8]

Mowat et al, (1976) studied the hypothalamic-pituitary-gonadal function in adult males with cirrhosis of liver. 37 adult males with cirrhosis of liver were studied, out of which 25 were alcoholics. Out of the 12 non alcoholics, 5 had crytogenic cirrhosis, one patient had chronic granulomatous liver disease. and 4 had hemochromatosis. These patients were in the age group of 22-74 years. Blood samples for hormonal studies were taken between 9 and 10 am. Cirrhotic patients were found to have significantly decreased testosterone levels and thus, reduced spermatogenesis. Basal levels of LH and FSH were nearly normal. 14 cirrhotic patients were studied for the pituitary's ability to secrete LH and FSH after stimulation with exogenous GnRH. 7 of these patients also had gynecomastia., out of which 4 had an increased response of LH

which implies Leydig cell failure. Patients in whom gynecomastia was absent had nearly normal FSH responses to GnRH stimulation. 6 patients with gynecomastia gave an evidently exaggerated response of FSH and they also had reduced spermatogenesis. The pituitary cells can therefore react to GnRH and the Leydig cells also respond to exogenous gonadotrophin. If the basal FSH and LH were normal, low testosterone and defective spermatogenesis were attributed to gonadal defects and abnormal hypothalamic and pituitary function. Leydig cells also responded to HCG stimulation by increasing more testosterone. As such abnormalities can also be found in non alcoholic cirrhotics, alcohol cannot be blamed for the endocrine changes of chronic liver disease. Also, as the pituitary is responding normally to stimuli, it indicates that these patients have some degree of hypothalamic dysfunction.[9]

McClain et al, (1981) conducted a study to assess hyperprolactinemia in portosystemic encephalopathy. 21 patients with alcoholic live disease and clinical evidence of portosystemic encephalopathy were included in the study. 19 had liver disease proven by liver biopsy, 17 of whom had liver cirrhosis and 2 had only alcoholic hepatitis. They used Parsons Smith criteria to grade the hepatic encephalopathy from Grade 1 to 4. 15 patients with active enteritis and normal liver function were put in the control group. Fasting prolactin was measured by a radio immune assay. In addition, liver function tests and prothrombin time were also measured. Cirrhotics without hepatic encephalopathy had moderately elevated prolactin (18.7) with a p value of 0.05. Cirrhotics with hepatic encephalopathy had significantly raised prolactin levels (39.2) and a p value $<0.01$ as compared to the patients in the control group. The cases with portal systemic encephalopathy were divided into 2 groups, those having slightly raised prolactin (12) and those having markedly elevated prolactin(9). The higher the prolactin levels, the greater the

derangement in levels of serum albumin, PT(INR), serum bilirubin. Serum prolactin level also correlated with the mortality of the patients in 100% of the population. They opined that patients with chronic alcoholic liver disease especially those with hepatic encephalopathy had altered neurotransmitter function. Patients with higher prolactin levels also had more grave prognosis. They suggested that serum prolactin could be used to monitor severity in patients with hepatic encephalopathy. Therefore, they hypothesized that encephalopathy patients with higher prolactin levels may benefit from drugs that correct the neurotransmitter levels. They decided that prolactin could be an indicator for therapeutic intervention aimed at correcting neurotransmitter abnormalities in dysfunction of hypothalamic pituitary axis seen in alcoholic cirrhotics.[11]

Arafa et al,(2012) described the features of hormonal disturbances in cirrhotic patients with hepatic encephalopathy. The study was conducted on 75 cirrhotic patients with hepatic encephalopathy and 50 cirrhotics without hepatic encephalopathy. Biochemical tests, endoscopy findings, sonographic reports were used to diagnose liver cirrhosis. Patients with neurologic disorders, on antidepressants and sedatives or other drugs causing hyperprolactinemia were excluded from the study. The participants were then assessed according to their Child-Pugh score and classified into Child A, B and C. In addition to regular blood investigations, serum albumin, INR, serum bilirubin, serum prolactin, total T3, cortisol and TSH were evaluated. 40 patients belonged to Child A and B each, 45 patients belonged to Child C. Cortisol, total T3 levels were found to be considerably less in hepatic encephalopathy patients on comparison with patients without encephalopathy. Prolactin concentration was markedly increased in patients with hepatic encephalopathy as compared to those without. In addition, prolactin levels increased progressively from Grade 1 to Grade 4 of hepatic encephalopathy. TSH levels showed no

substantial variation. Serum T3, serum cortisol positively correlated with serum albumin and prothombin time. Serum prolactin showed negative correlation with serum albumin and prothrombin time. Prolactin level was 14 ng/ml in Grade 1 and 2 of hepatic encephalopathy, 22 ng/ml in grade 3 of encephalopathy, and 35 ng/ml in grade 4 of hepatic encephalopathy. There was a consistent 24 hour elevation in serum prolactin level in these patients thus demonstrating that cirrhotic patients do not have diurnal variation of serum prolactin levels. They concluded that these hormonal disturbances may help to predict impending hepatic encephalopathy, thus enabling physicians to take steps to avert grave consequences.[6]

Koller et al,(2009) desired to study the effect of prolactin levels and how it varied along with the adverse events in cirrhotic patients. 90 patients mostly males were enrolled and followed up for a period of 434 days. Routine blood investigations were done, ascites and hepatic encephalopathy were looked for. Complications such as portal hypertension, gastrointestinal varix bleeding, hepatorenal syndrome, and death were documented. 16.7 percent of the patients were detected to have raised serum prolactin. These patients were also found to have higher Child Pugh scores, Meld scores and more advanced grades of hepatic encephalopathy. Higher prolactin levels were correlated with events such as ascites, coagulopathy, and hepatic encephalopathy. There was a positive correlation of prolactin values (above 10.5 microg/ml) and hepatic encephalopathy ($p<0.05$). Prolactin levels >11.91 microg/ml were also shown to predict death. Thus, they opined that basal prolactin levels may be used as an unconventional marker of hepatic encephalopathy in cirrhotic patients.[66]

Mukherjee et al, conducted a study titled 'Observation of serum prolactin level in hepatic cirrhosis' in 1991. They measured serum prolactin in patients of liver cirrhosis. Serum prolactin was estimated to be high, around 27.2 ng/ml in males and 38.4 ng/ml in females. P value was significant(<0.05). Patients with portal systemic encephalopathy had markedly elevated serum prolactin than those without encephalopathy ($p < 0.05$). Those with higher values on admission also had increased mortality($p<0.01$). All the hepatic parameters also showed a correlation with prolactin levels. Thus, they concluded that serum prolactin had diagnostic and prognostic values in clinical and subclinical hepatic encephalopathy.[13]

In 2007, Sanjay Kumar et al, attempted to predict large esophageal varices in cirrhotic patients using clinical, biochemical and imaging parameters. 101 patients of liver cirrhosis with no previous episodes of gastrointestinal bleeding were included in the study. Cirrhosis was diagnosed with the help of blood investigations, clinical characters and imaging. Patients were evaluated for ascites, hepatic encephalopathy, serum bilirubin and serum albumin. Etiology of liver cirrhosis was also worked up. Tests for HBsAg, HCV, ceruloplasmin, autoantibodies, iron studies were also undertaken. Ultrasonography of the abdomen was done to estimate liver and spleen size, ascites and presence of portosystemic collaterals. All patients were taken up for upper gastrointestinal endoscopy to asses presence of gastrointestinal or gastric varices. Grading for the varices was also done. 12 patients did not have esophageal varices at endoscopy, 43 were found to have small esophageal varices, and 46 were seen to have large esophageal varices. Gastric varices were seen in 15 patients.81 patients had ascites and 40 patients presented with hepatic encephalopathy. Platelet counts and size of the spleen could predict the presence of large esophageal varices. Using an equation which was derived for prediction, 65 of 95 patients were

correctly predicted to have or not have large esophageal varices. Basically, according to their study, a platelet count below 40,000/cumm could be considered to be a pointer towards large esophageal varices. Their study indicates that these independent variables may be used to predict large esophageal varices, thus preventing the need for screening endoscopies which are both costly and invasive.[14]

Corenblum et al, opined in 1989 that hyperprolactinemia in hepatic encephalopathy may be due to compromised central dopaminergic neurotransmission.

Ten patients with liver disease and hepatic encephalopathy (HE) and eight normal controls were included. Five of the 10 hepatic encephalopathy patients had hyperprolactinemia. The administration of L-dopa resulted in a fall of serum prolactin in all of the patients. Previous intake of Carbidopa, a peripheral decarboxylase inhibitor, did not alter the prolactin suppression by L-dopa in the normal patients or in those with normal basal prolactin levels. In the group with hyperprolactinemia, Carbidopa significantly subdued the response to L-dopa. Defective central neurotransmission, at least comprising the hypothalamic-pituitary dopaminergic system, may cause the hyperprolactinemia in Hepatic encephalopathy.[67]

# METHODOLOGY

## MATERIALS AND METHODS

### SOURCE OF DATA:

This study was conducted on 102 patients attending Medicine OPD and admitted in the wards and ICU of General Medicine at KLES Dr. Prabhakar Kore Hospital, Belgaum fulfilling the inclusion criteria, during January 2018 to December 2018.

**Inclusion criteria:**

1.Age >18 years

2.Patients clinically, biochemically and USG suggestive of liver cirrhosis

**Exclusion criteria:**

- Pregnant and lactating women
- Trauma to chest
- Cranial surgery/irradiation
- Chronic kidney disease
- Known patients of thyroid disease
- Herpes zoster
- Patients with history suggestive of raised intracranial pressure/ prolactinoma
- Patient on medications known to alter prolactin levels such as neuroleptics, tricyclic antidepressants, metoclopramide, domperidone, aldosterone antagonists, morphine, L-dopa, clomiphene citrate, tamoxifen.

### DATA COLLECTION

Informed consent was taken from all patients to be enrolled for the study. In all the patients relevant information was collected in a predesigned proforma. The patients were selected based

on clinical findings of liver disease, biochemical parameters and ultrasound abdomen. Prolactin level was measured in all the subjects enrolled in the study and it was correlated with Child Pugh score. In addition, patients were evaluated for the etiology of cirrhosis and the presence of various complications like portal hypertension, spontaneous bacterial peritonitis and hepatic encephalopathy.

**LABORATORY INVESTIGATIONS**

- All patients fulfilling inclusion criteria were subjected to a questionnaire and thorough clinical examination, to identify possible etiology of liver cirrhosis and to identify presence of complications of liver disease.
- Routine workup for chronic liver disease is done
- Complete blood counts, renal function tests
- Liver function tests including coagulation profile
- Serum prolactin at time of admission via radioimmunoassay
- Ascitic fluid analysis for glucose, proteins, cytology
- Upper gastrointestinal endoscopy
- Ultrasound abdomen including echotexture and size of the liver, splenic enlargement and portal vein diameter
- Hepatitis B Antigen (HBsAg) and anti Hepatitis C Virus (HCV) antibodies via ELISA method.
- The patients were then classified based on the modified Child Pugh scoring system and divided into Classes A, B or C based on the score obtained. The complications of

cirrhosis such as ascites, portal hypertension, oesophageal varices, hepatic encephalopathy, hepatorenal syndrome and spontaneous bacterial peritonitis were identified.

Sample size was calculated by the following formula:

N= 4PQ/D2 Where N=Sample size

P = Prevalence of the disease Q= 100- P

D = Absolute error taken as 12%of P

(P = 73; Q = 27; D^2=76.73)

Therefore, N=102. 73

Thus, the sample size of this study was taken as 102.

Sample Method : Cross-sectional Study,

All consecutive patients fulfilling the inclusion criteria were included in the study, statistical analysis was done by SPSS using descriptive analysis and chi-square test.

# RESULTS

## RESULTS

**Methods used:** Data analysis was done using R i386 3.5.1. Categorical variables are represented using percentages. Correlation between 2 variables are studied using Kendall tau. P-value <0.05 is considered as significant.

**Summary:**

Here 102 subjects of age group 49.46±12.15 years (range: 25-78) were considered for the study. Out of these, 93 were male and 9 were female subjects.

**Table 1: Distribution of subjects based on the age groups**

| Age group | Frequency | Percentage |
|---|---|---|
| **21-40** | 25 | 24.51 |
| **41-60** | 59 | 57.84 |
| **61-90** | 18 | 17.65 |

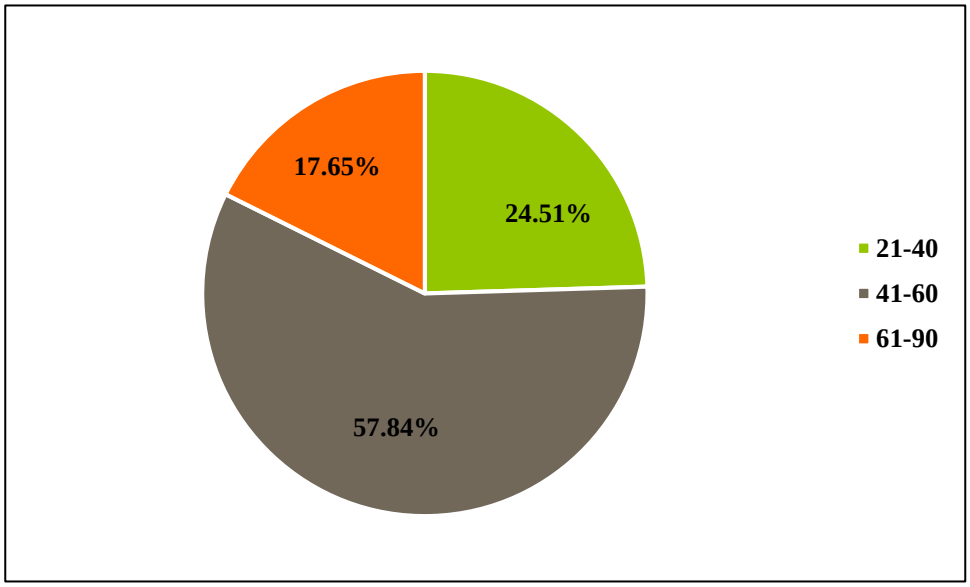



**Figure 1: Pie diagram for Age group**

From table 1, we observe that majority of subjects (57.84%) were in the age group “41-60 years” followed by “21-40 years” and 18(17.65%) subjects were in the age group “60-90 years”. The minimum and maximum age of subjects was 25 and 78 years respectively.

**Table 2: Distribution of subjects by gender**

| Gender | Frequency | Percentage |
|---|---|---|
| **Male** | 93 | 91.18 |
| **Female** | 9 | 8.82 |

93(91.18%) male subjects and 9(8.82%) female subjects were included in the sample.

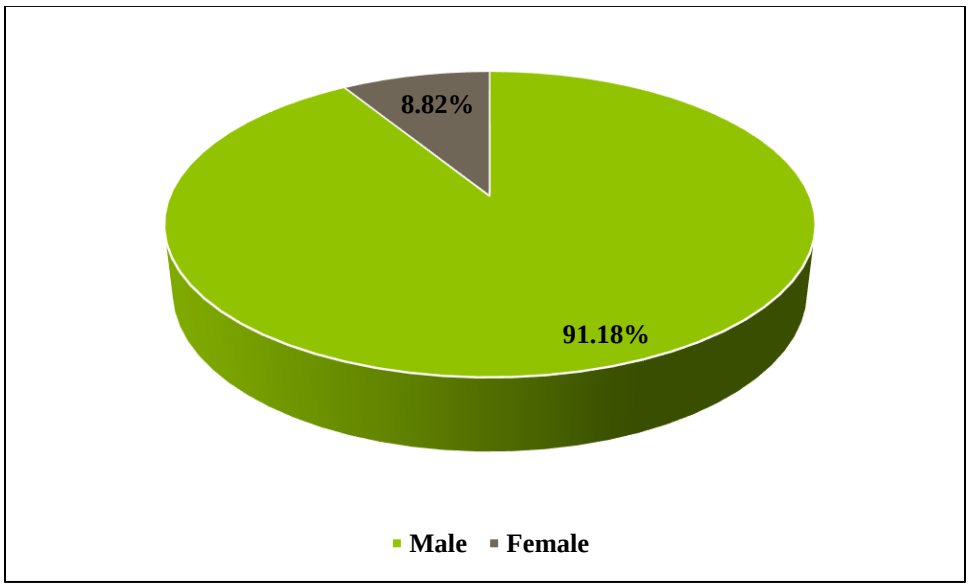



**Figure 2: Pie diagram for Gender**

**Table 3: Distribution of subjects based on diagnosis**

| Diagnosis | Frequency | Percentage |
|---|---|---|
| **ALD** | 80 | 78.43 |
| **HEP B** | 5 | 4.9 |
| **HEP C** | 2 | 1.96 |
| **NAFLD** | 12 | 11.76 |
| **UNKNOWN CAUSE** | 3 | 2.94 |

*Abbreviation: ALD: Alcoholic Liver Disease; HEP B: Hepatitis B; HEP C: Hepatitis C; NAFLD: Nonalcoholic fatty liver disease;*

From table 3, we observe that 78.43% of subjects in the sample were diagnosed with Alcohol liver disease followed by Nonalcoholic fatty liver disease in 11.76% patients, Hepatitis B in 4.9% patients. No obvious cause was seen in 2.94 % of patients. 1.96 % of patients were diagnosed with Hepatitis C.

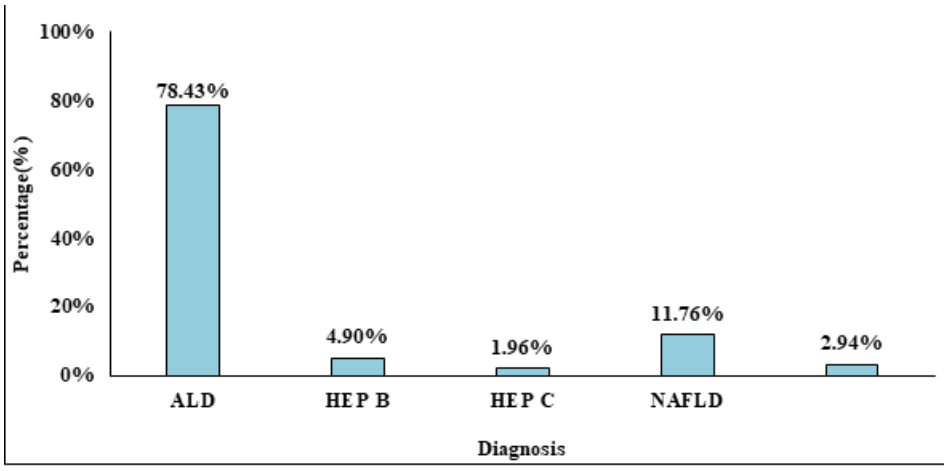



**Figure 3: Bar plot for Distribution of subjects based on diagnosis**

**Table 4: Distribution of subjects based on Child Pugh score.**

| **Child Pugh Class** | Frequency | Percentage |
|---|---|---|
| A | 8 | 7.84 |
| B | 35 | 34.31 |
| C | 59 | 57.84 |

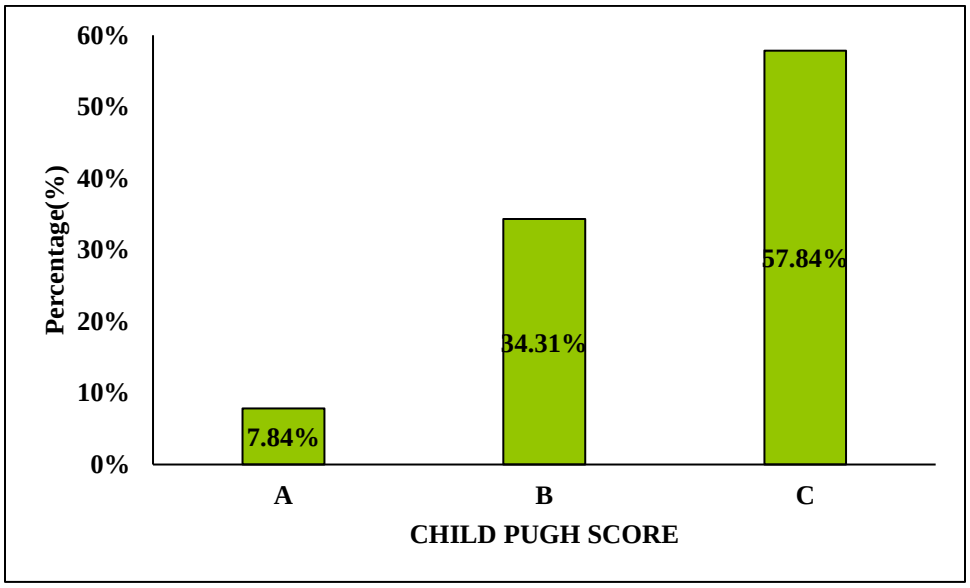



**Figure 4: Distribution of subjects based on CHILD PUGH score.**

From the table 4, we observe than majority (57.84%) of the subjects in the sample belonged to the Child Pugh class “C”, 34.31% of subjects belonged to the Child Pugh class “B” and remaining 7.84% of subjects belonged to the Child Pugh class “A”.

**Table 5: Distribution of subjects based on Bilirubin levels.**

| Bilirubin(mg/dl) | Frequency | Percentage |
|---|---|---|
| <2 | 13 | 12.75 |
| 2-3 | 34 | 33.33 |
| >3 | 55 | 53.92 |

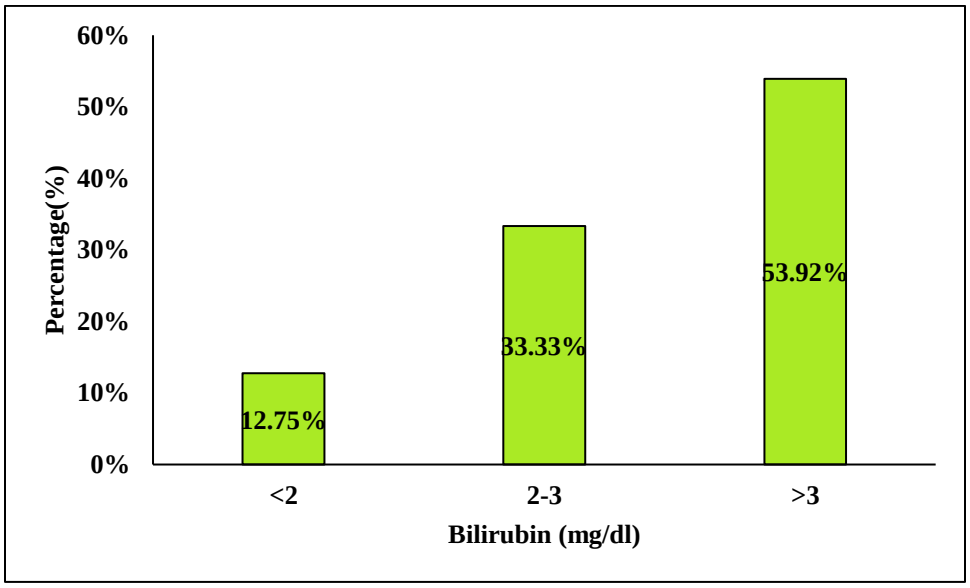



**Figure 5: Distribution of subjects based on Bilirubin levels.**

From table 5, we observe that 55(53.92%) subjects in the sample had bilirubin more than 3 mg/dl and 34 subjects had bilirubin in between 2mg/dl and 3mg/dl and 13(12.75) subjects had bilirubin less than 2 mg/dl. The average bilirubin in the sample was 8.11 mg/dl. The minimum bilirubin in the sample was 0.40 mg/dl while the maximum bilirubin was 50.74 mg/dl.

**Table 6: Distribution of subjects based on Albumin levels.**

| Albumin (g/dl) | Frequency | Percentage |
|---|---|---|
| <2.8 | 62 | 60.78 |
| 2.8-3.5 | 33 | 32.35 |
| >3.5 | 7 | 6.86 |

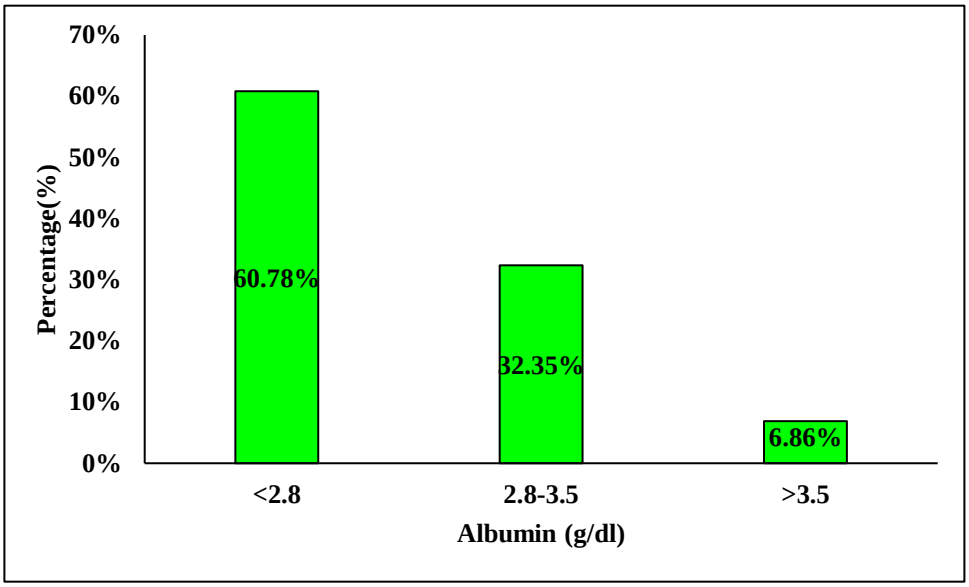



**Figure 6: Distribution of subjects based on albumin levels.**

From table 6, we observe that 60.78% of total subjects in the sample had albumin less than 2.8 g/dl, 33(32.35%) subjects in the sample had albumin in between 2.8 to 3.5 g/dl. Few (6.86%) of the subjects in the sample had albumin more than 3.5 g/dl. Mean Albumin in the sample was 2.63±0.63 g/dl.

**Table 7: Distribution of subjects based on INR.**

| INR | Frequency | Percentage |
|---|---|---|
| <1.7 | 44 | 43.14 |
| 1.7-2.3 | 28 | 27.45 |
| >2.3 | 30 | 29.41 |

Abbreviation: *INR: International normalized ratio*

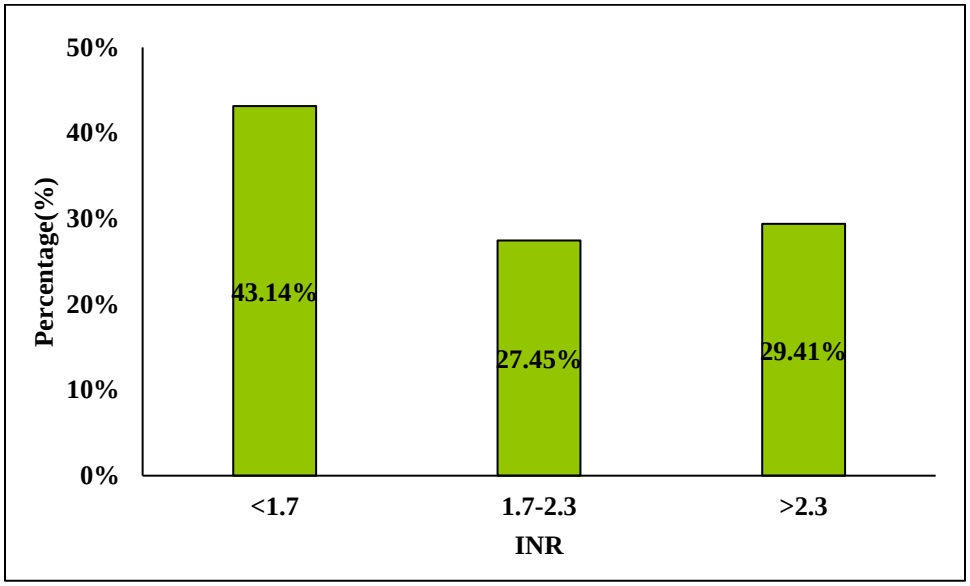



**Figure 7: Distribution of subjects based on INR value.**

From table 7, we observe that 43.14% of total subjects in the sample had international normalized ratio value less than 1.7 . 29.41% of subjects had international normalized ratio more than 2.3 and only 27.45% of subjects had INR in between 1.7 -2.3 .The mean INR value in the sample was 2.18±1.26 .

**Table 8: Distribution of subjects based on severity of ascites**

| Ascites degree | Frequency | Percentage |
|---|---|---|
| No Ascites | 42 | 41.18 |
| Easily Controlled Ascites | 54 | 52.94 |
| Poorly Controlled Ascites | 6 | 5.88 |

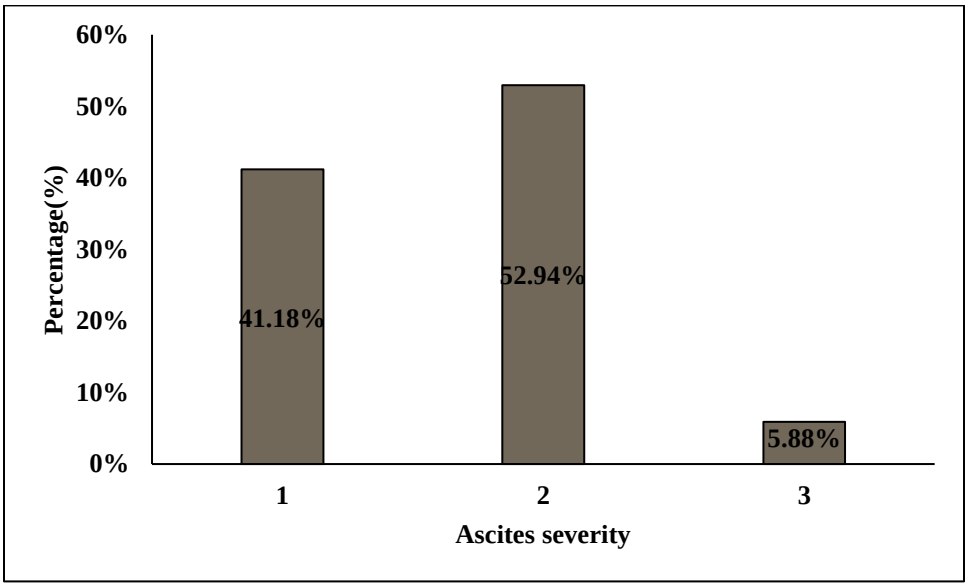



**Figure 8: Distribution of subjects based on severity of ascites.**

From table 8, we observed that, majority (52.94%) of the subjects had easily controlled ascites, which responded to diuretics, 41.8% patients who did not have ascites. The remaining 5.88% of the subjects had poorly controlled ascites, which did not respond to diuretics.

1=no ascites, 2= easily controlled ascites, 3=poorly controlled ascites

**Table 9: Distribution of subjects based on presence of hepatic encephalopathy.**

| Hepatic encephalopathy | Frequency | Percentage |
|---|---|---|
| **Yes** | 29 | 31.37 |
| **No** | 73 | 68.63 |

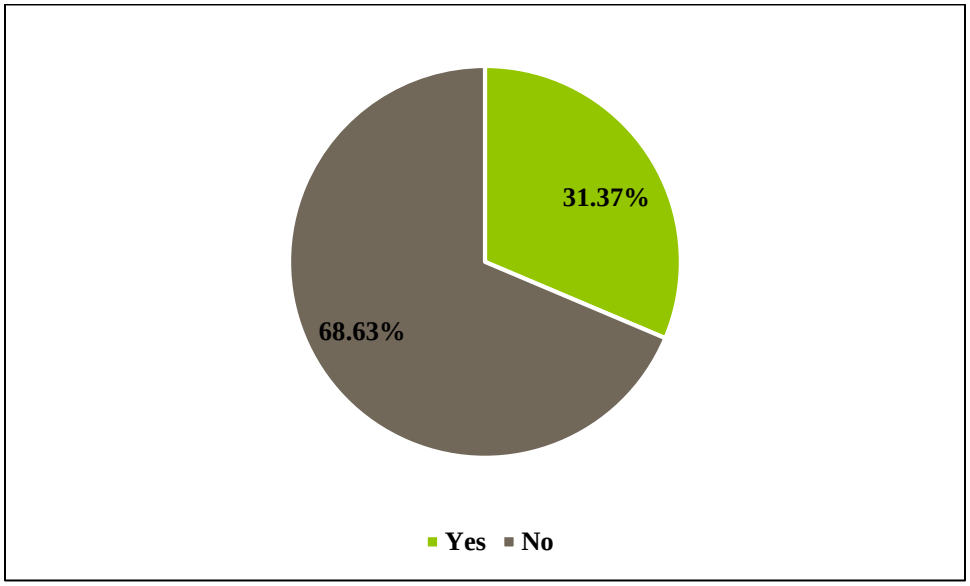



**Figure 9: Distribution of subjects based on presence of Hepatic encephalopathy.**

From table 9, we observe that 32(31.27%) subjects had Hepatic encephalopathy .

**Table 10: Distribution of subjects based on grade of hepatic encephalopathy.**

| Grade of hepatic encephalopathy | Frequency | Percentage |
|---|---|---|
| No hepatic encephalopathy | 73 | 71.57 |
| Minimal hepatic encephalopathy | 15 | 14.71 |
| Advanced hepatic encephalopathy | 14 | 13.73 |

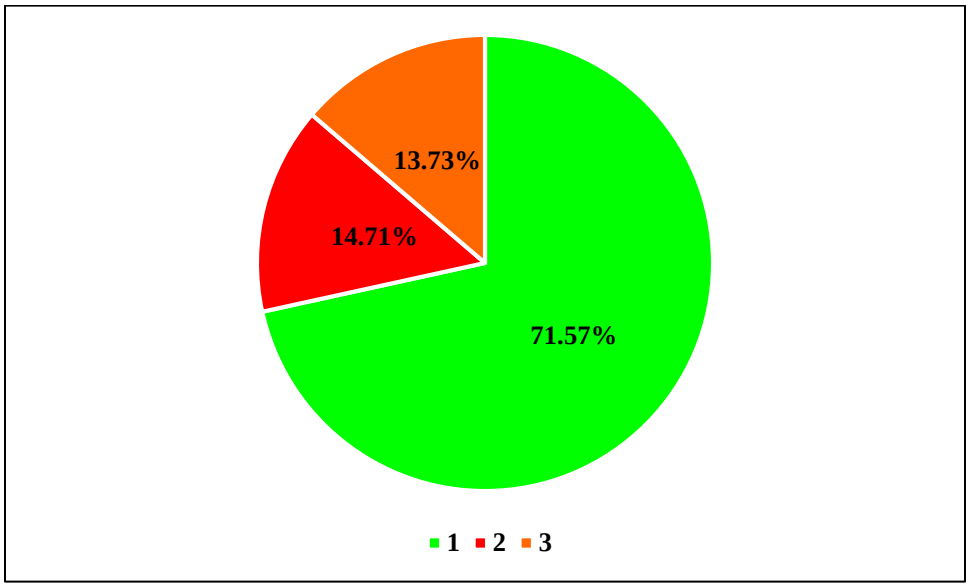



**Figure 10: Distribution of subjects based on grade of Hepatic Encephalopathy.**

1=no hepatic encephalopathy, 2=minimal hepatic encephalopathy, 3=advanced hepatic encephalopathy

From table 10, we observe that, among the total samples, 71.57% of subjects had no hepatic encephalopathy followed by 14.71% subjects having minimal hepatic encephalopathy. The remaining 13.73% of the total subjects had advanced hepatic encephalopathy.

**Table 11: Distribution of patients based on presence of Spontaneous Bacterial Peritonitis.**

| Spontaneous Bacterial Peritonitis | Frequency | Percentage |
|---|---|---|
| Yes | 10 | 9.8 |
| No | 92 | 90.2 |

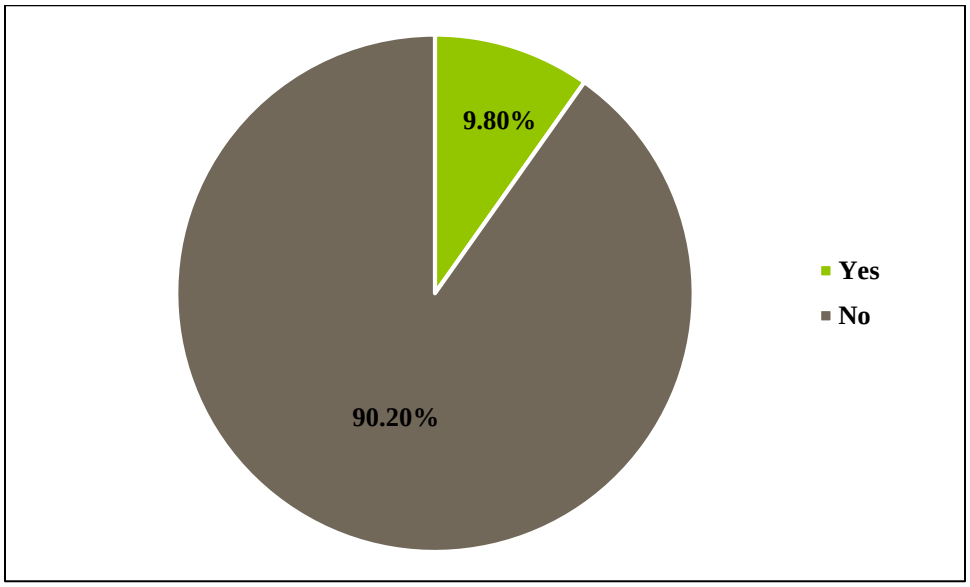



**Figure 11: Distribution of subjects based on presence of Spontaneous Bacterial Peritonitis**

From table 11, we observe that 90.20% of the total subjects in the sample had spontaneous bacterial peritonitis.

**Table 12: Distribution of subjects based on presence of Portal Hypertension.**

| Portal Hypertension | Frequency | Percentage |
|---|---|---|
| Yes | 75 | 73.53 |
| No | 27 | 26.47 |

From table 12, we observe that 73.53% of the total subjects in the sample had Portal hypertension while remaining 27 subjects had no portal hypertension. The following figure 12 depicts the same.

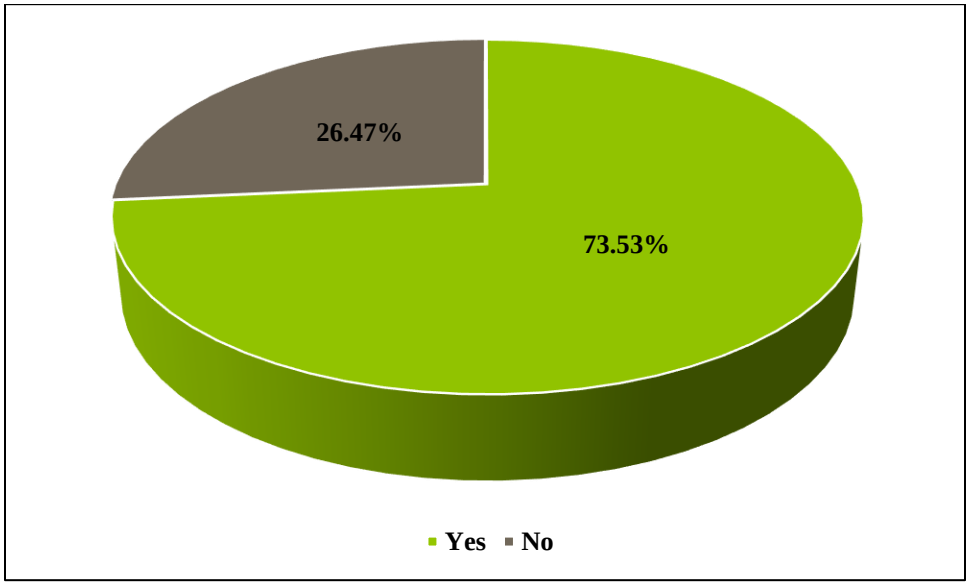



**Figure 12: Distribution of subjects based on presence of portal hypertension**

**Table 13: Distribution of subjects based on prolactin levels**

| Prolactin (ng/ml) | Frequency | Percentage |
|---|---|---|
| <15 | 20 | 19.61 |
| 15-40 | 49 | 48.04 |
| >40 | 33 | 29.41 |

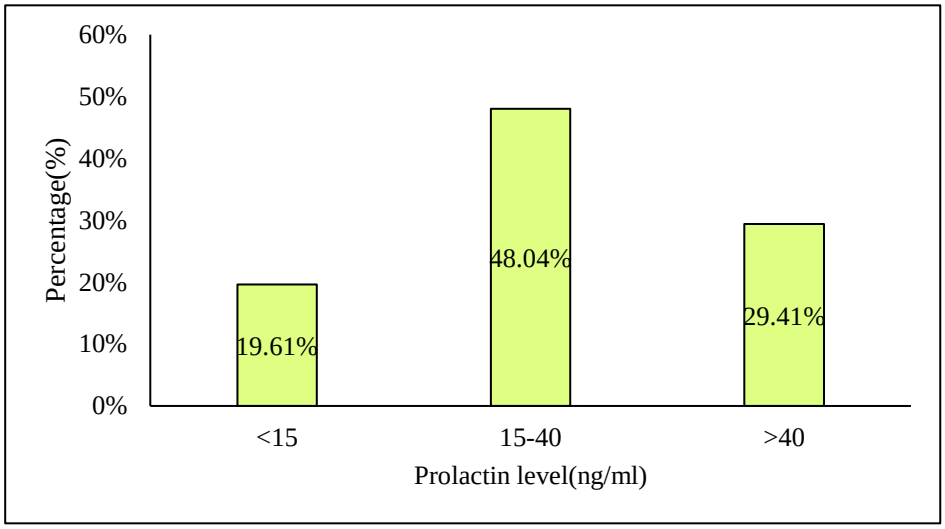



**Figure 13: Distribution of subjects based on prolactin levels**

From table 13, we observe that, 48.04% of subjects in the sample had prolactin level between 15-40ng/ml and 29.41% of subjects had prolactin level more than 40 ng/ml and remaining 19.61% had prolactin less than 15 ng/ml. The mean prolactin value was 50.3 ng/ml.

**Table 14: Correlation of serum Prolactin level with Child Pugh score**

| CHILD PUGH SCORE | PROLACTIN LEVEL <15 ng/ml | PROLACTIN LEVEL 15-40 ng/ml | PROLACTIN LEVEL > 40 ng/ml | TOTAL PATIENTS |
|---|---|---|---|---|
| A | 5 | 3 | 0 | 8 |
| B | 12 | 22 | 1 | 35 |
| C | 3 | 24 | 32 | 59 |
| TOTAL PATIENTS | 20 | 49 | 33 | 102 |

Out of the 59 patients belonging to the Child Pugh class C, 3 patients had prolactin levels <15 ng/ml, 24 patients had prolactin levels from 15ng/ml to 40 ng/ml and 32 patients had prolactin levels greater than 40 ng/ml.

Out of the 35 patients belonging to Child Pugh class B, 12 had prolactin levels <15 ng/ml, 22 had prolactin levels between 15 ng/ml to 40 ng/ml, 1 patient had prolactin level above 40ng/ml.

Out of the 8 patients belonging to Child Pugh class A, 5 patients had prolactin levels <15 ng/ml, 3 patients had prolactin levels between 15ng/ml to 40 ng/ml.

**Table 15: Correlation of prolactin with different factors**

| Factors | Prolactin | |
|---|---|---|
| | Tau | P value |
| Child Pugh score | 0.4688 | <0.0001* |
| Bilirubin | 0.1403 | 0.0368* |
| Albumin | -0.1350 | 0.0491* |
| INR | 0.1767 | 0.0087* |
| Ascites degree | 0.3829 | <0.0001* |
| Hepatic encephalopathy grade | 0.4897 | <0.0001* |

** indicates significance*

From table 15, using Kendall tau correlation, we conclude that Prolactin significantly correlates with Child Pugh score, Bilirubin, Albumin, International normalized ratio, degree of ascites and grade of hepatic encephalopathy

# DISCUSSION

## DISCUSSION

A total of 102 patients with cirrhosis of the liver admitted in the Dept. of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical research Centre were studied during the period January 2018 to December 2018 with an objective to correlate the serum prolactin levels with the CHILD-PUGH score in patients of cirrhosis of liver .

### AGE DISTRIBUTION

The average age in our study population was 49.46 ± 12.15 years with most of the patients (57.84%) in the age group off 41-60 years. This was in concordance with a study conducted by Kannan Sridharan et al., in an Uttar Pradesh where the mean age was 56 years.[2] Similarly, in another study done in Madurai by Pravin Prabhu et al., the mean age was found to be 45.8 years.[71]

### GENDER DISTRIBUTION

In the present study, 93% of the patients with cirrhosis were males, which is similar to a study done by Balakrishna et al., in which 83 % of the subjects were males[1]. In a study done by Metwally et al. 62% were male and 38 % were female.[3]

### ETIOLOGY OF CIRRHOSIS

Alcohol was the most common etiology for cirrhosis in our study, i.e. 78.43 %. This is in concordance with the study done by Balakrishna et al., in a teaching hospital in Karnataka,in which majority of the cases (73%) were alcoholic liver disease.[1] Similarly, C.Ress conducted a

study in 2014, 34 % were alcoholic liver disease patients and 30 % were patients with viral hepatitis[4].

**CLINICAL SIGNS**

**BILIRUBIN**

In the present study, the value of total bilirubin ranged between 0.4mg/dl to 50 mg/dl with a mean of 8.11mg/dl. Similarly, in a study published in BMJ, the mean bilirubin was 1.7 mg/dl and the values of total bilirubin from 0.3 mg/dl to 12 mg/dl among cirrhotic patients.[44]

**ALBUMIN**

In our study the mean value of albumin among cirrhotic patients was found to be 2.63±0.63g/dl, and it ranged from 1.4g/dl to 4.4g/dl. However, a similar study done in Europe showed a mean albumin level 3.5g/dl with a range of 2.4g/dl to 5g/dl[44].

**INR**

In the same study done in Europe, the mean INR value was 1.6 with a range of 1.0 to 2.9. [44] Our findings are concordant with the study, with mean INR of 2.18±1.26. 29.4 % patients had INR of >2.3.

**ASCITES**

In our study, 60 patients had ascites. A majority of the subjects (52.94%) had easily controlled ascites. 5.88% of the subjects were detected to have poorly controlled ascites. In contrast, results obtained by Balakrishna et al., showed that 83% of the subjects had ascites[1]. A study conducted by Vellisaris in 2009 showed only 2 out of 26 subjects had ascites.[17]

**HEPATIC ENCEPHALOPATHY**

Our study showed that 29 subjects (31.37%) had hepatic encephalopathy and 73 subjects (68.62%) did not have hepatic encephalopathy. Out of those who had hepatic encephalopathy, 15 subjects had minimal hepatic encephalopathy, the rest (14 subjects) had advanced hepatic encephalopathy. Balakrishna et al., showed that 25% of the subjects in his study had hepatic encephalopathy.[1]

**SPONTANEOUS BACTERIAL PERITONITIS**

Our study detected that 10 subjects (9.8%) had spontaneous bacterial peritonitis. Similarly, Balakrishna et al., noted that 8.3 % of the subjects in his study had spontaneous bacterial peritonitis.[1]

**PORTAL HYPERTENSION**

In our study, 75 subjects (75.53%) had portal hypertension while the rest did not have evidence of portal hypertension. In a similar study conducted in Southern India, 83.3 % of the subjects had portal hypertension. [1]

**PROLACTIN LEVELS**

Our study showed 20 subjects (19.6%) had prolactin values <15 ng/ml, 49 subjects (48.04 %) had values between 15-40 ng/ml, 33 subjects (29.41) had values above 40 ng/ml. Mukherjee et al., conducted a study in 1991 which showed that mean prolactin values were around 27.2 ng/ml in males and 38.4 ng/ml in females. The highest prolactin value in our study was 211 ng/ml. A

similar study conducted by Balakrishna et al, showed that the mean prolactin level in their study population was 60 ng/ml.[1]

**CHILD PUGH SCORE**

The observations in our study showed that majority of the subjects, 59 (57.84%) were categorized as Child Pugh class C. 35 subjects (34.31%) were classified as Child Pugh class B and the rest belonged to Child Pugh class A. Kannan Sridharan et al., observed that 12 subjects in his study were Child Pugh Class A and 8 were Child Pugh Class B.[2] In a study conducted by C. Ress et al., in 2014, 35 patients were defined as Child Pugh class A, 98 patients as Child Pugh Class B, and 45 patients as Child Pugh Class C, respectively.[4]

**CORRELATION OF CHILD PUGH SCORE & ITS COMPONENTS WITH PROLACTIN**

Prolactin was found to have a highly significant positive correlation with both Child Pugh score and hepatic encephalopathy in our study(p value <0.0001). Similarly, bilirubin, albumin, ascites also had significant positive correlation with prolactin level. There was a negative correlation between albumin and prolactin level. In a study by Koller et al., there was a positive correlation of prolactin values (above 10.5 microg/ml) and hepatic encephalopathy ($p<0.05$).[66] A study by Mukerjee et al., also showed concordant results, patients with hepatic encephalopathy had markedly elevated serum prolactin than those without encephalopathy ($p <0.05$). [13]

In our study, prolactin value were found to be higher in Child Pugh class C as compared to class A and B. 32 patients had prolactin level >40 ng/ml among the 59 patients of Child Pugh class C.

Pravin et al., conducted a study in which mean prolactin value was found to be 8.0ng/ml, 26 ng/ml and 56 ng/ml in Child Pugh Class A ,B and C respectively. Mean prolactin values were found to be increasing along with the severity of the disease.[71]

In contrast, a study conducted by Metwally et al., in Austria in 2017 suggested that raised prolactin value was actually a negative prognostic indicator of severity in liver cirrhosis.[3]

In our study, the mean prolactin value in those with minimal hepatic encephalopathy was 55.46 ng/ml and it was 105.05 ng/ml in those with advanced hepatic encephalopathy.

Our results were different from those of a study conducted by Arafa et al., in which mean prolactin level was 14 ng/ml in Grade 1 and 2 of hepatic encephalopathy, 22 ng/ml in grade 3 hepatic encephalopathy, and 35 ng/ml in grade 4 of hepatic encephalopathy. [6]

# CONCLUSION

## CONCLUSION

102 patients were included in our study based on clinical, biochemical and sonography findings of cirrhosis of liver. The study was done to analyze the prolactin levels in chronic liver disease patients and observe whether they correlate with the severity of liver disease, as calculated by the different parameters of the Child Pugh scoring system.

Our findings revealed that there is a significant positive correlation between prolactin levels and the severity of cirrhosis of liver.

The average age in our study was 49.46 ± 12.15 years with most of the patients (57.84%) in the age group of 41-60 years.

In the present study, 93% of the patients with cirrhosis were males .

Alcohol was the most common etiology for cirrhosis in our study, i.e. 78.43 %.

In the present study, the value of total bilirubin ranged between 0.4mg/dl to 50 mg/dl with a mean of 8.11mg/dl.

The mean value of albumin among cirrhotic patients was found to be 2.63±0.63g/dl, and it ranged from 1.4g/dl to 4.4g/dl.

Mean INR of the population is 2.18±1.26. 29.4 % patients had INR >2.3.

In our study, 60 patients had ascites and 29 patients had hepatic encephalopathy.

Majority (52.94%) of the subjects had easily controlled ascites followed by 41.18% patients with no ascites and the remaining 5.88% of the subjects had poorly controlled ascites.

Out of those who had hepatic encephalopathy, 15 subjects had minimal hepatic encephalopathy, the rest (14 subjects) had advanced hepatic encephalopathy.

We detected 10 subjects (9.8%) to have spontaneous bacterial peritonitis.

75 subjects (75.53%) had portal hypertension.

20 subjects (19.6%) had prolactin values <15 ng/ml, 49 subjects (48.04 %) had values between 15-40 ng/ml, 33 subjects (29.41) had values above 40 ng/ml.

The observations in our study showed that majority of the subjects, 59 (57.84%) were categorized as Child Pugh class C. 35 subjects (34.31%) belonged to Child Pugh class B and the rest belonged to Child Pugh class A.

Prolactin was found to have a highly significant positive correlation with both Child Pugh score and hepatic encephalopathy in our study (p value <0.0001). Similarly, bilirubin, albumin, ascites also had significant positive correlation with prolactin level. There was a negative correlation between albumin and prolactin level. In our study, prolactin value were found to be higher in Child Pugh class C as compared to Child Pugh class A and B. 32 patients had prolactin level >40 ng/ml among the 59 patients of Child Pugh class C.

Thus, from this study, we are able to conclude that serum prolactin could serve as a valuable indicator of severity of liver disease. Currently, the CHILD PUGH score is being used for severity assessment. Calculating the scores attributed to each component can be a cumbersome

process. Hence, a single parameter like serum prolactin, has a significant association with the severity of cirrhosis of liver, and can be used as a simple diagnostic test to assess the severity of cirrhosis of liver.

# LIMITATIONS

## LIMITATIONS

The main limitation of our study is that there are many confounding factors which could lead to raised prolactin levels, including undiagnosed comorbid conditions. While we have attempted to exclude as many of these factors as possible, we cannot definitely rule out certain conditions like prolactinomas since we have not subjected our patients for routine MRI screening.

The other limitation is the limited sample size. A larger number of study subjects could have established a stronger correlation between prolactin levels and certain components of CHILD PUGH score like bilirubin, ascites and INR.

# SUMMARY

## SUMMARY

The study of prolactin in cirrhotic patients of various etiologies helps to identify the severity of liver damage.

As per our study, an elevation of prolactin in patients with cirrhosis was significantly associated with worsening liver function as determined by higher Child-Pugh scores.

These results suggest that prolactin may be used as a tool for evaluation of liver functions in cirrhosis. Prolactin may also help to predict patients likely to develop complications. Studies on a larger scale with follow-up are required to include prolactin levels into prognostic scoring systems of liver disease.

Future studies could compare the prolactin levels with the other complications of liver disease like hepatopulmonary syndrome and hepatorenal syndrome.

Cohort studies can be undertaken to analyze whether the patients with raised prolactin levels had higher rates of mortality. Similarly, value of serial prolactin monitoring can also be studied.

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# ANNEXURES

**INFORMED CONSENT**

**Title Of Research Study: CORRELATION OF SERUM PROLACTIN LEVEL TO CHILD-PUGH SCORING SYSTEM IN LIVER CIRRHOSIS-A CROSS SECTIONAL STUDY**

- **Introduction and Purpose:-** Liver cirrhosis can lead to various hormonal disturbances.

Human prolactin is a hormone of pituitary origin, whose production is controlled by dopamine and its biological actions relate exclusively to lactation and reproductive functions [2].

Prolactin secretion is mainly regulated by tonic hypothalamic inhibition through dopamine and the stimulatory influences of hypothalamic releasing factors and circulating oestrogen.[1]

Circulating oestrogen is elevated in liver cirrhosis .

Oestrogen stimulate prolactin release by interfering with the dopamine secretion from the hypothalamus, and through a direct effect on the anterior pituitary .

Decompensated liver function leads to a change in the type of amino acids entering the central nervous system.

Circulating concentrations of aromatic amino acids have been found to increase leading to an increase in the synthesis of false neurotransmitters. These false neurotransmitters may inhibit the dopamine release contributing to hyperprolactinemia .

High prolactin levels have been associated with greater derangement of components of Child Pugh score, greater mortality and increased complications of chronic liver disease. Hence, the use of a single biomarker such as prolactin, whose levels give us an idea about the severity of the disease and the possibility of complications, is a very vital tool in EARLY INTERVENTION in such cases.

**Procedure**:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations like routine investigations and Hepatitis B and Hepatitis C workup. You will be subjected to sonography and upper gastrointestinal endoscopy.

**Risk and Benefits:**

You may experience discomfort while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

You may also experience discomfort during upper GI endoscopy. Possible risks include perforation of viscous and gastrointestinal bleeding but these are rare.

You may not be benefitted by these investigations but you will be part of this study which is going to be useful to others in the future.

**Alternatives:**

Taking part in this study is voluntary. You may choose not to take part in this study.

If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

**Privacy and Confidentiality:**

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

**Institution / Sponsor's policy:**

Does not apply to this research

**Financial incentives for participation:**

You will not be paid / offered any gifts /incentives for participating in the study.

**Authorization to publish the results:**

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

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

1. Dr. Roopa M Bellad, Chairman,

J.N.M.C Ethical Committee for Human Research

9448113403

## 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

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name :……..

Signature / Left thumb impression: ……..

of the participant

Name of the legally authorized :……..

representative / guardian

Signature / Left thumb impression :……..

Witness' name :……..

Signature / Left thumb impression :……..

Investigator's name and signature :……..

Date:

Place:

**PROFORMA**

**CASE NO:**

**NAME:**

**AGE/SEX:**

**IP NO.:**

**ADDRESS:**

**OCCUPATION:**

**COMPLAINTS AT PRESENTATION:**

**Past history:**

**Family history**

**Personal history**

**Treatment history**

PHYSICAL EXAMINATION:

GENERAL CONDITION:

PALLOR- YES/NO

ICTERUS-YES/NO

LYMPHADENOPATHY-YES/NO

CYANOSIS- YES/NO

CLUBBING-YES/NO

EDEMA-YES/NO

VITALS:

TEMPERATURE

PULSE

RESPIRATORY RATE

BLOOD PRESSURE

SIGNS OF HEPATOCELLULAR FAILURE:

Loss of axillary hair

Leuconychia

Dupuytren'contracture

Gynecomastia

Spider Naevi

Ascites

Testicular atrophySIGNS OF HEPATIC ENCEPHALOPATHY:

Asterixis

Constructional Apraxia

SYSTEMIC EXAMINATION:

R. S.:

C.V.S.:

**C.N.S.:**

P.A.:

**INVESTIGATIONS**

CBC

LFT, including INR

Serum Prolactin via Radioimmunoassay

Ascitic fluid analysis for glucose, proteins, cytology

Upper GI endoscopy

USG abdomen including echotexture of liver, size of liver, splenic enlargement and portal vein diameter

HBsAg and HCV via ELISA

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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**Ref: MDC/DOME/** 47 **Date: 22/11/2017**

To,

PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"CORRELATION OF SERUM PROLACTIN LEVEL TO CHILD –PUGH SCORING SYSTEM IN CIRRHOSIS OF LIVER – A ONE YEAR CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

**(Dr. Arathi Darshan)**
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

**(Dr. Roopa M Bellad)**
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

# Key for Masterchart

DIAGN-DIAGNOSIS

BILI-BILIRUBIN

ALB-ALBUMIN

ASC-ASCITES SEVERITY

(1=NO ASCITES, 2=EASILY CONTROLLED ASCITES

3=POORLY CONTROLLED ASCITES)

H.E-HEPATIC ENCEPHALOPATHY

(1=NO HEPATIC ENCEPALOPATHY, 2= MINIMAL HEPATIC

ENCEPHALOPATHY, 3=ADVANCED HEPATIC ENCEPHALOPATHY)

PRL-PROLACTIN

CTP-CHILD TURCOTTE PUGH

SBP-SPONTANEOUS BACTERIAL PERITONITIS

P.H-PORTAL HYPERTENSION

UN-UNKNOWN CAUSE

# MASTERCHART

| S.NO | NAME | IP | SEX | AGE | DIAGN | BILI | ALB | INR | ASC | SBP | P.H | H.E | H.E SCORE | PRL | CTP SCORE | CTP CLASS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | UDAY | 4832781 | M | 39 | ALD | 2 | 2.3 | 1.55 | 2 | YES | YES | NO | 1 | 19.23 | 8 | B |
| 2 | ARJUN | 4825130 | M | 55 | ALD | 24.8 | 2 | 2.7 | 2 | NO | YES | NO | 1 | 13.13 | 12 | C |
| 3 | VIJAY | 4790059 | M | 52 | ALD | 0.7 | 3.6 | 1.14 | 2 | NO | YES | NO | 1 | 11.64 | 6 | A |
| 4 | ASHWINI | 586889 | F | 30 | UN | 0.8 | 4.2 | 1.2 | 2 | NO | YES | NO | 1 | 10.82 | 6 | A |
| 5 | GAJANAN | 4412830 | M | 55 | ALD | 5.3 | 1.5 | 1.7 | 1 | NO | NO | NO | 1 | 16.3 | 9 | B |
| 6 | KADAPPA | 884534 | M | 58 | ALD | 2.03 | 2.8 | 1.54 | 3 | NO | YES | YES | 2 | 57.59 | 10 | C |
| 7 | YALLAPPA | 4703772 | M | 69 | HEP B | 4.5 | 2 | 1.42 | 3 | NO | YES | YES | 3 | 98.84 | 13 | C |
| 8 | MALLAPPA | 888801 | M | 53 | ALD | 3.15 | 3.2 | 1.2 | 1 | NO | NO | NO | 1 | 17.74 | 8 | B |
| 9 | MARUTI | 889733 | M | 50 | HEP C | 3.42 | 2.4 | 1.35 | 1 | NO | NO | NO | 1 | 22.87 | 9 | B |
| 10 | SIDRAM | 888504 | M | 48 | ALD | 4.69 | 2.5 | 2.05 | 2 | NO | YES | YES | 3 | 62.39 | 13 | C |
| 11 | BHIMU | 889158 | M | 52 | ALD | 4.24 | 2.6 | 4 | 2 | NO | YES | NO | 1 | 24.52 | 12 | C |
| 12 | VIJAYA | 889856 | F | 61 | NAFLD | 2.33 | 2.8 | 2.39 | 1 | NO | NO | NO | 1 | 14.59 | 9 | B |
| 13 | KENCHAWWA | 889895 | F | 57 | NAFLD | 2.75 | 2.2 | 1.16 | 1 | NO | NO | YES | 3 | 61 | 10 | C |
| 14 | KADAPPA | 890252 | M | 54 | ALD | 2.3 | 2.8 | 3.2 | 2 | YES | YES | NO | 1 | 57 | 10 | C |
| 15 | PRAVEEN | 890461 | M | 39 | ALD | 4.57 | 2.5 | 1.7 | 1 | NO | NO | NO | 1 | 13.48 | 9 | B |
| 16 | BASAVRAJ | 889907 | M | 45 | ALD | 7.6 | 2.2 | 1.34 | 2 | YES | YES | NO | 1 | 20 | 10 | C |
| 17 | SHASHIKANT | 890545 | M | 48 | ALD | 10.11 | 2.6 | 1.62 | 3 | NO | YES | NO | 1 | 73.82 | 10 | C |
| 18 | MAHARUDRA | 891153 | M | 71 | ALD | 5 | 2.7 | 1 | 2 | NO | YES | YES | 2 | 37.07 | 11 | C |
| 19 | DINKAR | 889629 | M | 46 | ALD | 1.66 | 2.7 | 1.5 | 1 | NO | YES | NO | 1 | 22.58 | 7 | B |
| 20 | LAXMAN | 891990 | M | 42 | ALD | 3.5 | 3 | 1.18 | 1 | NO | NO | NO | 1 | 14.19 | 8 | B |
| 21 | MAHESH | 892624 | M | 47 | ALD | 3.08 | 2.7 | 1.65 | 3 | NO | YES | YES | 3 | 154.8 | 13 | C |
| 22 | GIRIMALLAPPA | 892906 | M | 67 | NAFLD | 2.08 | 2.7 | 1.31 | 1 | NO | NO | NO | 1 | 17.96 | 9 | B |
| 23 | AMRUT | 895974 | M | 72 | NAFLD | 4.73 | 2.6 | 1.46 | 2 | YES | YES | YES | 2 | 40.21 | 11 | C |
| 24 | MALLIKARJUN | 894254 | M | 44 | ALD | 28.19 | 2.8 | 2.62 | 1 | NO | YES | NO | 1 | 3.51 | 9 | B |
| 25 | NITIN | 894202 | M | 38 | ALD | 28.49 | 2.9 | 5.2 | 2 | NO | YES | NO | 1 | 26.42 | 11 | C |
| 26 | UMESH | 894134 | M | 60 | ALD | 3.6 | 2.6 | 2.5 | 2 | NO | YES | YES | 2 | 59.46 | 13 | C |
| 27 | CHANNAMALLAPPA | 897620 | M | 40 | HEP B | 0.96 | 4 | 1.1 | 1 | NO | NO | NO | 1 | 2.72 | 5 | A |
| 28 | RAVINDRA | 895580 | M | 54 | ALD | 3.79 | 2.9 | 1.36 | 1 | NO | YES | NO | 1 | 34.11 | 8 | B |
| 29 | JOHNY | 894827 | M | 43 | NAFLD | 3.84 | 2.9 | 1.55 | 1 | NO | NO | NO | 1 | 10.14 | 8 | B |
| 30 | BISMILLA | 896318 | F | 25 | UN | 1.8 | 2.9 | 10 | 1 | NO | NO | NO | 1 | 2.7 | 9 | C |
| 31 | UMESH | 896780 | M | 65 | ALD | 5.45 | 3.3 | 2.39 | 2 | NO | YES | YES | 3 | 70.71 | 13 | C |
| 32 | KHAJASAB | 898977 | M | 54 | NAFLD | 9.29 | 2.9 | 2.23 | 1 | NO | YES | NO | 1 | 18.21 | 9 | B |
| 33 | RAHUL | 905928 | M | 34 | ALD | 21.72 | 2.7 | 2.94 | 2 | YES | YES | YES | 2 | 92.94 | 13 | C |
| 34 | SHIVARAM | 907869 | M | 31 | ALD | 5 | 1.4 | 1.02 | 1 | NO | NO | YES | 2 | 20.97 | 10 | C |
| 35 | RAJARAM | 907898 | M | 50 | ALD | 10.51 | 2.4 | 2.16 | 3 | NO | YES | YES | 3 | 84 | 14 | C |
| 36 | BASAVANT | 5013128 | M | 45 | ALD | 1.9 | 3.3 | 1.6 | 1 | NO | YES | NO | 1 | 11.51 | 6 | A |
| 37 | MOHAMMAD | 910142 | M | 48 | HEP B | 16 | 3 | 2.89 | 1 | NO | NO | NO | 1 | 38.3 | 10 | C |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 38 | SUDAM | 910171 | M | 32 | ALD | 50.74 | 2.8 | 6.25 | 1 | NO | NO | NO | 1 | 24.04 | 10 | C |
| 39 | VINAYAK | 912080 | M | 46 | ALD | 19.43 | 2.6 | 5.46 | 1 | YES | YES | YES | 2 | 39 | 12 | C |
| 40 | PRAVEEN | 913245 | M | 40 | ALD | 11.35 | 1.9 | 2.31 | 1 | NO | NO | NO | 1 | 13.48 | 11 | C |
| 41 | CHANABASAPPA | 918911 | M | 56 | ALD | 6.84 | 2.7 | 1.81 | 2 | NO | YES | YES | 3 | 103.1 | 14 | C |
| 42 | SANJAY | 884593 | M | 53 | ALD | 3.2 | 3 | 1.59 | 2 | NO | YES | YES | 3 | 115 | 11 | C |
| 43 | SATYAPPA | 4322951 | M | 61 | ALD | 1.98 | 4.2 | 1.39 | 1 | NO | NO | NO | 1 | 20.16 | 5 | A |
| 44 | BASANGOUDA | 884687 | M | 64 | HEP B | 2.19 | 2.7 | 1.45 | 2 | NO | YES | NO | 1 | 15 | 9 | B |
| 45 | LOVAKUMAR | 885127 | M | 45 | ALD | 2.7 | 4.4 | 1.9 | 2 | NO | YES | NO | 1 | 38.1 | 8 | B |
| 46 | AJAY | 885437 | M | 44 | ALD | 3.07 | 3.2 | 1.63 | 2 | NO | YES | NO | 1 | 65.43 | 9 | B |
| 47 | SOMASEKHAR | 890428 | M | 40 | ALD | 16.16 | 2.4 | 5.26 | 2 | YES | YES | NO | 1 | 60.46 | 12 | C |
| 48 | SHIVALINGAPPA | 886237 | M | 53 | ALD | 8.49 | 2 | 1.43 | 1 | NO | YES | NO | 1 | 20.23 | 9 | B |
| 49 | BALASAHEB | 886684 | M | 78 | NAFLD | 2.5 | 1.1 | 2.23 | 1 | NO | YES | NO | 1 | 5.56 | 9 | B |
| 50 | RAMESH | 934848 | M | 54 | ALD | 7.5 | 2.1 | 3.41 | 2 | NO | YES | NO | 1 | 54.7 | 13 | C |
| 51 | VIVEKANAND | 885903 | M | 39 | ALD | 25.77 | 2.3 | 2.56 | 2 | NO | NO | NO | 1 | 35.85 | 12 | C |
| 52 | DEVARAJ | 885941 | M | 41 | ALD | 3.02 | 2.3 | 1.5 | 2 | NO | YES | NO | 1 | 24.47 | 9 | B |
| 53 | FLORIANO | 885842 | M | 54 | ALD | 0.74 | 2.3 | 1.41 | 1 | NO | NO | NO | 1 | 17.4 | 6 | A |
| 54 | SANTHOSH | 883927 | M | 26 | ALD | 0.4 | 4.4 | 1.18 | 1 | NO | NO | YES | 2 | 21.11 | 6 | A |
| 55 | LALITA | 885211 | F | 76 | NAFLD | 2.15 | 2.9 | 1.22 | 2 | NO | YES | NO | 1 | 18.22 | 8 | B |
| 56 | RAMEJA | 882934 | F | 68 | NAFLD | 2.39 | 2.4 | 1.61 | 3 | NO | YES | YES | 3 | 211 | 11 | C |
| 57 | AMEER | 925595 | M | 47 | NAFLD | 2.54 | 2.9 | 1.37 | 1 | NO | NO | NO | 1 | 37.1 | 7 | B |
| 58 | GOPAL | 925384 | M | 31 | ALD | 5.47 | 2.1 | 2.23 | 2 | NO | YES | NO | 1 | 41.03 | 11 | C |
| 59 | MALLIKARJUN | 925029 | M | 78 | NAFLD | 3.46 | 3.3 | 1.4 | 2 | NO | YES | NO | 1 | 10.45 | 9 | B |
| 60 | SHRISHEL | 924732 | M | 43 | ALD | 18.56 | 2.8 | 1.94 | 2 | NO | YES | NO | 1 | 39.54 | 10 | C |
| 61 | ASHOK | 4661394 | M | 48 | ALD | 0.7 | 1.5 | 0.94 | 2 | YES | YES | YES | 2 | 18.93 | 9 | B |
| 62 | KRISHANAND | 843898 | M | 62 | ALD | 1.8 | 2.9 | 1.31 | 1 | NO | YES | NO | 1 | 13.56 | 6 | A |
| 63 | DUNDAPPA | 879732 | M | 41 | ALD | 28.82 | 2.9 | 3.1 | 2 | NO | YES | YES | 2 | 76.52 | 12 | C |
| 64 | MALLIKARJUN | 941275 | M | 45 | ALD | 15.4 | 2.8 | 3.5 | 2 | NO | YES | YES | 2 | 56.6 | 13 | C |
| 65 | ASHOK | 881815 | M | 48 | ALD | 8.57 | 3.3 | 1.44 | 1 | NO | YES | NO | 1 | 47.29 | 8 | B |
| 66 | BASAVANT | 880915 | M | 54 | ALD | 2.27 | 2.3 | 1.27 | 2 | NO | YES | NO | 1 | 13.7 | 9 | B |
| 67 | PRAVIN | 843332 | M | 46 | ALD | 12.5 | 3.2 | 3.12 | 2 | NO | YES | YES | 2 | 18.41 | 12 | C |
| 68 | DODAPPA | 883253 | M | 26 | ALD | 25.73 | 2.6 | 2.23 | 1 | NO | YES | NO | 1 | 23.6 | 11 | C |
| 69 | RAMCHANDRA | 896759 | M | 60 | ALD | 3.47 | 2.8 | 1.59 | 2 | NO | YES | YES | 3 | 51.53 | 10 | C |
| 70 | BHEEMAPPA | 876035 | M | 49 | ALD | 4.45 | 2 | 1.82 | 2 | NO | YES | NO | 1 | 68.87 | 11 | C |
| 71 | ANADENAPPA | 883253 | M | 27 | ALD | 25.75 | 2.6 | 2.23 | 2 | NO | YES | NO | 1 | 23.6 | 12 | C |
| 72 | BASAVANT | 880915 | M | 54 | ALD | 2.68 | 2.5 | 1.6 | 1 | NO | YES | NO | 1 | 13.1 | 8 | B |
| 73 | SAGAR | 940378 | M | 37 | ALD | 17.46 | 2.6 | 2.5 | 1 | NO | YES | YES | 3 | 159.8 | 13 | C |
| 74 | SURESH | 877691 | M | 40 | ALD | 28.23 | 2.6 | 1.86 | 1 | NO | YES | NO | 1 | 21.7 | 10 | C |
| 75 | RAJASEKHAR | 883782 | M | 68 | ALD | 17.32 | 2.7 | 1.43 | 1 | NO | YES | NO | 1 | 36.7 | 9 | B |
| 76 | RAJAK | 883303 | M | 57 | ALD | 4.93 | 3.2 | 1.66 | 2 | NO | YES | NO | 1 | 10.23 | 9 | B |
| 77 | UMESH | 926018 | M | 35 | NAFLD | 6.2 | 1.5 | 2.57 | 2 | NO | NO | NO | 1 | 143.8 | 12 | C |
| 78 | NARAYAN | 922503 | M | 51 | ALD | 23.76 | | 2.31 | 2 | NO | YES | NO | 1 | 17.78 | 12 | C |
| 79 | SURESH | 922448 | M | 41 | ALD | 7.32 | 1.8 | 3.9 | 2 | NO | YES | NO | 1 | 25.98 | 12 | C |
| 80 | KASTURI | 922796 | F | 58 | HEP B | 2.53 | 2.5 | 1.7 | 2 | NO | NO | NO | 1 | 3.89 | 9 | B |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 81 | RANGANATH | 922827 | M | 52 | ALD | 6.75 | 2.6 | 1.95 | 1 | NO | NO | NO | 1 | 15.8 | 9 | C |
| 82 | TUKARAM | 923447 | M | 40 | ALD | 21.7 | 3 | 1.52 | 2 | NO | YES | NO | 1 | 34.7 | 9 | B |
| 83 | VISHVESHWAR | 924331 | M | 36 | ALD | 4.7 | 3.3 | 2.25 | 2 | NO | YES | NO | 1 | 48.37 | 10 | C |
| 84 | DUNDAPPA | 850573 | M | 63 | ALD | 5.72 | 2.6 | 2.14 | 1 | NO | YES | YES | 3 | 47.52 | 12 | C |
| 85 | UMESH | 4253490 | M | 28 | ALD | 3.7 | 1.4 | 3.09 | 1 | NO | YES | YES | 2 | 34.34 | 12 | C |
| 86 | GAUSSAB | 4748864 | M | 45 | ALD | 9 | 3.5 | 1.8 | 1 | NO | NO | NO | 1 | 35.97 | 7 | B |
| 87 | ADIVEPPA | 4471897 | M | 39 | ALD | 5.5 | 1.7 | 1.99 | 2 | NO | YES | YES | 2 | 66.45 | 12 | C |
| 88 | PRAKASH | 4782408 | M | 60 | ALD | 0.6 | 1.7 | 3.2 | 2 | NO | YES | YES | 2 | 192.3 | 11 | C |
| 89 | GURUSIDDA | 879841 | M | 34 | ALD | 9.4 | 2.5 | 1.96 | 2 | NO | YES | NO | 1 | 30.7 | 11 | C |
| 90 | SHEKHAR | 4783386 | M | 50 | ALD | 2.5 | 1.5 | 2.51 | 2 | NO | YES | YES | 3 | 163.6 | 13 | C |
| 91 | SUDEEP | 883520 | M | 51 | ALD | 3.49 | 2 | 1.84 | 2 | YES | YES | NO | 1 | 59.6 | 11 | C |
| 92 | SHANKAR | 883123 | M | 54 | ALD | 14.65 | 2.5 | 1.99 | 2 | NO | YES | NO | 1 | 20 | 11 | C |
| 93 | LAXMIKANT | 882332 | M | 68 | ALD | 3.69 | 2.7 | 1.68 | 1 | NO | YES | NO | 1 | 21.98 | 9 | B |
| 94 | PRAHLAD | 881161 | M | 43 | ALD | 9.01 | 2.7 | 2.1 | 2 | NO | YES | NO | 1 | 51.99 | 11 | C |
| 95 | MAHADEV | 882193 | M | 48 | ALD | 11.75 | 2.2 | 4.62 | 2 | NO | NO | NO | 1 | 23.35 | 12 | C |
| 96 | AKKAVVA | 882091 | F | 78 | HEP C | 6.6 | 3 | 1.4 | 2 | YES | YES | NO | 1 | 35.46 | 12 | C |
| 97 | DODDAYYA | 883284 | M | 55 | ALD | 6.72 | 2.6 | 1.77 | 2 | NO | YES | NO | 1 | 16.71 | 11 | C |
| 98 | VEERENDRA | 881275 | M | 46 | ALD | 3.51 | 3.7 | 2.19 | 1 | NO | YES | NO | 1 | 20.39 | 8 | B |
| 99 | SIDAPPA | 942280 | M | 40 | ALD | 3.8 | 2.3 | 1.99 | 2 | NO | YES | NO | 1 | 37 | 11 | C |
| 100 | PRAKASH | 942406 | M | 41 | ALD | 2.35 | 1.6 | 2.37 | 2 | NO | YES | YES | 3 | 87.43 | 13 | C |
| 101 | MAHANTESH | 942407 | M | 62 | ALD | 4.01 | 2.9 | 1.7 | 1 | NO | NO | NO | 1 | 33.63 | 8 | B |
| 102 | SWATI | 942552 | F | 55 | UN | 1.84 | 2.7 | 2.65 | 1 | NO | NO | NO | 1 | 12.6 | 9 | B |