" USE OF CLOCK AND STAR DRAWING, AS A MARKER OF NEUROPSYCHOLOGICAL ASSESSMENT IN THE GRADING OF HEPATIC ENCEPHALOPATHY AND COMPARE WITH WEST HAVEN CRITERIA AND PORTOSYSTEMIC ENCEPHALOPATHY SCORE AND INDEX "

By

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Dissertation submitted to BLDE (Deemed to be) University, Vijayapura

In partial fulfilment of the requirements for the award of the degree of

DOCTOR OF MEDICINE IN

GENERAL MEDICINE

Under the guidance of

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Dr. NIMMAGADDA VIRAJA

LIST OF ABBREVIATIONS USED

NASH	:	Non alcoholic steato hepatitis
SAAG	:	Serum to ascites albumin gradient
TGF	:	Transforming growth factor
IgA	:	Immunoglobulin A
PMN	:	Polymorphoneuclear Leukocyte
SBP	:	Spontaneous bacterial peritonitis
MNB	:	Monomicrobial non-neutrocytic bacterascites
CNNA	:	Culture-negative neutrocytic ascites
TIPS	:	Transjugular intrahepatic portosystemic shunt
NSBBs	:	Nonselective β-adrenergic blocking agents
SSTR	:	Selective serotonin receptor
HVPG	:	Hepatic venous pressure gradient
PKC	:	Protein kinase C
EVL	:	Endoscopic variceal ligation
ICA	:	International Ascites Club
HRS	:	Hepato renal syndrome
ADQI	:	Acute Dialysis Quality Initiative
FENa	:	Fractional excretion of sodium
ACEIs	:	Angiotensin-converting enzyme inhibitors
ARBs	:	Angiotensin receptor blockers
NSAIDs	:	Non steroidal anti inflammatory drugs
RAAS	:	Renin angiotension aldosterone System
BUN	:	Blood Urea Nitrogen

Tc - 99m	:	Metastable nuclear isomer of technetium
PAMPs	:	Pathogen associated molecular pattern molecules
AKI	:	Acute kidney injury
NAKI	:	Non acute kidney injury
AKD	:	Acute kidney disease
CKD	:	Chronic kidney disease
ECAD	:	Extracorporeal albumin dialysis
MARS	:	Molecular adsorbent recirculating system
MELD	:	Model for End stage Liver Disease
HPS	:	Hepatopulmonary Syndrome
POPH	:	Portopulmonary hypertension
PaO_2	:	Partial pressure of oxygen
mPAP	:	Mean pulmonary artery pressure
PVR	:	Pulmonary vascular resistance
MAP	:	Mean arterial pressure
P(A-a) O_2	:	Alveolar arterial pressure gradient
L-NAME	:	N^G-nitro-L-arginine methyl ester
HCC	:	Hepatocellular carcinoma
HE	:	Hepatic encephalopathy
SHE	:	Subclinical hepatic encephalopathy
MHE	:	Minimal hepatic encephalopathy
HRQoL	:	Health-related quality of life
Ach	:	Acetylcholine
AchE	:	Acetylcholinesterase
BBB	:	Blood brain barrier

GABA	:	Gamma aminobutyric acid
Gln Synth	:	Glutamine synthetase
NMDA	:	N methyl D aspatic acid
NT	:	Neurotransmitter
RNS	:	Reactive oxygen species
THDOC	:	Tetrahydrodeoxycorticosterone
ALF	:	Acute liver failure
CDR	:	Cognitive Drug Research
CFF	:	Critical flicker frequency
EP	:	Evoked potentials
HE	:	Hepatic encephalopathy
ICT	:	Inhibitory control test
MHE	:	Minimal hepatic encephalopathy
MRS	:	Magnetic resonance spectroscopy
PHES	:	Psychometric Hepatic Encephalopathy Score
RBANS	:	Repeatable Battery for the Assessment of Neurophysiological Status
EEG	:	Electroencephalogram
SONIC	:	Spectrum Of Neurocognitive Impairment In Cirrhosis
CHESS	:	Clinical Hepatic Encephalopathy Staging Scale
HESA	:	Hepatic Encephalopathy Severity Algorithm
WHC	:	West Haven Criteria
PSEI	:	Portosystemic Encephalopathy Index
PSE_{SUM}	:	Portosystemic Encephalopathy Sum
VEP	:	Visual evoked potential
AEP	:	Auditory evoked potential

SEP	:	Somatosensory evoked potential
IGCF	:	Index Of Global Cortical Function
IBSC	:	Index Of Brainstem Conduction
BCAAs	:	Branched chain amino acids
LOLA	:	L-ornithine L-aspartate
MCH	:	Mean corpuscular hemoglobin
MCV	:	Mean corpuscular volume
MCHC	:	Mean corpuscular hemoglobin concentration
SGOT	:	Serum glutamic oxaloacetic transaminase
SGPT	:	Serum glutamic pyruvic transaminase
ALP	:	Alkaline Phosphatase

ABSTRACT

NEED FOR STUDY:

Cirrhosis being usually irreversible is the end stage of many diseases affecting the liver. Hepatic Encephalopathy, the commonest complication of cirrhosis of liver, develops in 50-70% of patients with cirrhosis, and its occurrence is a poor prognostic indicator. Constructional apraxia is a well recognized manifestation of hepatic encephalopathy. Grading of hepatic encephalopathy is necessary to assess the evolution of the condition and the response to the effects of therapy. Current hepatic encephalopathy grading tools are limited because of complexity or subjectivity. Hence a simple, objective, low cost, bedside method of assessing the grade of hepatic encephalopathy using clock and star drawing which depict the level of constructional apraxia may be useful.

METHODS :

Patients diagnosed with clinical and sonological evidence of cirrhosis admitted from November 2018 to June 2020 in Shri B.M.Patil Medical college were graded according to West Haven Criteria and Porto Systemic Encephalopathy score and compared with the degree of constructional apraxia which were judged by patient's ability to copy a star and clock face.

RESULTS :

Most common cause of cirrhosis in our study was alcohol with mean age study group being 45.36 $\pm$ 11.972 and with male preponderance. Mean volume of alcohol was 120.76$\pm$44.42 grams/day and mean duration of alcohol 17.74 $\pm$ 8.231 in our study. Macrocytic anemia was predominant with a mean hemoglobin of 9.16 $\pm$ 2.69 and thrombocytopenia was observed with a mean platelet count of 1.27 $\pm$ 0.89. Total bilirubin ranged from 8.1 $\pm$ 7.7 with SGOT levels much higher than SGPT with mean values being 137.3 $\pm$ 243.5 and 96.1 $\pm$ 235.8 respectively. Most common finding in upper gastrointestinal endoscopy was esophageal varices (30%). Statistically significant correlation was observed between ammonia and Child Pugh score. And

also statistically significant association was observed between ammonia and severity of hepatic encephalopathy. It was observed in our study that statistically significant association was present between clock drawing and WHC grades and PSEI as well as star drawing and WHC grades and PSEI. The sensitivity and specificity of star and clock in our study was 90.7%, 88.37% and 57.14%, 57.14% respectively.

CONCLUSION :

Clock and star drawings which are simple, bedside, less time consuming neuropsychological methods could be used to assess the severity of hepatic encephalopathy on a routine basis.

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INTRODUCTION

Liver being the largest organ in the body, weighing about 1.5 kilograms (2% of the total body weight) and receiving 1350ml of blood per min (27% of cardiac output) performs multiple complex interrelated functions of the body which become specially evident when there is any damage/disease[1] and many of the chronic diseases of the liver cause significant morbidity, decline in the quality of life and mortality.

Even with today's medical knowledge and modern technology, 2 million deaths are caused due to diseases of liver per year worldwide and being the end stage of many liver diseases, cirrhosis and its complications account for leading cause of liver related deaths, which is 1 million deaths per year[2]. The most common causative factors of cirrhosis globally stand out as alcohol, non-alcoholic steato hepatitis (NASH) and hepatitis which can be dealt with by lifestyle modification or immunization and are treatable if diagnosed early enough[3].

OBJECTIVE OF THE STUDY:

To grade the hepatic encephalopathy with the help of neuropsychological tests like clock and star drawing and compare with West Haven criteria and Portosystemic encephalopathy score and index.

REVIEW OF LITERATURE

CIRRHOSIS

In 1819, Rene-Theophile-Hyacinthe Laennec used the term "Cirrhosis" that is derived from the Greek "kirrhos" meaning tawny (light brown/yellowish color) but before his time, it was synonymous with 'hardening of the liver'[4].

Vesalius and Morgagni described it as shrunken liver though it is not just that[4].

Mallory said: "To the clinician the term cirrhosis means a chronic, progressive destructive lesion of the liver combined with reparative activity and contraction on the part of the connective tissue. The contraction of the connective tissue may lead to obstruction of the bile ducts, causing more or less jaundice, and it can interfere with the flow of blood through the blood vessels resulting in portal congestion and ascites. The pathologist uses the term cirrhosis in a broader sense. He applies it to all sclerosed conditions of the liver, whether progressive or not, in which destruction of liver cells is associated with real or apparent increase in connective tissue"[4].

Harvey in 1616, described 12 cases of which few are mentioned as "russet, hard or contracted, almost bloodless" and few as "large, hard liver like a scirrhous tumor, almost bloodless and with a rough surface"[4].

Payne in 1626, described liver as "scirrhosum et induratum, and juiceless, like rotten wood" in a person with intemperate habits with jaundice and ascites[4].

Matthew Baillie in 1793 said that forming tubercles in liver is one of the most common forms of its diseases and also observed that it is associated with drinking habits and more commonly observed in men more than females and described present day "nodule" in cirrhosis, as "common tubercule of the liver"[4].

Best and his colleagues' experiments point that alcohol supplies only calories without proteins, aminoacids like choline and methionine whereas Klatskin said that alcohol increases the requirement of choline[4].

Presently, "cirrhosis is defined as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules".

It is characterised by[5] :

1. Involving most of the liver,

2. Fibrous septa which may be reversible or irreversible based on reversibility of disease process (zone of hypoperfusion),

3. Parenchymal nodules which are either micro (<3mm) or macro (>1cm) composed of both senescent and novel hepatocytes which are usually derived from hematopoietic stem cell niche (zone of hyperperfusion).

Clinically cirrhosis is described as uncomplicated/compensated which is detected by routine examination/other investigations or complicated/decompensated in which patients present usually with ascites, jaundice or gastrointestinal bleeding[6].

Once decompensation occurs, the mortality and morbidity resulting from cirrhosis increase sharply, and depending on the cause of decompensation, the 1-year case-fatality rate can be as high as 80%[7].

GLOBAL BURDEN AND EPIDEMIOLOGY :

Prevalence of cirrhosis from autopsy studies arrays from 4.5% to 9.5% (50 million adult population) of the general population globally which is often underestimated owing to its asymptomatic patients. Cirrhotic deaths have increased from being ranked 14th leading cause of death in world in 2001 to 12th in 2020[3].

In Asia, the incidence of cirrhosis ranges from 16.5 per 100,000 in East Asia to 23.6 per 100,000 in Southeast Asia[8].

Globally alcohol consumption and hepatitis being the major causes of cirrhosis and being addressed with screening tools, immunization, antiviral therapies there is a trend change towards increasing incidence of cirrhosis secondary to non alcoholic fatty liver disease secondary to obesity and the metabolic syndrome[8,9].

Number of global prevalent cases of compensated, decompensated cirrhosis have almost been doubled from 1990 to 2017[7].

Prevalence, age-standardised death rates, disability adjusted life years are globally lower in females than in males[7].

Number of deaths are highest in 50–74 years age group and higher rates are observed with increasing age[3].

Central Asia, Western, eastern, and central sub-Saharan Africa, Southeast Asia and Eastern Europe are the top 6 regions with age-standardised death rates due to cirrhosis in 2017. In Central Asia and Eastern Europe, the majority of the cirrhotic deaths are related to alcohol whereas in the other regions, it is hepatitis[7].

Australasia, East Asia, high-income Asia Pacific, Western Europe, Southern Sub-Saharan Africa, and high-income North America are 6 regions with low age standardized death rates due to cirrhosis in 2017, alcohol being the major cause of cirrhosis in Western Europe and in the rest, it is hepatitis[7].

Overall around 2.3 billion people of the world consume alcohol and the global burden of alcoholic liver disease continues to escalate along with the per-capita alcohol consumption from 5.5 L in 2005 to 6.4 L in 2016 worldwide and alcohol related cirrhotic deaths were 27.3% in 2017[7,8].

Worldwide 57% of cirrhotic deaths were due to hepatitis in males and 50.7% in females in 2017 despite the available screening tools and treatment[7].

In 2017, 7·7% of the cirrhotic deaths were due to NASH and prevalence of compenasated cirrhotics due to NASH have doubled and decompensated cirrhotics due to NASH have tripled from 1990 to 2017[7]

Chronic liver disease patients have greater levels of unemployment (65.3% vs 31.4%), inability to work due to disability (30.5% vs 6.6%), and reported days of disability per year (10.2 vs 3.4) when compared with age matched controls and the disability increases with cirrhotic complications[8].

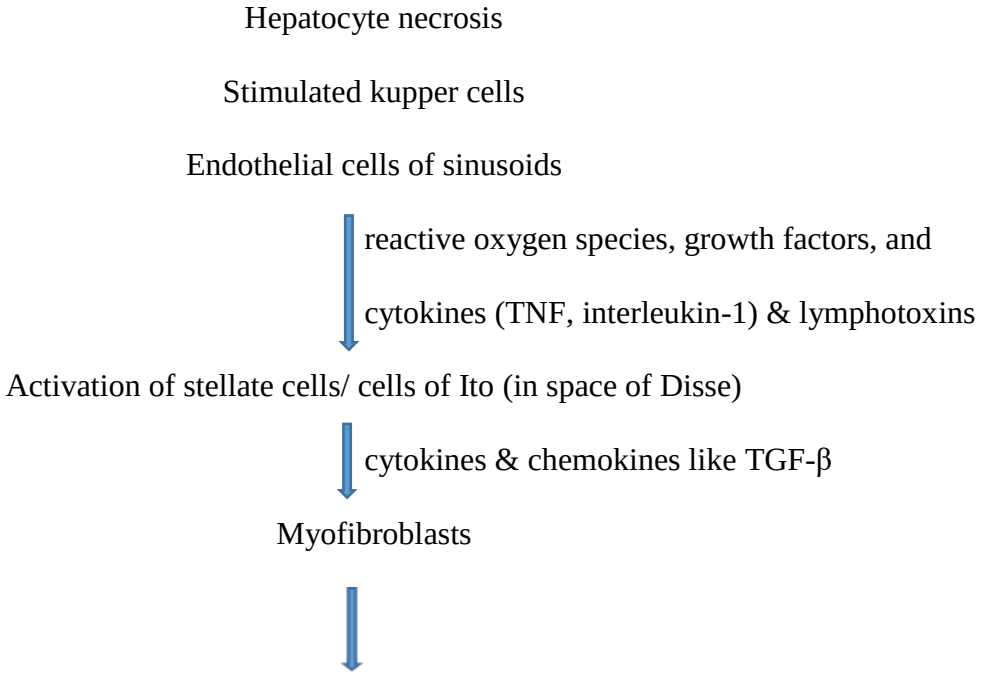
PATHOGENESIS :

Pathogenesis of cirrhosis is majorly explained by[5]:

1. Hepatocyte necrosis,

2. Dynamic process of extracellular matrix synthesis, deposition, and resorption controlled by altering balances between metalloproteases and its tissue inhibitors elucidating the possibility of cirrhotic regression even in late-stage disease, if the disease process is terminated.

FIGURE 1 : PATHOGENESIS OF CIRRHOSIS



3. Vascular injuries, changes, shunts[5]. Normally even with such a high blood flow of about 1050 ml/min from the portal vein and 300 ml/min from the hepatic artery, liver still maintains low vascular resistance which is shown by smaller pressure gradient between 9 mmHg average pressure in the portal vein leading into the liver and 0 mmHg average pressure in the hepatic vein leading from the liver into the vena cava[1].

a) Loss of sinusoidal endothelial cell fenestrations,

b) Development of portal vein-hepatic vein and hepatic artery-portal vein vascular shunts,

c) Increased basement membrane formation

convert thin-walled sinusoids into higher pressure, fast-flowing vascular channels reducing the solute (particularly protein like albumin, lipoprotein, clotting factors) exchange between hepatocytes and the plasma resulting in portal hypertension[5].

The transport deficit is further aggravated by the loss of hepatic microvilli and thus cause liver cell dysfunction[5].

TABLE 1 : ETIOLOGY AND HISTOPATHOLOGY OF CIRRHOSIS :

Cirrhosis is a multifactorial disease.

Its etiological agents, specific histopathological changes and specific treatment are a follows[6]:

ETIOLOGY	HISTOPATHOLOGY	SPECIFIC TREATMENT
Alcohol related cirrhosis	Micro/macro nodular changes with acidophilic bodies and mallory's hyalin	Abstinence
Hepatits B & C	Micro/macro nodular changes with acidophilic bodies and ground glass hepatocytes	Antivirals

NASH	Steatosis with reversible cirrhosis	Reduction of weight
Hemochromatosis	Micronodular pattern with deposition of iron	Venesection
Wilson's disease	Macronodular pattern with deposition of copper, acidophilic bodies and mallory's hyalin.	Chelation of copper
α 1-antitrypsin deficiency	Micro/macro nodular pattern with acidophilic bodies, mallory's hyalin and PAS positive globules.	?Transplant
Indian childhood cirrhosis	Macronodular changes with cholestatis, acidophilic bodies and mallory's hyalin.	?Transplant
Primary biliary cirrhosis & Primary sclerosing cholangitis	Cholestasis, acidophilic bodies and mallory's hyalin.	?Transplant
Venous outflow obstruction	Reversible cirrhosis	Relieve the vein Block/ ? Transplant. Treat the cardiac cause if heart failure is the etiology.
Galactosemia	Reversible cirrhosis	Withdraw milk and its products
Tyrosinemia	Reversible cirrhosis	Withdraw dietary tyrosine

Intestinal bypass surgery	Micronodular changes with steatosis, acidophilic bodies and mallory's hyalin.	? Transplant
Toxins and drugs(Methotrexate, Amiadarone, Enalapril)	Micro/macro nodular changes with steatosis, mallory bodies, periportal and pericellular fibrosis	Recognise and withdraw

CLINICAL FEATURES :

SKIN :

ARTERIAL SPIDERS :

Potent steroid, oestrogen not only acts on the endometrial spiral arterioles in pregnancy but also on the cutaneous vessels making them appear in upper part of body with a body and legs, structure analogous to spiders. They are either end arteries in skin or coiled artery in subcutis with aggregates of glomus cells or the pericytes of Zimmermann which break into many feeding vessels. These are pulsatile and blanch on pressure with a glass slide[10].

PALMAR ERYTHEMA :

In 1899, Chambers noticed red colour of palms in habitants of the Gold Coast. Lane described the red colour of palms in few patients as hereditary/familial. Association of palmar erythema and arterial spiders was described by Walsh and Becker in pregnant females but first, Forman described palmar erythema in pregnant females in 1934. Liver palms or palmar erythema appearing in chronic liver disease was described in 1942 and 1943 by Ratnoff and Patek, Perera and William Bean.

"An older Miss Muffett

Decided to rough it

And lived upon whisky and gin.

Red hands and a spider

Developed outside her

Such are the wages of sin" mentioned Dr.William Bean[10].

2 types of palmar erythema[6,10] :

1. Familial/simple exaggeration of speckled mottling without true accentuation of blood flow regionally.
2. Liver palms with warmth and intense red in hypothenar, thenar eminences and finger pulps which may extend onto dorsum of hands in horse shoe pattern at base of nails.

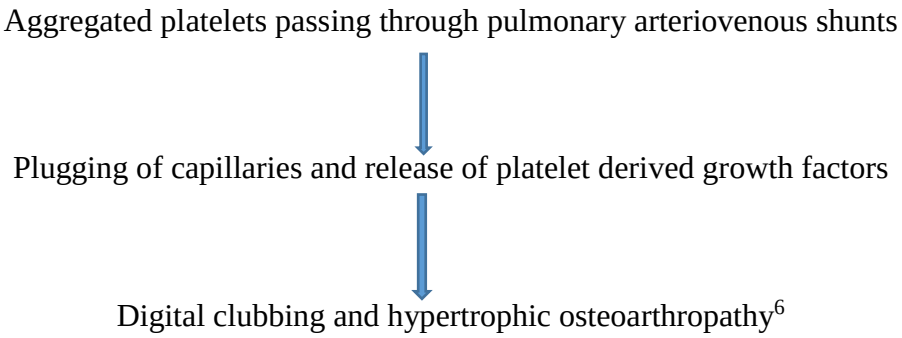
Arterial spiders are twice more common in liver disease than palmar erythema.

LEUCONYCHIA :

White finger nails are due to hypoalbuminaemia[6].

CLUBBING :

FIGURE 2 : MECHANISM OF CLUBBING



Other nail changes like Onychorrhexis, pitting, longitudinal melanonychia, brittle nails, dystrophic nails occur due to[11] :

1. Decreased cell-mediated immunity,
2. Immunosuppression,
3. Anemia (Iron deficiency).

DUPUYTREN ' S CONTRACTURE :

Due to thickened palmar fascia, may be due to vitamin E deficiency. It is named after Aron Guillaume Dupuytren who observed this deformity as a result of retraction of palmar aponeurosis[12].

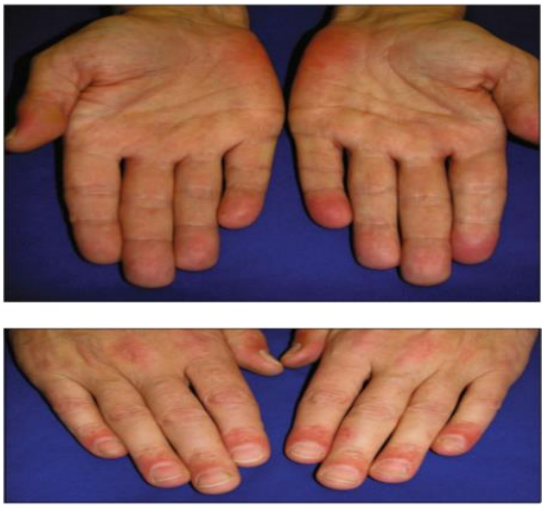


FIGURE 3 : Palmar erythema in a hepatitis patient involving both palmar and dorsal surfaces[13]

Figure 4 : Leukonychia

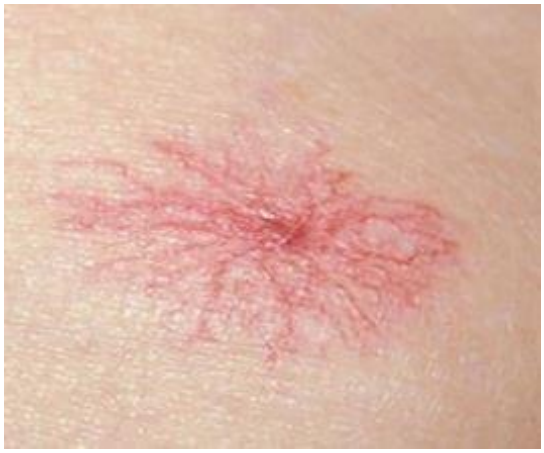
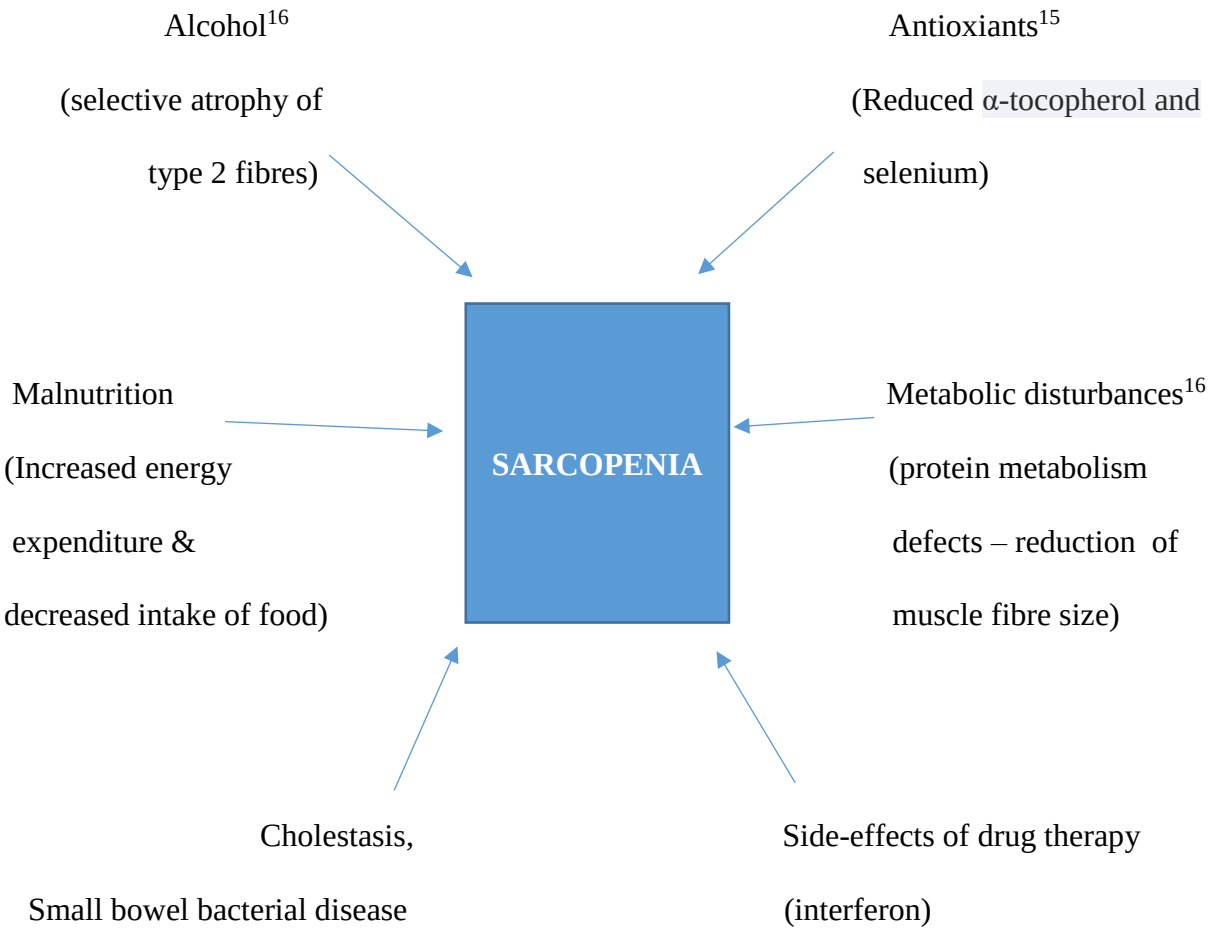


Figure 5 : Arterial spider

MYOPATHY / SARCOPENIA :

It is caused by many factors[14].

FIGURE 6 : FACTORS CAUSING SARCOPENIA



Proximal myopathy is seen usually.

Apparent diffusion coefficient on MRI of skeletal muscles is recently reported to be high in liver disease[14].

FOETOR HEPATICUS :

Sweetish, slightly faecal smell of the breath due to dimethyl sulphide and ketones in alveolar air. Wide spectrum antibiotics altering the gut flora and post defaecation, smell is observed to be less intense thus, the thought of its origin from intestine. In patients of coma, this smell gives a diagnostic clue[6].

FIGURE 7 : HYPOGONADISM[6]

Hepatocellular dysfunction,

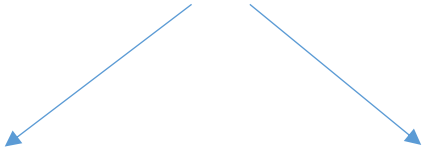
Cholestasis

Reduced conjugation of steroid hormones,

Reduced excretion of oestrogen,

Upturning of hepatic oestrogen receptors,

Downturning of hepatic testosterone receptors



Males	Females
Soft and small testis, Prostatic hypertrophy,	Ovulatory failure,
Diminished libido and potency	Loss of breast and pelvic fat,
Loss of secondary sexual hair,	Erratic menstruation, Infertility.
Gynaecomastia.	

HAEMATOLOGICAL MANIFESTATIONS :

These include combination of cytopenias like thrombocytopenia, anemia, leukopenia as well as coagulopathies[17].

Factors predisposing to hemorrhage[17] :

Thrombocytopenia

Decreased levels of factors II, V, VII, IX, X, XI

Dysfibrinogenemia

Decreased alpha-2-antiplasmin

Factors predisposing to thrombosis[17] :

Increase in factor VIII and Von Willebrand factor

Decreased protein C and protein S

Decreased antithrombin

Reduced plasminogen

In early stages of cirrhosis, prothrombotic condition is observed whereas in later stages, hemorrhagic manifestations are seen[17].

GASTROINTESTINAL FEATURES :

Parotid gland enlargement,

Splenomegaly,

Abdominal wall collaterals, Ascites,

Peptic ulceration (duodenal ulcers > gastric ulcers),

Small bowel bacterial overgrowth (more common in those with ascites than without),

Abdominal herniae,

Chronic relapsing pancreatitis and,

Pancreatic calcification are the gastrointestinal manifestations in cirrhosis of liver[6].

RENAL MANIFESTATIONS :

Redistribution of blood flow away from cortex results in hepatorenal syndrome which further may lead to intrinsic renal failure that inturn result in hypotension and shock[6].

Cirrhotic glomerular sclerosis is seen with thickening of the mesangial stalk and capillary walls. IgA deposition in basement membrane of glomerulus is seen in alcoholic cirrhosis[6].

Chronic hepatitis C infection is associated with cryoglobulinaemia and membrano proliferative glomerulonephritis[6].

NEUROLOGICAL MANIFESTATIONS :

Range from tremors, confusion, stupor to coma[6].

History of Occupation, age, sex, domicile, fatigue and weight loss, anorexia and flatulent dyspepsia, abdominal pain/distention, jaundice, itching (deposition of bile salts in cutis), colour of urine and faeces, bleeding manifestations like haemorrhage-nose, gums, skin, alimentary tract, loss of libido, menstrual irregularities should be enquired[6].

Past history of jaundice, hepatitis, drugs ingested, blood transfusion, history of alcohol consumption, family history of liver disease/ autoimmune disease should also be enquired and taken into consideration[6].

TABLE 2 : INCIDENCE OF VARIOUS SIGNS IN CIRRHOSIS[18]

SIGNS	**REPORTED PERCENTAGE**
Jaundice	30-70
Telangiectasia	17-45
Spider nevi	15-62
Collateral circulation	19-63
Cyanosis or clubbing	5-18
Edema	35-69
Ascites	48-93
Hepatomegaly	70-79
Splenomegaly	24-55
Hemorrhoids	9-34
Sexual changes	5-50

DIAGNOSIS OF CIRRHOSIS :

Liver biopsy, an invasive procedure is the gold standard for diagnosis and is associated with risk of organ injury[6].

Transient elastography (fibroscan) is a rapid non invasive method of evaluating liver fibrosis/ cirrhosis. Liver stiffness ranges from 12.5 to 75.5 kilo Pascals in cirrhotic patients. Alcohol induced liver cirrhotics have higher liver stiffness values compared to other causes. To diagnose histologically alcoholic cirrhosis takes longer time than compared to hepatitis induced cirrhosis[19].

In most of the cases of cirrhosis, diagnosis is made with combination of clinical and radiological features[6].

COMPLICATIONS OF CIRRHOSIS :

Many complications are due to decreased liver cell function, arterial dilatation & hyperdynamic circulation resulting in portal hypertension, and a high risk of hepatocellular carcinoma[5].

Jaundice, ascites, bleeding varices, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, hyponatraemia, high output cardiac failure and hepatocellular carcinoma are the complications of cirrhosis[6].

JAUNDICE :

Jaundice is yellowish discoloration of skin and mucus membrane when systemic retention of bilirubin is above 2.0 mg/dL[5]. The term ‘Icterus’, derived from the Greek word ‘ikteros’ which actually refers to a plant disease in which the leaves turn into yellow or yellow-green is used as a synonym to jaundice. Hepatic or cholestatic types of jaundice occur with cirrhosis[20]. Jaundice is milder and not persistent in alcoholic cirrhosis compared to post necrotic / post hepatitic cirrhosis.

It is severe in 3 conditions in alcoholic cirrhosis[18] :

1. Early stage of cirrhosis with acute illness,
2. When cirrhosis is well established with onset of complications/decompensation,
3. Hepatic precoma.

In case of biliary cirrhosis, jaundice deepens as the disease process progresses.

ASCITES :

Ascites occurs in more than 50% of patients within 10 years of the diagnosis of cirrhosis[21]. It is the accumulation of fluid in peritoneum which when 500ml is present, becomes clinically detectable. Ascites due to cirrhosis is a serous fluid with high protein of around 3 g/dL of protein (albumin) and the serum to ascites albumin gradient(SAAG) is more than or equal to 1.1 g/dL[5].

3 mechanisms of ascites formation[5,22] :

1. Initiation of ascites formation by increased sinusoidal pressure (minimal portal pressure gradient of 12 mmHg).
2. Maintainence of ascites formation by vascular changes (Underfill/Overfill theories) leading to sodium and water retention.
3. Leakage of fluid from hepatic lymph into peritoneum as a result of excessive lymph flow of around 20 litre per day (normal thoracic duct lymph flow is around 1 litre/day). Hepatic lymph has high protein content and low level of triglycerides, thus the protein-rich ascitic fluid.

Most widely accepted theory is underfill / vasodilatory theory which is explained as below[22].

FIGURE 8 : UNDERFILL / VASODILATORY THEORY[22]

Peripheral vasodilatation (production of vasodilators like nitic oxide, adrenomedullin, carbon monoxide, endocannabinoids, prostacyclin, tumour necrosis factor alpha and urotensin & inhibition of nitric oxide synthase)

↓

Reduction of effective arterial blood volume

Reduction of systemic blood pressure

↓ Carotid sinus baroreceptors

Rise in renin, aldosterone, vasopressin

Sympathetic system stimulated

↓ Increased luminal uptake and basolateral passage of sodium

Sodium and water retention

Renal vasoconstriction

↓

Plasma volume expansion

+

portal hypertension

↓

Ascites

FIGURE 9 : OVERFILL THEORY[22]

Hepatic signal (baroreceptor, reduced hepatic synthesis of a natriuretic agent, reduced hepatic clearance of a sodium retaining hormone / a ‘ hepatorenal reflex ’ of unknown etiology)

↓

Renal Na+ and H2O retention

↓

Increased plasma volume

Increased cardiac output

Reduced systemic vascular resistance

+

Portal hypertension

↓

Overflow into peritoneal cavity

GRADES OF ASCITES[21]

Grade 1 : Mild ascites with no clinical detection, only detectable by ultrasonography.

Grade 2 : Moderate ascites presenting as umiform distension of abdomen.

Grade 3 : Gross ascites with marked abdominal distension.

UNCOMPLICATED ASCITES : Uncomplicated ascites is defined as “ascites that is not infected and that is not associated with the development of the hepatorenal syndrome (HRS)”[21].

COMPLICATIONS OF ASCITES :

1. REFRACTORY ASCITES : International Ascites Club(1996) defined refractory ascites as "ascites that cannot be mobilized or the early recurrence of which cannot be satisfactorily prevented by medical therapy". It constitutes 5% to 10% of all the ascitic patients[21].

It is further of 2 types :

a. Diuretic-resistant ascites - Fluid overload that is unresponsive to dietary salt restriction and to high doses of diuretics.

b. Diuretic-intractable ascites - Ascites wherein there is inability to treat ascites with maximum doses of diuretics because of their side effects[23, 24].

Refractory ascites has significantly been associated with hepato renal syndrome type-2, ascitic infection, dilutional hyponatraemia, myopathy and hepatic hydrothorax. It has an omnious prognosis with 2-year probability of survival among patients with refractory ascites of 30% compared to a minimum of 40% patients with uncomplicated ascites being alive at 5 years[24].

"Revised diagnostic criteria of refractory ascites

1. Treatment duration: Patients must be on intensive diuretic therapy (spironolactone 400 mg/day and furosemide 160 mg/day) for at least 1 week and on a salt-restricted diet of less than 90 mmoles/ day or 5.2 g of salt/day.

2. Lack of response: Mean weight loss of o 0.8 kg over 4 days and urinary sodium output less than the sodium intake.

3. Early ascites recurrence: Reappearance of grade 2 or 3 ascites within 4 weeks of initial mobilization.

4. Diuretic-induced complications:

a. Diuretic-induced hepatic encephalopathy: development of encephalopathy in the absence of any other precipitating factor.

b. Diuretic-induced renal impairment: increase of serum creatinine by 4100% to a value 42 mg/dl in patients with ascites responding to treatment.

c. Diuretic-induced hyponatraemia: decrease of serum sodium by 410 mmol/L to a serum sodium of o125 mmol/L.

d. Diuretic induced hypo or hyperkalaemia: change in serum potassium to o 3 mmol/L or 46 mmol/L despite appropriate measures"[24].

FIGURE 10 : PATHOGENESIS OF DIURETIC-RESISTANT ASCITES[24]

Systemic and portal haemodynamic abnormalities,

Activation of neurohumoural vasoactive systems,

Renal re-absorption of sodium and water

+

Progressive decline in renal perfusion and glomerular filtration rate

↓

Sodium re-absorption at the proximal convoluted tubule markedly increases

Delivery of sodium to distal segments of the nephron is markedly decreases

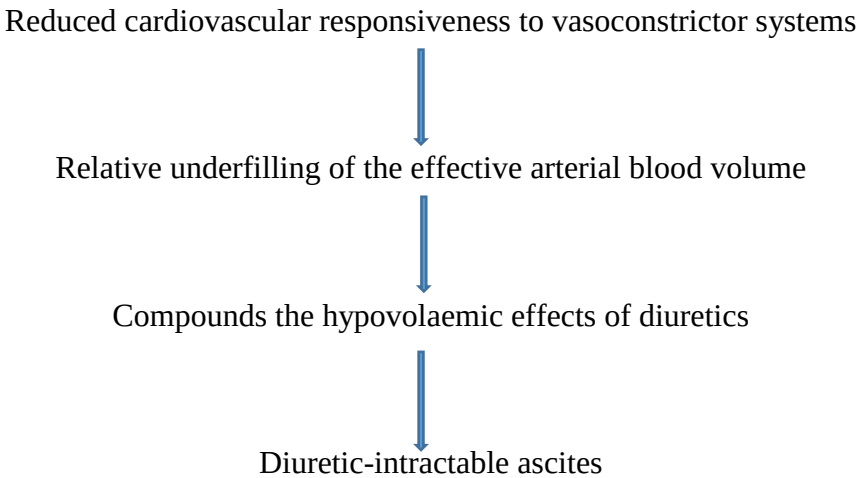
↓

Renal sodium retention mainly occurs proximal to the site of action of both anti mineralocorticoid as well as loop diuretics

↓

Diuretic-resistant ascites

FIGURE 11 : PATHOGENESIS OF DIURETIC INTRACTABLE ASCITES[24]



NON REFRACTORY ASCITES :

- **RECIDIVANT / RECURRENT ASCITES :** Defined as the "Peritoneal effusion that recurs on at least three occasions within a 12-month period inspite of reduction in dietary salt and adequate diuretic doses"[24].
- Massive/tense ascites is also not considered as refractory unless the failure to respond to treatment has been demonstrated[24].

2. ASCITIC INFECTION :

In 1975, Correia and Conn coined the term spontaneous bacterial peritonitis because it is without any inflammatory focus intra abdominally and without any continguous source of infection[22,25].

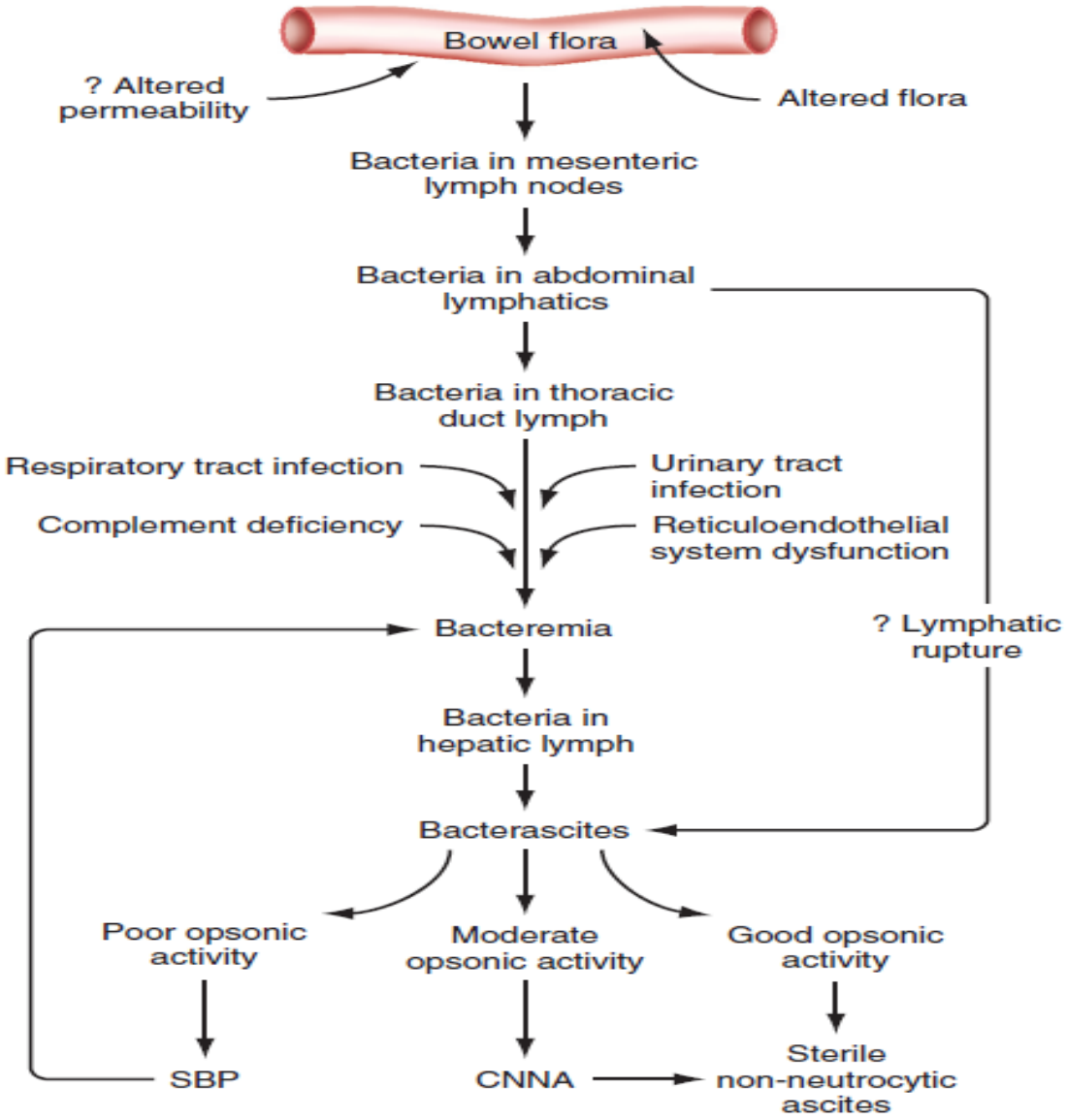
5 types of ascitic infection based on ascitic culture results, neutrophil count, and presence or absence of a surgical source of infection[25] :

TABLE 3 : DIFFERENT TYPES OF ASCITIC INFECTION AND THEIR DIAGNOSTIC CRITERIA

ENTITY	DIAGNOSIS
SBP(Spontaneous bacterial peritonitis)	1. Positive ascitic fluid culture 2. High ascitic absolute PMN count (at least 250 neutrophils/mm3)
MNB(Monomicrobial non-neutrocytic bacterascites)	1. Positive ascitic fluid culture for a single organism, 2. Ascitic fluid PMN count 250/mm3 3. No evidence of an intra abdominal surgically treatable source of infection
CNNA(Culture-negative neutrocytic ascites)	1. Ascitic fluid culture grows no bacteria 2. Ascitic fluid PMN count $\geq$ 250/mm3 3. Not even a single dose of antibiotic has been given 4. No other explanation for an elevated ascitic PMN count (hemorrhage into ascites/ peritoneal carcinomatosis/TB/pancreatitis)
Secondary bacterial peritonitis	1. Ascitic fluid culture is positive (usually for multiple organisms) 2. PMN count $\geq$ 250/mm3 3. Intra-abdominal surgically treatable primary source of infection (perforated intestine, perinephric abscess) has been identified.
Polymicrobial bacterascites (needle perforation of the bowel)	1. Multiple organisms seen on Gram stain or cultured from the ascetic fluid 2. PMN count $\leq$ 250/mm3

Most common organism causing SBP is Escherichia coli. Streptococcus viridans, Staphylococcus aureus, Enterococci are other organisms responsible for ascitic infection[26]

FIGURE 12 : PATHOGENESIS OF ASCITIC INFECTION[25]



3. UMBILICAL HERNIAE :

Diastasis of recti or herniae occur in the umbilical, femoral or inguinal regions or through old incisions as a result of increased intra abdominal pressure. 20% of the cirrhotics with ascites develop herniae and may be in upto 70% in long standing ascites/tense ascites. These herniae are prone to rupture or incarceration. Thus, after effective treatment of ascites, definitive mesh repair of these herniae is to be planned[22].

4. HEPATIC HYDROTHORAX :

Trans-diaphragmatic movement of fluid from peritoneal to plueral cavity results in right sided pleural effusion in 85%, left sided in 13% and bilateral in 2%. Detection of radiotracer (intraperitoneal injection of Tc - 99m - labelled sulphur colloid or macroaggregated serum albumin) in the pleural space is demonstrated generally within 2 hours of injection gives the diagnosis. Ascites should be effectively treated and TIPS is proven more successful than drainage and pleurodesis[22].

5. PERIPHERAL OEDEMA :

Due to a functional inferior vena caval block due to high intrabdominal pressure due to the ascitic fluid[22].

TABLE 4 : TREATMENT OF ASCITES AND ITS INFECTION[26]

Grade 1	Salt restriction(to <2g/day)
Grade 2	Spirinolactone (max dose: 400mg/day), Furosemide (max dose : 160mg/day).
Grade 3/ Refractory ascites	Large volume paracentesis, Lee Van shunt (TIPS), Liver transplant.

Ascitic infection	Prophylaxis : Oral norfloxacin (400 mg/day every 12 hrs for a minimum of 7 days)[22] Treatment : Third generation cephalosporins like cefotaxime 2 g iv every 8 hours usually for 5 days but duration of antibiotic is determined based on clinical response and serial ascitic fluid PMN counts and cultures[25,26]. • In case of secondary bacterial peritonitis & polymicrobial bacterascites, anti anaerobic drug such as metronidazole is added. • In case of secondary bacterial peritonitis, emergency surgical intervention is indicated.

PROGNOSIS OF CIRRHOTICS WITH ASCITES :

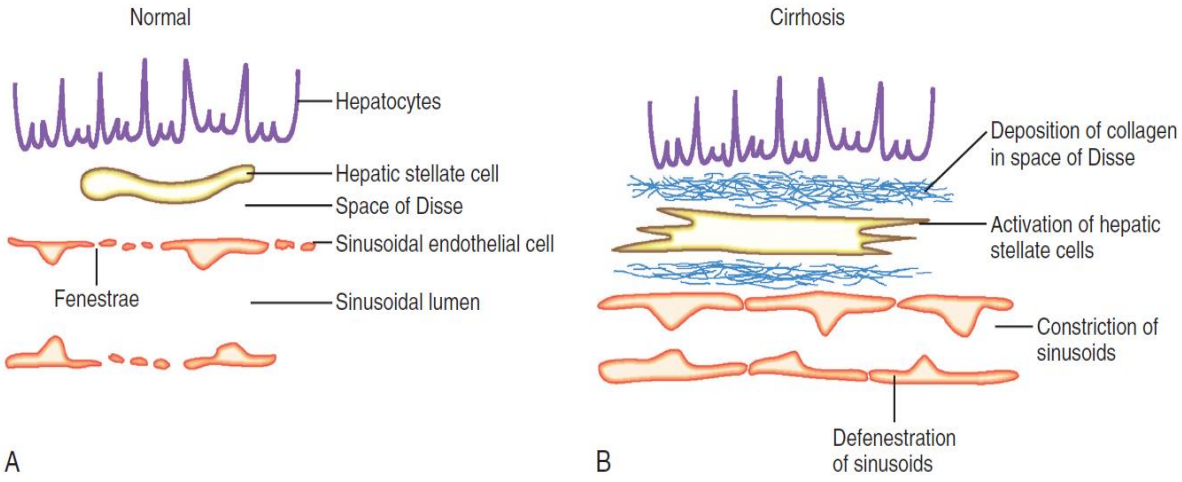
Cirrhotics with ascites indicates a poor prognosis, especially with refractory ascites and those who develop SBP. At 2 years, the probability of mortality in hospitalized cirrhotics with ascites is 40%[21]. 10-20% of the patients with SBP die at hospital admission and the median survival at 1 year is 9 months. Immediate survival and resolution of SBP is 100% in uncomplicated community acquired SBP[22].

PORTAL HYPERTENSION AND BLEEDING VARICES :

The superior mesenteric vein and the splenic vein just behind the head of the pancreas at about the level of the second lumbar vertebra form the portal vein. It has segmental intrahepatic distribution along with the hepatic artery. Portal blood flow is about 1- 1.2L/min

and portal pressure is about 7mmHg. When the portal circulation is obstructed, collateral circulation develops to carry the portal blood into the systemic veins[27].

FIGURE 13 : PATHOGENESIS OF PORTAL HYPERTENSION



According to Ohm's law, the portal pressure gradient(ΔP) is given by portal flow(F) multiplied by the resistance to its flow(R)[28].

$$\Delta P = F*R$$

In cirrhosis, both portal flow and resistance offered to it are increased, thus the pressure gradient leading to portal hypertension[28].

New vascular structures sprout (angiogenesis) and the collaterals dilate(collateralization) occur connecting the high-pressure portal venous system with lower-pressure systemic veins, but even these 2 processes are not enough for normalizing portal pressure and inturn causes complications of portal hypertension, such as esophageal varices, hemorrhoids[28].

COLLATERAL CIRCULATION AND VARICES :

Normally blood flow is towards the portal circulation through the collaterals but as the portal pressure increases in cirhhosis, the blood flow is reversed and flows away from the portal circulation[28]**.** Portal pressure should be a minimum of 10mmHg for the varices to develop and 12mmHg for the varices to bleed[28]. The major sites of porto-systemic or porto-caval shunts are lower part of esophagus, umbilicus, rectum and have been depicted in the following picture[27].

FIGURE 14 : PORTO-CAVAL SHUNTS

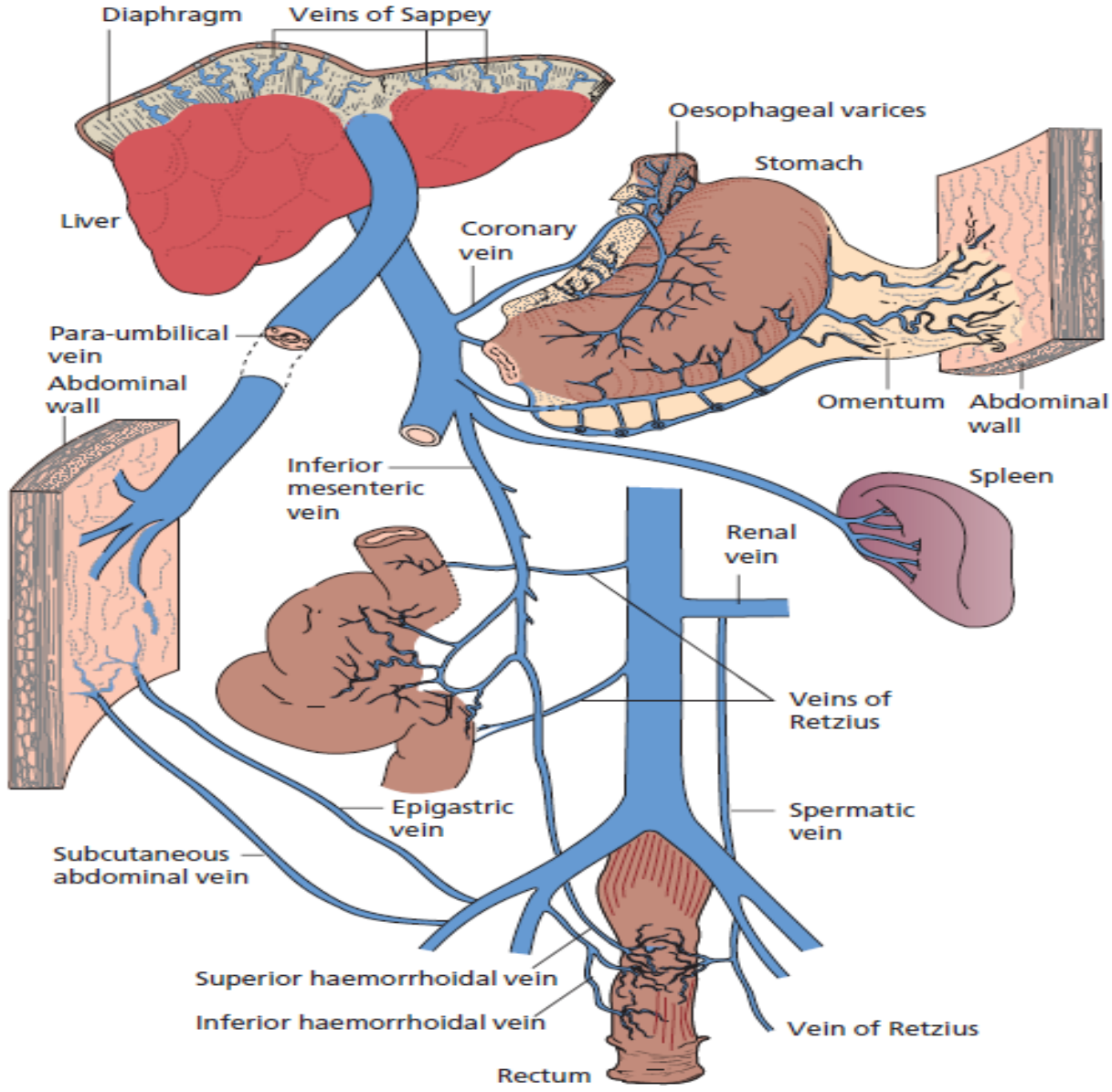
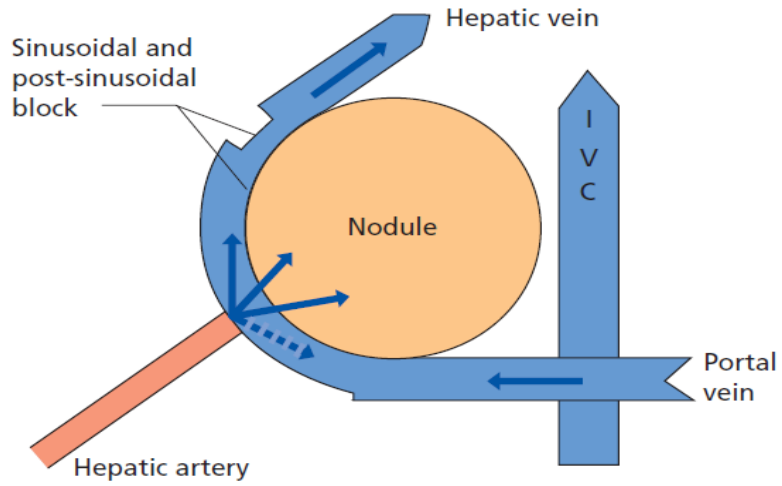


TABLE 5 : CLASSIFICATION OF PORTAL HYPERTENSION[28]

POST HEPATIC	INTRA HEPATIC	PREHEPATIC
Budd-Chiari syndrome	**PRE SINUSOIDAL**	Portal vein thrombosis
Constrictive pericarditis	Idiopathic portal hypertension	Splenic vein
Inferior vena caval	PBC	thrombosis
obstruction	Sarcoidosis	
Right-sided heart failure	Schistosomiasis	
Severe tricuspid regurgitation	**SINUSOIDAL**	
	Alcoholic cirrhosis	
	Alcoholic hepatitis	
	Cryptogenic cirrhosis	
	Postnecrotic cirrhosis	
	POST SINUSOIDAL	
	Sinusoidal obstruction	
	syndrome	

FIGURE 15 : CIRRHOTIC NODULE OBSTRUCTING THE HEPATIC VESSELS



Nodules in cirrhosis mainly supplied by the hepatic artery obstructs the sinusoids and hepatic veins[27]

CLINICAL FEATURES OF PORTAL HYPERTENSION[27] :

Most common cause of portal hypertension is cirrhosis.

Most common presentation is hematemesis.

ABDOMINAL WALL VEINS : Dilated veins radiating from the umbilicus termed as caput Medusae. Cruveilhier-Baumgarten syndrome is the association of dilated abdominal wall collaterals and a loud venous murmur at the umbilicus.

SPLENOMEGALY : Fibrocongestive splenomegaly is more due to reticuloendothelial hyperplasia rather than the portal hypertension. It is larger in younger cirrhotics & in macronodular than in micronodular cirrhosis.

ASCITES : The portal hypertension increases the capillary filtration pressure and thus causes ascites.

GASTRIC & INTESTINAL VASCULOPATHY : Portal hypertensive gastropathy, Gastric antral vascular ectasia. Congestive jejunopathy and colonopathy are seen.

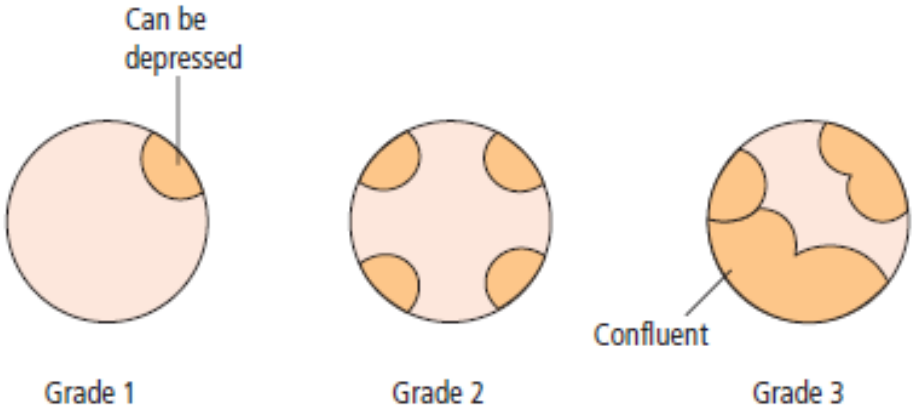
ANORECTAL VARICES : Present in 44% of patients with cirrhosis. They must be differentiated from simple haemorrhoids which are prolapsed vascular cushions which do not communicate with the portal system.

DIAGNOSIS OF PORTAL HYPERTENSION :

Ultrasound, Doppler studies, MRI, Venography, Portal pressure measurement help in diagnosis of portal hypertension[27].

For varices, barium studies & endoscopy are helpful. The following picture shows grades of varices on endoscopy[27].

FIGURE 16 : GRADES OF VARICES ON ENDOSCOPY



Grade 1: Small and straight

Grade 2 : Tortuous and occupying less than one third of the esophageal lumen

Grade 3 : Large and occupying more than one third of the esophageal lumen[28].

TREATMENT OF PORTAL HYPERTENSION

1. DRUGS THAT REDUCE PORTAL BLOOD FLOW :

A) Nonselective β-adrenergic blocking agents (NSBBs like propranolol, nadolol) should be used cautiously with close monitoring of blood pressure, serum sodium and serum creatinine[29].

B) Somatostatin and its analogs - Current recommended regimen is to start these drugs from the admission and to proceed with endoscopic therapy during the diagnostic endoscopy[30].

They act by : a)Glucagon suppression through SSTR 2 receptors

b)Potentiation of PKC-dependent vasoconstrictors through SSTR 2 receptors

c)Attenuation of stellate cells' contraction through SSTR 1 receptors

'a' and 'b' cause splanchnic vasoconstriction and thus decrease the portal and collateral blood flow & 'c' causes reduction of hepatic resistance[30].

A bolus injection is 250 microgram stat followed by 250 picogram/hr is given as continuous infusion usually and if responding to therapy, maintainence is continued for 2-5 days[31].

C) Vasopressin and terlipressin - Vasopressin, the most potent splanchnic vasoconstrictor has serious adverse effects like myocardial ischemia/infarction, arrhythmias, mesenteric ischemia, limb ischemia and stroke in about 25% of the patients making it to be withdrawn in such patients. Adjunctive nitroglycerine reduces these side effects[31].

Terlipressin (triglycyl lysine vasopressin) doesn't produce much fibrinolysis and longer bioavailability. 2 mg/4 hrs is given till a bleeding free period of 1-2 days is achieved. Maintainence dose of 1 mg/4 hrs is given for 5 days to prevent early rebleeding[31].

2. DRUGS THAT REDUCE INTRAHEPATIC RESISTANCE :

A) α1-Adrenergic blocking agents (Prazosin) - No statistically significant difference is observed between the propranolol & prazosin group and the propranolol & isosorbide mononitrate group in terms of clinical manifestations as well as hepatic venous pressure gradient (HVPG)[32].

B) Angiotensin receptor blocking agents - angiotensin blockade decreases vasoconstrictive hyperactivity in hepatic failure[33].

C) Nitrates - these increase intrahepatic nitric oxide bioavailability[33].

3. TIPS (TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT) : It is a side to side porto-systemic shunt. Cirrhotics with Child–Pugh class C/class B having persistent bleed at endoscopy are at high risk for treatment failure, hence early use of TIPS might be useful[34]. After TIPS, mortality rate is 5% and 50% in good risk (Child grade A and B) patients and high risk (Child grade C) patients respectively[27].

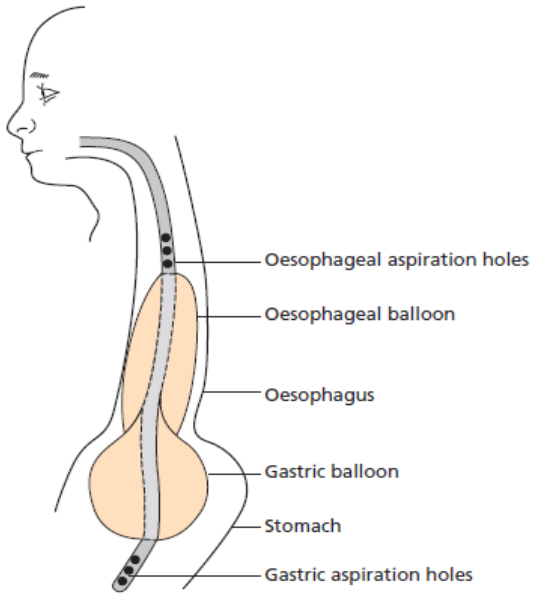
TIPS ENCEPHALOPATHY :

In 25-30% of the patients who undergo TIPS develop encephalopathy. The risk increases with the age of the patient, Child's class and shunt size. Its risk is high in first 3 months and later decreases as there is cerebral adaptation. Its risk can be reduced by placing a smaller stent but resistant encephalopathy may lead to the need of liver transplantation[27].

TABLE 6 : TREATMENT OF VARICES AND VARICEAL BLEEDING[35]

INDICATION	FIRST LINE THERAPY	SECOND LINE THERAPY	THIRD LINE THERAPY
Prevention of first variceal hemorrhage	Non selective beta blockers (NSBBs)	Endoscopic variceal ligation(EVL) in high risk varices	
Acute variceal bleeding	Endoscopic variceal ligation and or drug therapy(somatostatin/ terlipressin)	TIPS(Transjugular intrahepatic portosystemic shunt)	Balloon tamponade (bridge to TIPS)
Prevention of variceal bleeding	NSBBs or EVL	EVL+drug therapy(beta blockers±nitrates)	TIPS

FIGURE 17 : SENGSTAKEN BLAKEMORE TUBE IN POSITION



PROGNOSIS OF CIRRHOTICS WITH PORTAL HYPERTENSION AND VARICES[27] :

- Higher the hepatic venous pressure gradient poorer the prognosis.
- The 1 year survival in cirrhotic with varices good risk patients is about 85% and in bad risk (Child grade C) patients about 30%. 65% of varices in patients with cirrhosis will not rupture in 2 years of diagnosis.
- Abstinence from alcohol improves the prognosis in cirrhotics with ascites where as chronic hepatitis patients continue to do poor.

HEPATORENAL SYNDROME (HRS) :

Renal failure of kidneys associated with severe liver failure without any structural damage to kidneys or some amount of parenchymal damage[26,36].

In 1978 for the first time, a conference was held up in Sassari, Italy, to propose definition, diagnostic criteria for the HRS. International Ascites Club (ICA) founded in Florence, Italy, in 1990 reigned by a group of six members elected every 4 years once, is aimed to conduct research on mechanisms of hemodynamic and kidney dysfunctions in the presence of severe liver failure and on the pathogenesis and management of ascites and its infections, HRS[37].

Acute Dialysis Quality Initiative (ADQI) proposed to name renal failure in cirrhotics as hepatorenal disorders from hepatorenal syndrome[38].

International Club of Ascites (ICA) defined hepatorenal syndrome as renal failure in cirrhotics with those satisfying the following criteria[36] :

"1 Cirrhosis (acute/acute on chronic liver failure) with ascites,

2 Serum creatinine >1.5 mg/dL or increase in serum creatinine by more or equal to 0.3mg/dL within 48hrs or more/equal to 50% from baseline value with urine output $\leq$ 0.5ml/kgBW >6hrs,

3 No improvement in serum creatinine (decrease to 1.5 mg/dL or less) after at least 2 days of diuretic withdrawal and expansion of plasma volume with albumin (1 g/kg of body weight/day up to a maximum of 100 g/day),

4 Absence of shock,

5 No current or recent treatment with nephrotoxic drugs or vasodilators,

6 Absence of parenchymal kidney disease as indicated by proteinuria > 500 mg/day, microhaematuria (>50 red blood cells per high power field), urinary injury markers and/or abnormal renal ultrasonography, suggestion of renal vasoconstriction with FENa(fractional excretion of sodium) of <0.2% especially with levels <0.1% being highly predictive)."

A minor group of cirrhotics due to profound sarcopenia and urea synthesis result in decreased levels of serum creatinine and BUN levels, thus delaying the diagnosis of HRS[38].

CLINICAL FEATURES :

Hepatorenal syndrome usually presents in cases of severe liver damage with refractory ascites with worsening hemodynamic parameters like low mean arterial pressure, low cardiac output due to splanchnic vasodilataion[22].

Although many are asymptomatic, sodium and water retention presents as edema of the body, renal vasoconstriction decreases glomerular filtration rate leading to decrease in urinary output, increases blood urea nitrogen(BUN) and sometimes directly presents as hepatic encephalopathy[38].

Drugs like diuretics, lactulose, angiotensin-converting enzyme(ACEIs) inhibitors, angiotensin receptor blockers(ARBs), and NSAIDs which have an effect on patient's intravascular volume status and renal blood flow have to be withdrawn in the setting of acute kidney dysfunction. Thorough evaluation of spontaneous bacterial peritonitis should be done as 20% of SBP patients manifest with hepato renal syndrome[38]. Hepatomegaly, RAAS activation, Mean arterial pressure and serum electrolytes are the predictors of HRS development[39].

FIGURE 18 : PATHOGENESIS OF HEPATO RENAL SYNDROME[27,38,40]

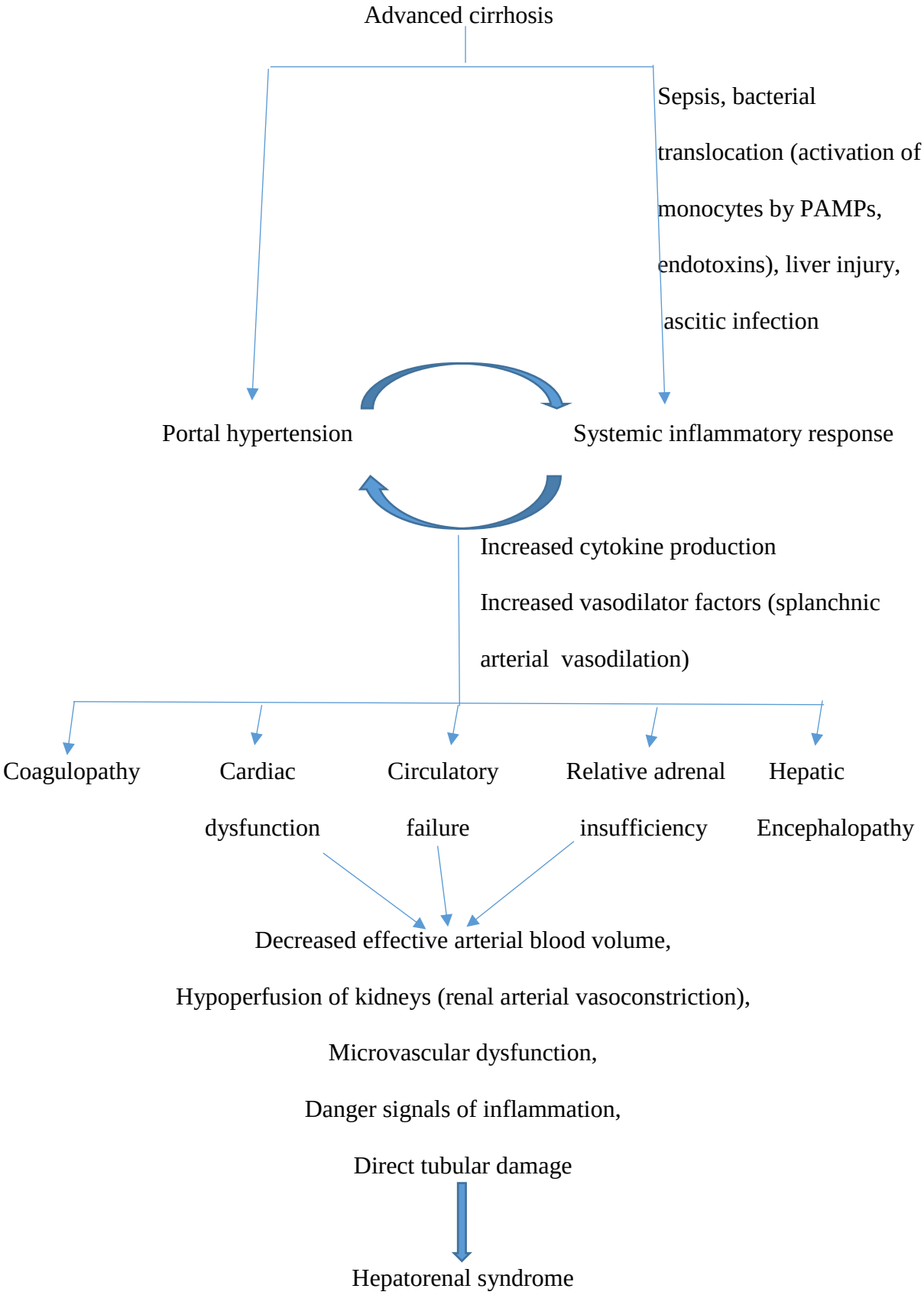


TABLE 7 : CLASSIFICATION OF HEPATO RENAL SYNDROME[36]

OLD CLASSIFICATION	NEW CLASSIFICATION	CRITERIA
HRS 1	**HRS-AKI**	a)Serum creatinine ≥0.3 mg/dl within 2 days and or b)Urinary output ≤ 0.5 ml/kgBW ≥6 hr or c)Serum creatinine ≥50% using the last available value of outpatient value within 3 months as the baseline value
HRS 2	**HRS-NAKI** **A)HRS-AKD** **B)HRS-CKD**	**A) HRS-AKD** a)Effective glomerular filtration rate <60 ml/min per 1.73 m^2 of body surface area for <3 months in the absence of other (structural) causes b) Serum creatinine ≥50% using the last available value of outpatient value within 3 months as the baseline value **B)HRS-CKD** Effective glomerular filtration rate <60 ml/min per 1.73 m^2 of body surface area for <3 months in the absence of other (structural) causes

PREVENTION OF HRS[38,40,41] :

1. Prevention of variceal bleeding (NSBBs, EVL)

2. Pentoxifylline for severe alcoholic hepatitis

3. Withdrawal of drugs causing decrease in intravascular volume

4. Cautious use of nephrotoxins (ACEIs, ARBs, NSAIDs, antibiotics)

5. Aggressive prophylaxis, diagnosis and treatment of ascitic infections with norfloxacin[41,]

6. Albumin

TREATMENT OF HRS[38,40] :

1. Withdraw all nephrotoxic agents (ACEIs, ARBs, NSAIDs, diuretics)

2. Prompt use of antimicrobials for infections

3. Inj human albumin bolus of 1 g/kg/day on presentation upto highest dose of 100 g/day followed by maintainence dose of 20-60 g/day to maintain central venous pressure between 10 to15 cm H2O

4. Vasopressor therapy for a maximum duration of 14 days until reversal of hepatorenal syndrome or liver transplantation (along with albumin):

a. Terlipressin : 1 mg/4 hr , can increase the dose to 2 mg/4 hr if creatinine level is not improved by 25% at day 3 of therapy

OR

b. Midodrine : 2.5-5 mg TID per oral can be increased till 15 mg TID to a mean arterial pressure of 15 mm Hg.

Octreotide : 100 μg s/c TID,can be increased to 200 μg TID, or start octreotide at a 25μg IV stat dose followed by maintainence dose of 25 μg/hr.

OR

c. Norepinephrine : 0.1-0.7 μg/kg/min as an IV infusion. Increased by 0.05 μg/kg/min every 4 hr and titrate to an MAP increase of at least 10 mm Hg

- Combination of vasopressors with albumin resolve 60% of the kidney dysfunctions in cirrhotics[40].
- Noradrenaline and terlipressin are equally effective pharmacologically but the former is cost effective[42].
- Terlipressin + albumin combination has higher efficacy than midodrine & octereotide + albumin[43].

5. TIPS[40]

6. Extracorporeal albumin dialysis (ECAD)[40]

Removal of albumin and its bound substances with the molecular adsorbent recirculating system (MARS) method can treat HRS, especially type 1[44].

7. Liver transplantation

PROGNOSIS OF CIRRHOTICS WITH HEPATORENAL SYNDROME :

HRS type 1 and those with lower Model for End stage Liver Disease (MELD) score have better prognosis[45].

HEPATOPULMONARY SYNDROME(HPS) :

Cirrhosis produces vascular changes in various organs. In the lungs, right-to-left intrapulmonary shunts, vascular dilatation are common[46]

1. In 5-30% of cirrhotics who are evaluated for liver transplantation, there occurs microvascular alterations impairing the gaseous exchange resulting in hepatopulmonary syndrome which inturn leads to profound hypoxemia which is very difficult to treat[27,47].

2. In 5% of cirrhotics, vasoconstriction and remodeling in resistance vessels increase pulmonary arterial pressures resulting in Portopulmonary hypertension(POPH) leading to right heart failure[27,47].

The prevalence of HPS ranges from 5-32% in cirrhotics and in1966, Berthelot et al. identified that pulmonary vascular dilatation may play a role in HPS[48].

FIGURE 19 : PATHOGENESIS OF HEPATOPULMONARY SYNDROME[38]

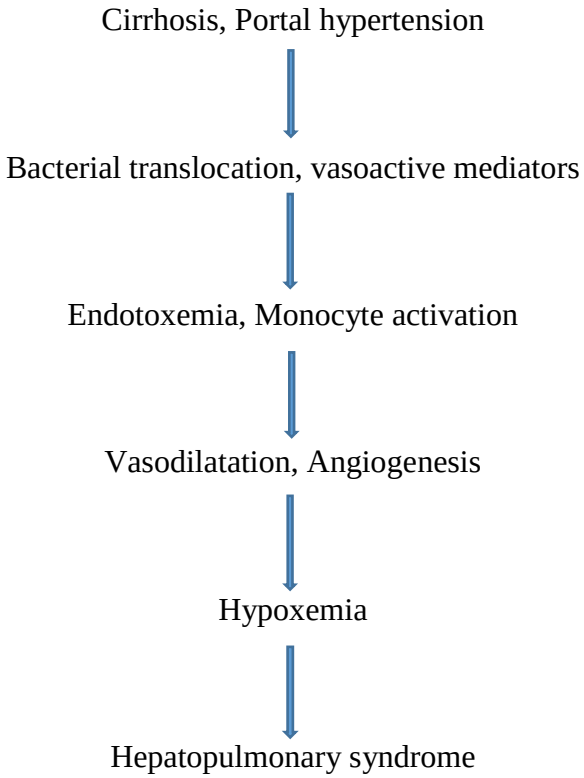


TABLE 8 : DIFFERENCES BETWEEN HPS AND POPH[49,50]

CHARACTERISTICS	HPS	POPH
Pathology	Arterial hypoxemia caused by intrapulmonary vasodilatation	Pulmonary artery hypertension
Clinical picture[50]	Respiratory symptoms (platypnea)	Usually asymptomatic
Diagnostic criteria	PaO_2 < 80 mm Hg	mPAP > 25 mm Hg; PVR > 3 wood units
Associated liver disorder	Cirrhosis but no correlation with its severity	Always portal hypertension but no correlation with its severity
Prevalence	5%-32%	5%-10%
Medical treatments	Supplementation of oxygen	Pulmonary vasoactive medications
5-Year survival rate	23% (no treatments)	4%-14%; 40% survival rate with pulmonary vasoactive medications
Liver transplant	Indicated	Contraindicated if mPAP > 45 mm Hg
Treatment outcomes	Complete resolution with liver transplant	Unpredictable, 50% resolution with liver transplant

CLINICAL FEATURES[51] :

1. Dyspnea on exertion

2. Platypnea(breathlessness on sitting up from lying position)

3. Orthodeoxia (PaO_2 reduction of more than 5% or more than 4 mm Hg on sitting up from lying position**)**

4. Clubbing and cyanosis

5. Diffuse telangiectasias

- Chest xray may be normal or show bilateral basal reticulonodular opacities
- Pulmonary function testing shows reduced diffusing capacity when carbon monoxide is made to inhale.

DIAGNOSTIC CRITERIA[52] :

1. Liver disease/failure with or without portal hypertension

2. Partial pressure of oxygen < 80 mmHg or alveolar–arterial oxygen gradient [P(A-a) O_2 gradient] ≥ 15 mmHg (or > 20 mmHg for patients > 65-years-old) while breathing ambient air

3. Positive contrast-enhanced echocardiography or lung perfusion scanning with radioactive albumin showing intrapulmonary vascular dilatation.

TABLE 9 : HEPATOPULMONARY SYNDROME-SEVERITY CLASSIFICATION[53]

Mild	P(A-a) O_2 gradient ≥ 15 mmHg, PaO_2 ≥ 80 mmHg
Moderate	P(A-a) O_2 gradient ≥ 15 mmHg, PaO_2 ≥ 60 mmHg to < 80 mmHg
Severe	P(A-a) O_2 gradient ≥ 15 mmHg, PaO_2 ≥ 50 mmHg to < 60 mmHg
Very severe	P(A-a) O_2 gradient ≥ 15 mmHg, PaO_2 < 50 mmHg

TREATMENT :

A) O_2 supplientation,

B) Pentoxyfylline,

C) TIPS with pulmonary angiography to embolize the vessels,

D)Intrapulmonary shunting

E) Anticoagulants if marked coagulopathy, varices are present

F) Withdrawal of NSBBs was found to improve right heart failure, early ligation of varices and withdrawal of regarding medical therapy is recommended.

G) Prostacyclin analogues(Epoprostenol, Iloprost, Treprostinil). Epoprostenol requires an intravenous complex pump with central venous line and continuous monitoring. Life threatening complications like rebound pulmonary vasoconstriction are known to occur if the drug delivering pump fails. Side effects with other drugs are minimal like flushing, headache, cough. Iloprost given for 1 year shows good results[54].

H) Oral endothelin receptor antagonists(bosentan, Ambrisentan). These inhibit the angiogenesis by inhibiting the endothelin A and B receptors[55].

I) Oral phosphodiesterase-5 inhibitors(sildenafil,Tadafil, Vardenafil)

J) N^G-nitro-L-arginine methyl ester (L-NAME), an inhibitor of nitric oxide synthesis[56]

K) Liver transplantation

PROGNOSIS OF CIRRHOTICS WITH HPS:

HPS individually worsens the prognosis of cirrhotics[57].

HEPATOCELLULAR CARCINOMA :

It is found that death rate in cirrhotics with hepatocellular carcinoma (HCC) is increasing in Europe and United states, whereas death rate in cirrhotics due to non HCC is decreasing or is stable. In compensated cirrhotics, HCC is the most common cause of liver related deaths. Hepatitis C virus (HCV) infection, herediatary hemochromatosis, hepatitis B infection are the major causes of HCC in cirrhotics[58]. Co-infections of the viruses increase the risk of HCC further[59]. Elderly males with severe liver failure are more prone for this complication. Metabolic syndrome is a preventable comorbidity of HCC risk in cirrhotics and even in non-cirrhotics, metabolic syndrome produces risk of HCC[60]. Endoglycosidase heparanase which plays a major role in tumor cell invasion, vascular sprouting and metastasis is associated with pathogenesis of HCC in liver cirrhosis[61].

HEPATIC ENCEPHALOPATHY :

Hepatic Encephalopathy, the most common complication of liver cirrhosis, occurs in half-three fourths of the cirrhotics[62]. In upto 84% of the patients unidentified neuropsychological deficits exist even with normal neurological examination, thus proving the point of having underlying neurobehavioural changes of the disease[6].

Hepatic encephalopathy consists of transient, subtle, reversible spectrum of neuropsychiatric deficits from clinically unidentifiable manifestations to clinically identifiable changes like alterations in behaviour, motor activity, cognition, conscious level[62].

EPIDEMIOLOGY

The incidence of hepatic encephalopathy ranges from 2% to 20% in an year(far eatern areas in Asia) but China reported upto 40%[63].

In a study done from 2001-2017, in Sweden by Nilsson E, Anderson H et al, the cumulative incidence of hepatic encephalopathy in 1317 cirrhotics is as shown in the following table[64].

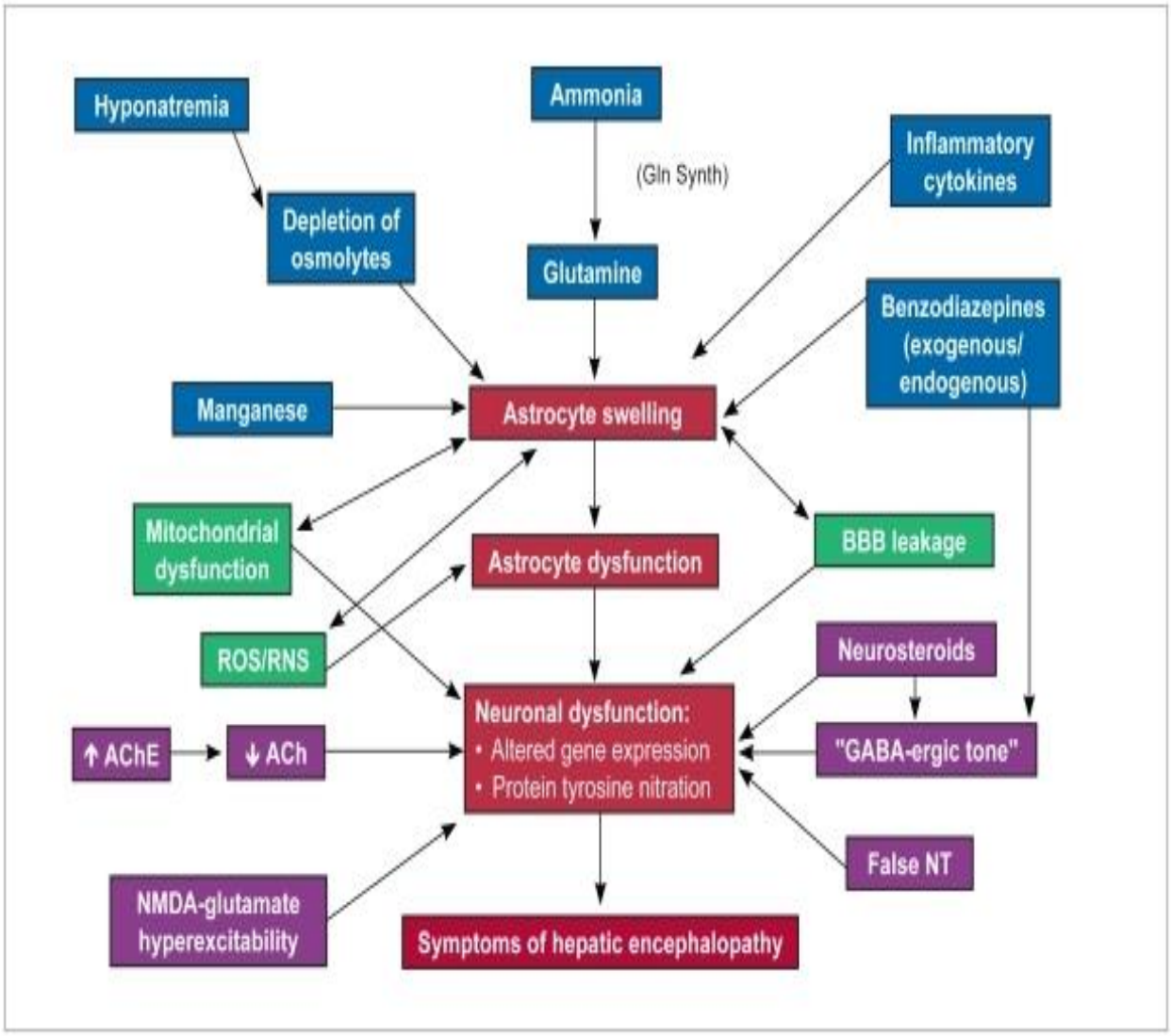
TABLE 10 : ETIOLOGY, INCIDENCE OF HEPATIC ENCEPHALOPATHY[65]

ETIOLOGY OF CIRRHOSIS	1YEAR INCIDENCE	10 YEAR INCIDENCE
Alcoholic cirrhosis	21%	42%
Hepatitis C infection	3%	23%
Cryptogenic cirrhosis	14%	22%
NASH	6%	30%
Primary biliary cholangitis	6%	24%
Primary sclerosing cholangitis	0%	7%
Autoimmune hepatitis	10%	14%
Other causes (Hepatitis B, Alpha 1 antitrypsin deficiency, Hemochromatosis)	6%	25%

In China, the incidence of subclinical hepatic encephalopathy(SHE) is found to be 50.9% of cirrhotic patients without any clinically identifiable manifestations. Its prevalence was found to increase with the severity of liver functions[65].

Wang and colleagues in 2013, assessed health-related quality of life (HRQoL) in minimal hepatic encephalopathy patients which reflected a poorer quality of life[66].

FIGURE 20 : PATHOGENESIS OF HEPATIC ENCEPHALOPATHY[67]



Ach-Acetylcholine, AchE-Acetylcholinesterase, BBB-Blood brain barrier, GABA-Gamma aminobutyric acid, Gln Synth-Glutamine synthetase, NMDA-N methyl D aspatic acid, NT-neurotransmitter, RNS-reactive oxygen species.

Neurosteroids like tetrahydroprogesterone (allopregnanolone) and tetrahydrodeoxycorticosterone (THDOC) are synthesized in astrocytes. These modulate the GABA-A receptors and increase the inhibitory transmission in neurons leading to manifestations of hepatic encephalopathy[68].

CONCEPT OF SYNERGISM :

Leslie Zieve in the 1970s, identified that toxins like phenols and mercaptans act synergistically with ammonia and enhance the neuronal damage.

Now the redefined concept of synergism says manganese, proinflammatory cytokines along with ammonia activate the peripheral-type (mitochondrial) benzodiazepine receptors resulting in increased amount of neurosteroids and thus increased neuroinhibition through GABAergic tone[69].

CLASSIFICATIONS IN HEPATIC ENCEPHALOPATHY :

1. WEST HAVEN CRITERIA[70]:

3 main types of Hepatic Encephalopathy

Type A : Associated with acute liver failure.

Type B : Associated with portosystemic shunts in the absence of liver disease.

Type C : Associated with chronic and end stage liver disease and portal hypertension.

Type C hepatic encephalopathy is the most common type and has been graded from 0 to 4 based on West Haven criteria(WHC) based on changes in conscious level, cognitive function, behavioral changes and also classified into episodic, persistent and minimal types[71].

FIGURE 21 : EPISODIC, PERSISTENT AND MINIMAL HEPATIC ENCEPHALOPATHY[71]

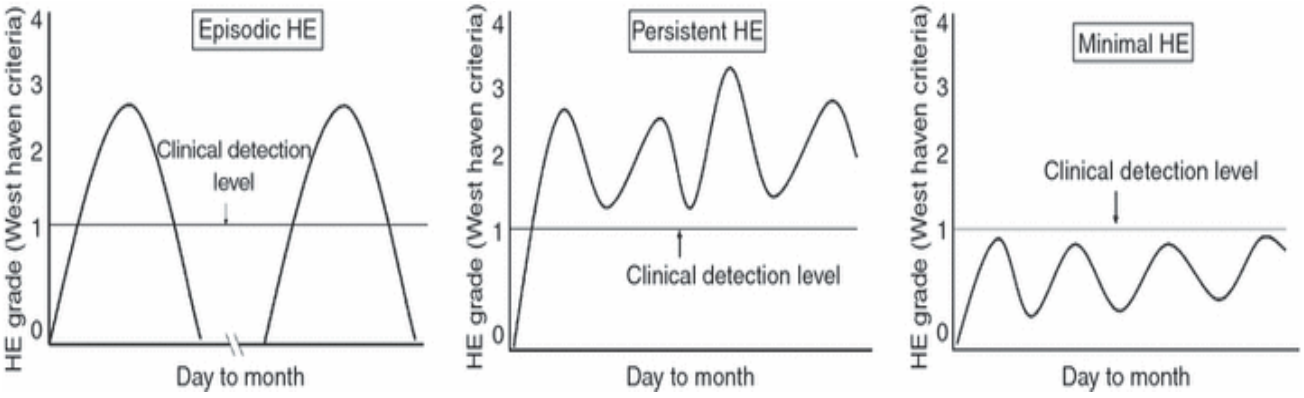


TABLE 11: WESH HAVEN CRITERIA GRADES

GRADE	NEUROLOGICAL MANIFESTATIONS
0	No alteration in the conscious level, no intellectual abnormalities or behavioural changes
1	Minimal lack of awareness, euphoria or anxiety, disorientation to time, reduced span of attention/concentration, inability to do addition/subtraction.
2	Lethargy, disorientation, behavioural changes
3	Somnolence to semistupor, confusion, bizarre behavior, responds to painful stimuli
4	Coma, no reponse to painful stimuli, cant test mental state

2. SONIC CLASSIFICATION[72]:

A consensus report in 2011 proposed a new SONIC (Spectrum Of Neurocognitive Impairment In Cirrhosis) nomenclature to reflect the wide spectrum of clinical findings and improve the clinical classification of hepatic encephalopathy for research studies. Based on SONIC classification, cirrhotic patients are divided into 3 categories **:** unimpaired, covert and overt hepatic encephalopathies.

- Unimpaired patients have no clinical, neurophysiologic or neuropsychometric abnormalities.
- Patients with covert hepatic encephalopathy have minimal hepatic encephalopathy(clinically normal patients with abnormal cognition or neurophysiologic test results) or grade 1 hepatic encephalopathy by West Haven criteria.

- Patients with overt hepatic encephalopathy have grade 2 hepatic encephalopathy or higher by West Haven Criteria.

This classification doesn't distinguish minimal hepatic encephalopathy from grade 1 hepatic encephalopathy, and takes the advantage of the recognition that disorientation , specifically to time distinguishes grade 1 from grade 2 hepatic encephalopathy and distinguishes covert from overt hepatic encephalopathy.

TABLE 12 : SONIC CLASSIFICATION

CLASSIFICATION	MENTAL STATUS	SPECIAL TESTS	ASTEREXIS
Unimpaired	Not impaired	Normal	Absent
Covert Hepatic Encephalopathy	Not impaired	Abnormal	Absent
Overt Hepatic Encephalopathy	Impaired	Abnormal	Present (absent in coma)

FIGURE 22 : DIFFICULTIES WITH CLINICAL CLASSIFICATIONS OF HEPATIC ENCEPHALOPATHY

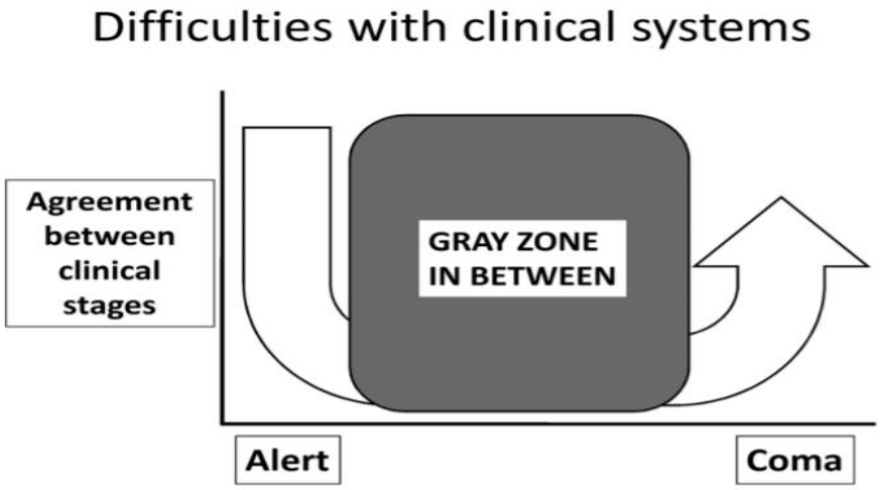
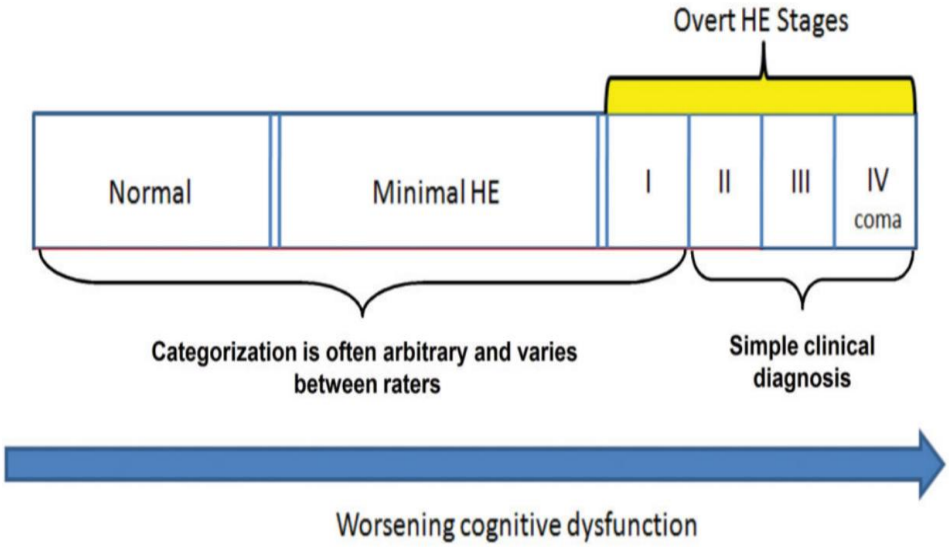


FIGURE 23 : SPECTRUM OF COGNITION IN HEPATIC ENCEPHALOPATHY



3.GLASGOW COMA SCALE[73]:

Glassgow Coma Scale is more reliable than the West Haven Criteria it is less sensitive in quantifying the mildest forms of hepatic encephalopathy and is much better suited for advanced hepatic encephalopathy.

4.CLINICAL HEPATIC ENCEPHALOPATHY STAGING SCALE (CHESS) [74]:

The Clinical Hepatic Encephalopathy Staging Scale(CHESS) differentiates minimal from overt hepatic encephalopathy but not helpful in severe hepatic encephalopathy.

5.HEPATIC ENCEPHALOPATHY SEVERITY ALGORITHM[75]:

This algorithm provides objective assessment of cognitive areas outlined in the West Haven Criteria, using clinical and neuropsychological indicators and has been validated in patients with WHC grades 3,4 encephalopathy but not in milder forms of hepatic encephalopathy.

6.PORTOSYSTEMIC ENCEPHALOPATHY SCORE AND INDEX[76]:

The portosystemic Encephalopathy index combines the assessment for mental state, ammonia levels, EEG, the number connection test/trail test, degree of asterixis.

TABLE 13 : PORTO SYSTEMIC ENCEPHALOPATHY SCORE[76]

SCORE	MENTAL STATE	TRAIL MAKING (SEC)	ASTEREXIS	VENOUS AMMONIA (MG/DL)	EEG (CYCLES/S)
0	No abnormality detected	≤30	Nil	≤80	Normal alpha waves 8.5-12
1	Trivial lack of awareness, Euphoria or anxiety, Shortened attention span. Impaired addition or subtraction	31-50	Rare flapping motion	81-105	7-8
2	Lethargy, Disorientation to time, Obvious personality change, Inappropriate behaviour	51-80	Occasional irregular flaps	106-135	5-7
3	Somnolence to semi stupor, Responsive to stimuli, Confused, Gross disorientation, Bizzare behaviour	81-120	Frequent flaps	136-160	3-5
4	Coma	>120	Continuous flapping	>160	≤3

PSE_{sum} (PORTO SYSTEMIC ENCEPHALOPATHY SUM) = 3 x mental status score + trail making score + asterixis score + ammonia score.

PSEI(PORTO SYSTEMIC ENCEPHALOPATHY INDEX) = PSE_{sum}/Highest possible sum.

TABLE 14 : DIAGNOSIS OF HEPATIC ENCEPHALOPATHY[77]

TEST	TYPE	MOST SUITABLE FOR	ADVANTAGES	DIS ADVANTAGES	RECOMMENDED
Arterial ammonia	Blood test	ALF	Simple to perform	Lacks diagnostic accuracy in low-grade HE	Only in ALF or high-grade type C HE
cGMP	Blood test	MHE	Simple to perform	Not widely available	Further validation
EEG	Neurophysiological	Any	Validated changes in HE	Lacks specificity	Use in conjunction with other tests
EP	Neurophysiological	Type C	Can reveal other pathologies	specific equipment required	Use in conjunction with other tests in research setting
PHES	Psychometric battery (pencil and paper)	Any	Well validated	Limited number of cognitive domains	Gold standard in Europe for MHE
RBANS	Psychometric battery (computerized)	MHE	Validated in chronic HE	Relatively time consuming	Gold standard in USA for MHE

CDR	Psychometric battery (computerized)	MHE	Validated, online version	Learning effect	Useful research tool
CFF	Psychophysical	Any	Simple, quick	Requires close supervision	Screening test
ICT	Neuropsychological	MHE	Well validated in non-HE populations	Requires standardization	Screening test
MRI	Imaging	Any	Highly objective	Difficult to use in severe HE; false-negative in MHE	Useful to rule out other pathology
MRS	Imaging/ spectroscopic	Any	Interrogates cellular processes	Requires standardization	Useful research tool
PET	Imaging/nuclear medicine	Type C	Interrogates cellular processes	Expensive	Research tool

ALF: Acute liver failure; CDR: Cognitive Drug Research; CFF: Critical flicker frequency; EP: Evoked potentials; HE: Hepatic encephalopathy; ICT: Inhibitory control test; MHE: Minimal hepatic encephalopathy; MRS: Magnetic resonance spectroscopy; PHES: Psychometric Hepatic Encephalopathy Score; RBANS: Repeatable Battery for the Assessment of Neurophysiological Status; EEG: Electroencephalogram

NEUROPSYCHOLOGICAL TESTS :

ELECTROENCEPHALOGRAM :

Normal or low frequency alpha rhythm (8.5 Hz) interrupted by random waves in the theta range (4-8 Hz) over both the hemispheres with haphazard appearance of rare high voltage waves in the delta region(<4 Hz) are the usual changes observed in hepatic encephalopathy on EEG. Triphasic waves are usually seen. Reduced or absent eye opening reactivity is observed[78]. It is costlier and time consuming test.

EVOKED POTENTIALS :

Evoked potentials are obtained either through the passive reception of sensory stimuli ('exogeneous' EPs) or cognitive treatment of sensory stimuli ['endogenous' EPs / 'cognitive' EPs (CEPs)].

Exogeneous EPs are further classified according to :

- The type of sensory stimulus used [visual (VEP), auditory (AEP) or somatosensory (SEP)]
- Analysis time window (short-latency, middle-latency or long-latency EPs).

Electroencephalogram assesses only cortical function whereas evoked potentials not assess both the brainstem and the cerebral cortex but also provide a quantitative assessment of some cognitive processes.

All the evoked potential parameters are briefed into two indices: the index of global cortical function (IGCF) and the index of brainstem conduction (IBSC).

IGCF was shown to be correlated with the Glasgow Coma and also highly significant relationship is observed between EEG and IGCF grades[79]. This test requires special equipment.

INHIBITORY CONTROL TEST :

A simple computerized psychometric test in which patients are shown a series of letters and are asked to respond by clicking the mouse key when an X is followed by a Y, or a Y is followed by an X (alternating presentation, termed targets). Patients are instructed not to respond to X following X or Y following Y (nonalternating presentation, termed lures). Target recognition requires cognitive functions like reaction time whereas avoidance of lures require response inhibition, attention, and working memory. High lure and low target response indicate poor psychometric performance. This test needs higher level of education to perform[80].

CRITICAL FLICKER FREQUENCY :

Critical flicker frequency is a highly reproducible parameter with little age which is done in day time and is dependent on training. The threshold frequencies at which light pulses are sensed as fused are termed fusion frequencies and that sensed as flickering light are termed as critical flicker frequencies [CFF]. Significantly lower frequencies were observed in hepatic encephalopathy[71].

COGNITIVE DRUG RESEARCH :

It consists of five psychometric subsets that test attention power, attention continuity, speed of memory and quality of episodic and working memory and has been developed by Cognitive Drug Research (CDR)[81]. It is a computerized test which needs higher level of education.

REPEATABLE BATTERY FOR THE ASSESSMENT OF NEUROPHYSIOLOGICAL STATUS :

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) serves dual purposes[82] :

- Identifies and characterizes abnormal cognitive decline in the elderly
- Neuropsychological screening battery for younger patients.

This test takes less than half an hour to administer, and yields scaled scores for five cognitive domains which are [82]:

1. Immediate Memory - a) List learning
   b) short memory
2. Visuospatial/Constructional – a) Figure copying
   b) Line orientation
3. Language – a) Picture naming
   b) Semantic fluency
4. Attention – a) Digit span
   b) Coding
5. Delayed Memory – a) List Recognition
   b) Story recall
   c) Figure recall.

PSYCHOMETRIC HEPATIC ENCEPHALOPATHY SCORE :

Schomerus and Hamster devised a psychometric battery comprising the Digit Symbol Test (DST), the Trail Making Test A & B(TMT-A, TMT-B), the Serial Dotting Test (SDT) and the Line Tracing Test (LTT). Score obtained by these series of tests was called Psychometric Hepatic Encephalopathy Score (PHES) by Weissenborn et al. It is considered the gold standard for minimal hepatic encephalopathy in Europe[83].

CONSTRUCTIONAL APRAXIA:

Intellectual deterioration in Hepatic Encephalopathy varies from slight impairment of mental function to gross confusion. Isolated abnormalities appearing in the setting of clear consciousness relate to disturbances in visuo spatial gnosis. These are most easily elicited as Constructional apraxia.

The clock-drawing test was originally developed in the early 1900s to evaluate soldiers who had suffered head wounds to the occipital or parietal lobes, injuries that often led to difficulty composing images correctly with the appropriate number of parts of correct size and orientation (i.e., constructional apraxia). To depict a clock, patients must be able to follow directions, comprehend language, visualize the proper orientation of an object, and execute normal movements.The clock-drawing test is unaffected by the patient's level of education[84].

Star drawing scores were given in a study by Edwin N, Peter JV et al. in 2011[76].

Clock and star drawing may serve as reproducible, inexpensive bedside tools for diagnosing and grading the severity of hepatic encephalopathy.

According to a study done by Edwin N et al, depicting the relationship between clock and star drawing and the degree of hepatic encephalopathy, the grading of hepatic encephalopathy was done as follows based on clock and star drawing[76].

TABLE 15 : SCORING SYSTEM FOR STAR DRAWING[76]

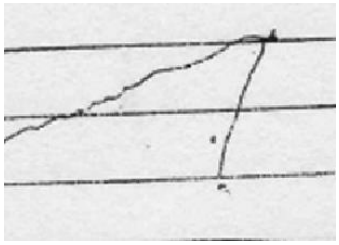
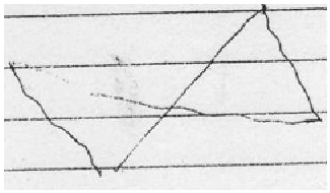
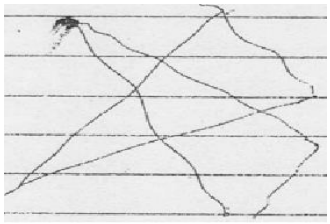
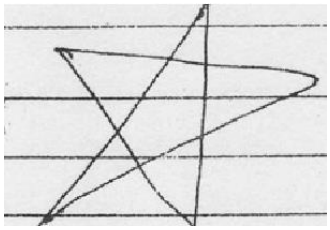
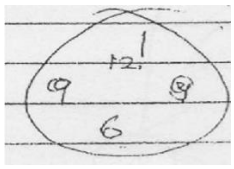
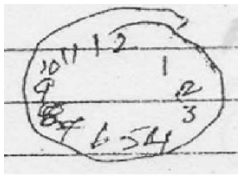
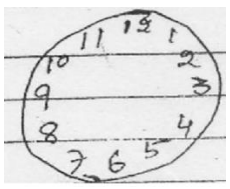
SCORE	CRITERIA FOR STAR DRAWING, SAMPLE FIGURE
0	Unable to draw.
1	Scribble. 
2	Able to draw lines but unable to connect sensibly to form the desired figure. 
3	Able to draw but imperfect 
4	Perfect star 

TABLE 16 : SCORING SYSTEM FOR CLOCK FACE DRAWING[76]

SCORE	GRADE FOR CLOCK DRAWING	CRITERIA FOR GRADE OF CLOCK DRAWING AND SAMPLE FIGURE
0	Poor	Non-recognisable drawing or gross distortion of the basic gestalt. 
1	Fair	Clock should contain an approximately circular face or the numbers 1 through12. 
2	Good	Clock should contain 2 of the following: circular face/ Numbers 1 through 12/ Symmetric number placement. 
3	Excellent	Near perfect representation of the items with all appropriate components placement and perspective. 

TREATMENT OF HEPATIC ENCEHALOPATHY :

1. Nutritional management[85] :

- Weight reduction and correction of vitamin deficiencies.
- 35–45 kcal gram per day of energy products with small quantity meals with proper distribution throughout the day are recommended and in the late-night ended with complex carbohydrates so that protein usage by the body is reduced.
- Normal amount of protein1.2–1.5 g kg/day is recommended.

2. Ammonia-lowering strategies :

a) Non-absorbable disaccharides like lactulose and lactitol : in 1966, Johannes Bircher first used these for hepatic encephalopathy. These interfere with glutamine uptake by intestinal cells, causes catharsis and increases transit time, beneficially effect the flora of intestine[86].

b) Antibiotics: neomycin, rifaximin

Rifaximin prevented remissions of hepatic encephalopathy thus the hospitalizations effectively[87].

c) Branched chain amino acids (BCAAs) like valine, leucine, and isoleucine increase the degradation of ammonia in voluntary muscles[88].

d) L-ornithine L-aspartate (LOLA): Mixture of 2 aminoacids stimulates urea synthesis by hepatocytes and ammonia removal via glutamine synthesis in voluntary muscles[89].

e) Benzoate, phenylacetate

f) L-carnitine

3. Neuropharmacological approaches :

a) GABA receptor modulators inhibit the increased GABAergic tone[90].

b) Anti-inflammatory agents: Minocycline is known to reduce the astrocytic activation and edema of the brain[91].

c) Centrally-acting agents

d) Liver transplantation

PROGNOSIS OF CIRRHOTICS WITH HEPATIC ENCEPHALOPATHY :

- Psychometric hepatic encephalopathy score ≤−6 has poor outcome[91].
- Patients even with severe HE with no organ dysfunction other than mechanical ventilation had good prognosis[92].

MATERIALS AND METHODS :

SOURCE OF DATA :

- Data was collected from patients who were admitted in BLDE (Deemed to be) University's Shri B.M.Patil's Medical College Hospital and Research Centre, Vijayapura.
- Period of study was from November 2018 to June 2020.

METHOD OF COLLECTION OF DATA :

INCLUSION CRITERIA :

All the patients who were admitted in medical wards of shri.B.M.Patil Medical college with cirrhosis, diagnosed with :

1)Clinical history,

2)By the presence of sonological evidence of shrunken liver or splenomegaly with collaterals and or endoscopically proven oesophageal varices constitute evidence.

Histological confirmation was not mandatory for inclusion in the study.

EXCLUSION CRITERIA :

Patients with Acute liver cell failure, those comatose or having an alternate non-hepatic cause for low sensorium such as hyponatraemia, sedative overdose, alcohol consumption, uraemia and hypoglycaemia were excluded.

METHOD OF CONDUCT OF STUDY :

Patients diagnosed with clinical and sonological evidence of cirrhosis admitted in Shri B.M.Patil Medical college were graded according to West Haven Criteria and Porto Systemic Encephalopathy index and compared with the degree of constructional apraxia which was judged by patient's ability to copy a star and clock face on the day of admission.

PSE_{sum} (PORTO SYSTEMIC ENCEPHALOPATHY SUM) and PSEI (PORTO SYSTEMIC ENCEPHALOPATHY INDEX) was calculated for all patients included in the study. For the trail making component, the patients were asked to connect a series of 25 arbitarily arranged numbered dots in sequence. Electroencephalography(EEG), which is not routinely done for the evaluation of hepatic encephalopathy, was not performed due to resource constraints as well as the fact that removal of EEG score doesn't alter the validity of PSEI test. As comatose patients were excluded, the highest possible mental score was 9. Thus PSE_{sum} ranged from 0-21 and PSEI from 0-1.

The diagnosis of hepatic encephalopathy was made if the WHC grade was > 0 or the PSEI was $\geq$ 0.33 in the setting of underlying cirrhosis and other causes of altered conscious state were excluded.

The drawings of clock face and star were scored depending on the person's ability to draw the clock and star diagrams given to them.

TYPE OF STUDY :

Cross sectional observational study

SAMPLE SIZE :

50

The proportion of Hepatic encephalopathy 15.4% in grade 0 and at 95% confidence level , at 10% absolute error, the sample size calculated is 50, using statistical formula,

$$N=(Z^2 * P*Q) / d^2$$

Z = Confidence level

P = Proportion value

d = Absolute error

STATISTICAL METHODS :

Distribution of demographic data, etiology of cirrhosis, mean values of alcohol consumption, laboratory values, PSEI were all computed. Association between ammonia and Child Pugh scores, ammonia and degree of hepatic encephalopathy (WHC grades) were tested. Associations were tested between PSEI, WHC each with clock and star scores. Sensitivity, specificity, positive predictive values, neagative predictive values of clock and star for the diagnosis of hepatic encephalopathy were computed. Relationship between PSEI and clock or star scores was also assessed using Kruskal-Wallis test. If the Kruskal-wallis was significant, Tukey all pairwise multiple comparisons were done to determine which pairs of scores were significantly different.

OSERVATIONS :

TABLE 17 : DISTRIBUTION OF AGE AMONG SUBJECTS

AGE	NO. OF PATIENTS	PERCENT
< 30	5	10.0
30 - 39	8	16.0
40 - 49	17	34.0
50 - 59	13	26.0
60 - 69	6	12.0
70+	1	2.0
TOTAL	50	100.0

TABLE 18 : MEAN AGE DISTRIBUTION

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
AGE	24	80	45.36	11.972

Table 17, 18 and figure 24 demonstrate the age distribution of the patients with cirrhosis observed in this study. The maximum number of patients lie in the age group of 40-49 and the mean age of subjects is 45.36 $\pm$ 11.972. Cirrhosis occurred at as less as 24 years of age and only one patient of above 70 years of age with 80 years was observed in this study.

FIGURE 24 : DISTRIBUTION OF AGE AMONG SUBJECTS

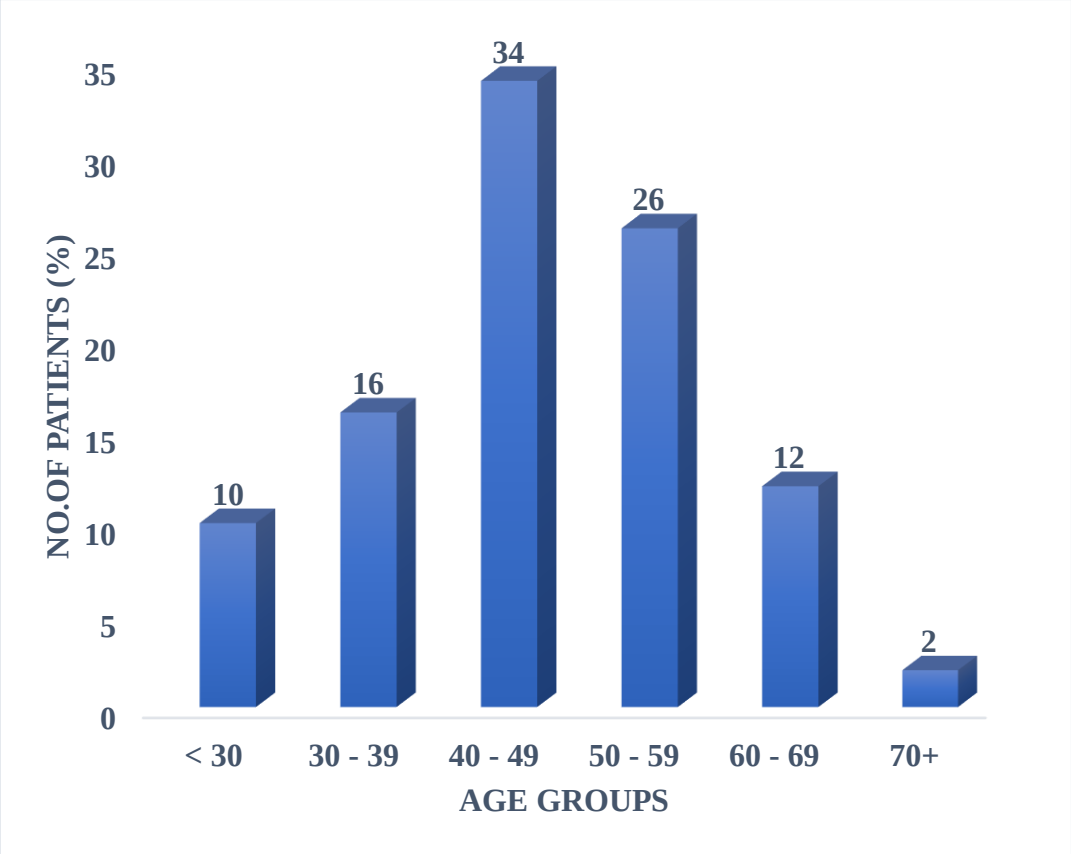


TABLE 19 : DISTRIBUTION OF GENDER AMONG SUBJECTS

GENDER	NO. OF PATIENTS	PERCENTAGE
FEMALE	2	4
MALE	48	96
TOTAL	50	100

Table 19 and figure 25 demonstrate the distribution of sex among the subjects with male preponderance of 96% with 48 males among 50 subjects.

FIGURE 25 : DISTRIBUTION OF GENDER AMONG SUBJECTS

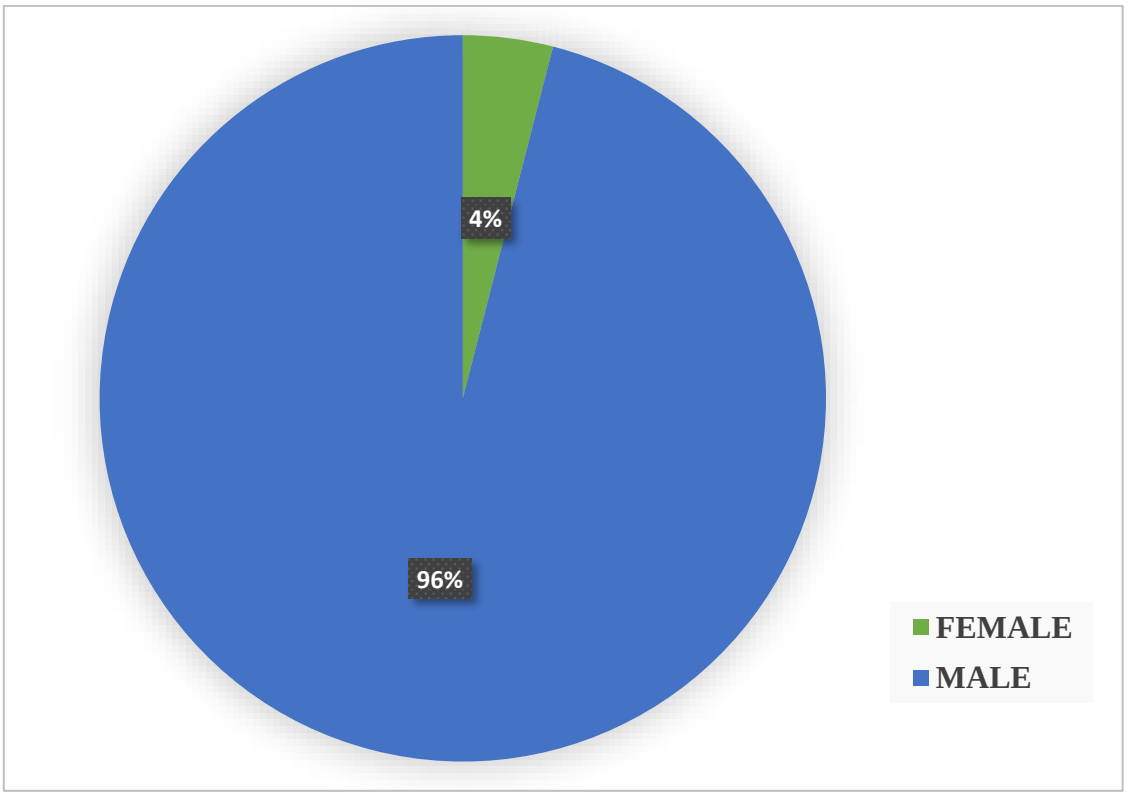


TABLE 20 : DURATION OF DURATION OF SYMPTOMS OBSERVED AMONG CASES

DURATION OF SYMPTOMS (MONTHS)	NO. OF PATIENTS	PERCENTAGE
<1	30	60.0
1 TO 3	14	28.0
3 TO 6	5	10.0
>6	1	2.0
TOTAL	50	100.0

Table 20 and figure 26 demonstrate that 60% of the subjects presented within 1 month of their exacerbated or new symptoms and only one patient presented after 6 months of symptoms.

FIGURE 26 : DURATION OF SYMPTOMS OBSERVED AMONG CASES

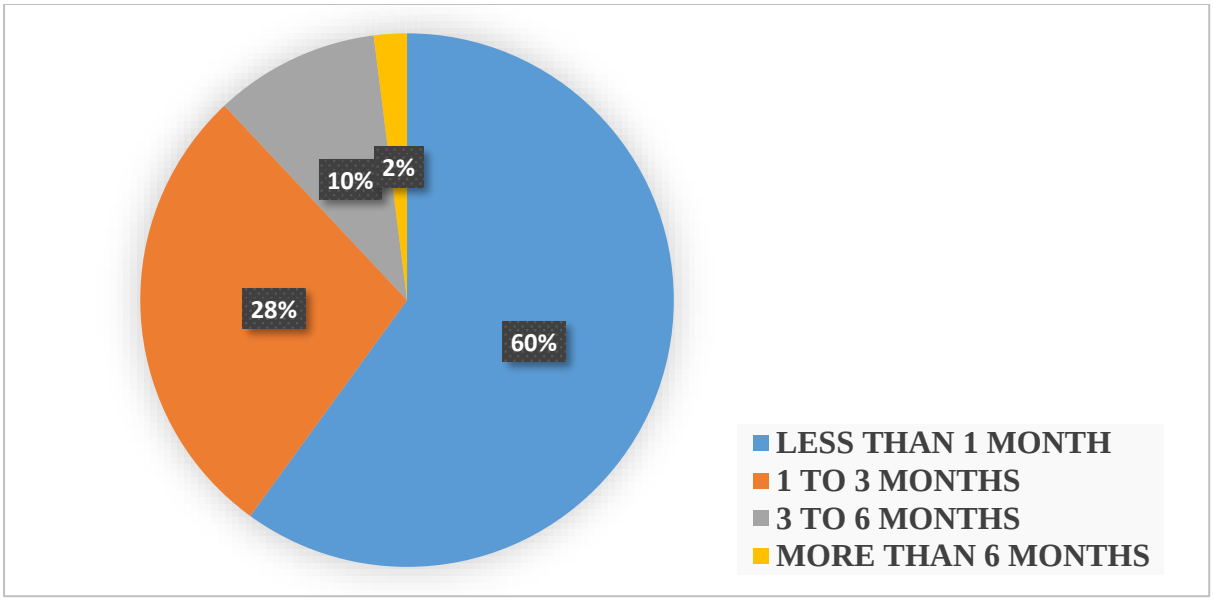


TABLE 21 : DIFFERENT PAST HISTORIES IN SUBJECTS

PAST HISTORY	NO. OF PATIENTS	PERCENTAGE
CIRRHOSIS 1 TO 3 MONTHS	3	6.0
CIRRHOSIS 3 TO 6 MONTHS	6	12.0
CIRRHOSIS MORE THAN 6 MONTHS	3	6.0
CIRRHOSIS MORE THAN 1 YEAR	7	14.0
T2DM, CIRRHOSIS 3 TO 6 MONTHS	1	2.0
T2DM, HTN, CIRRHOSIS 3 TO 6 MONTHS	1	2.0
RVD, HTN, CIRRHOSIS MORE THAN 6 MONTHS	1	2.0
T2DM, HTN, IHD	1	2.0
HIV	1	2.0
NIL	26	52.0
TOTAL	50	100.0

Table 21 and figure 27 show 44% of the patients already had previous history of cirrhosis of varying durations and thus implicating repeated admissions to hospitals though almost half of them had no significant past history.

FIGURE 27 : DIFFERENT PAST HISTORIES IN SUBJECTS

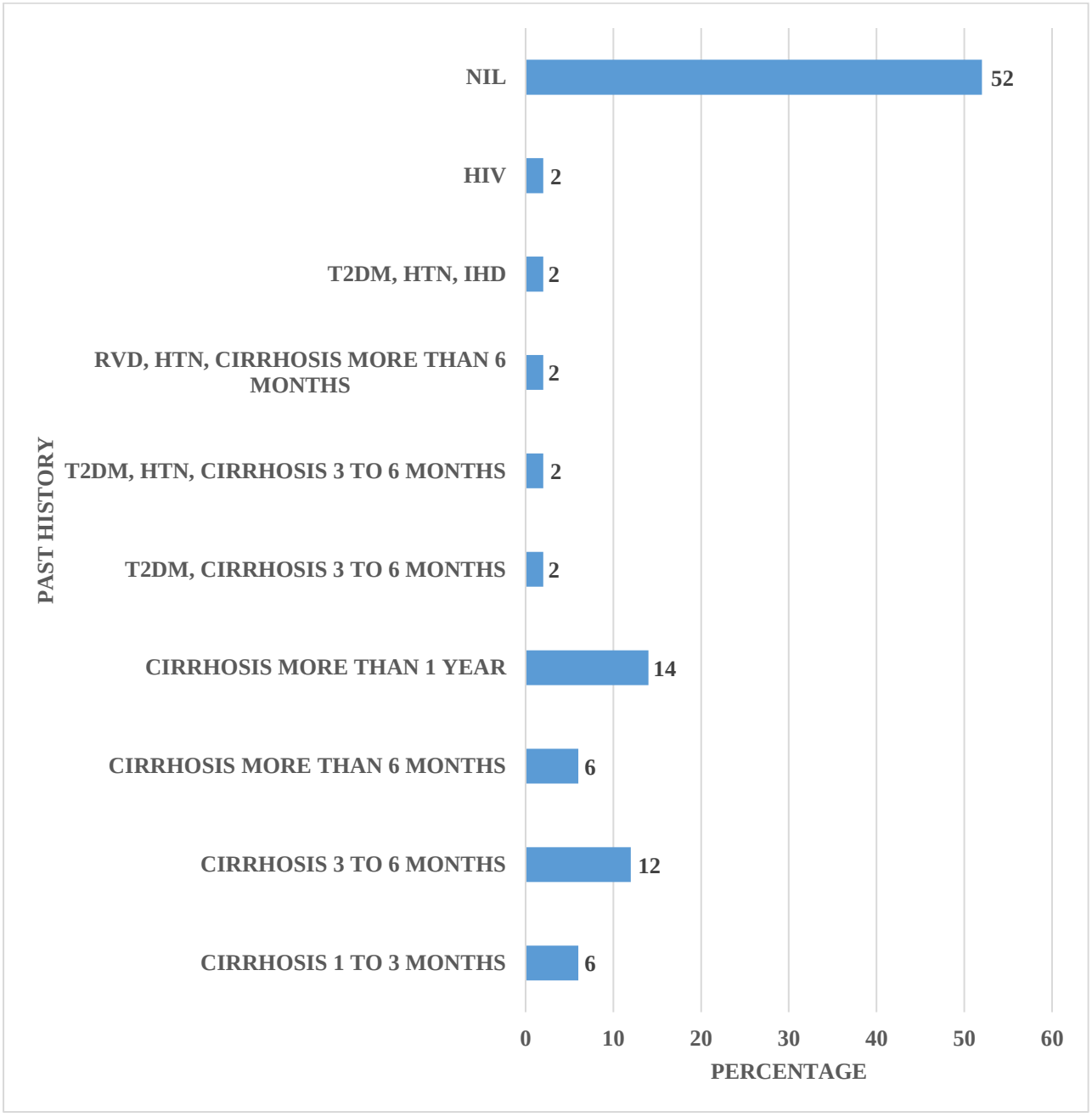


TABLE 22 : AVERAGE ALCOHOL CONSUMPTION

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
AVERAGE VOLUME OF ALCOHOL CONSUMPTION (G/DAY)	60	231	120.76	44.42
AVERAGE DURATION OF ALCOHOL CONSUMPTION (YEARS)	4	35	17.74	8.231

- Table 22 and figure 28 depict that in this study, minimum volume of alcohol consumption per day is 60 grams and a maximum of 231 grams per day is also observed.
- Duration of alcohol consumption varied from a minimum of 4 years to a maximum of 35 years.
- Mean volume of alcohol consumption is 120.76±44.42 grams/day and mean duration is 17.74±8.23 years in the observed subjects.
- Out of 50, 4 patients did not consume alcohol.

FIGURE 28 : AVERAGE ALCOHOL CONSUMPTION

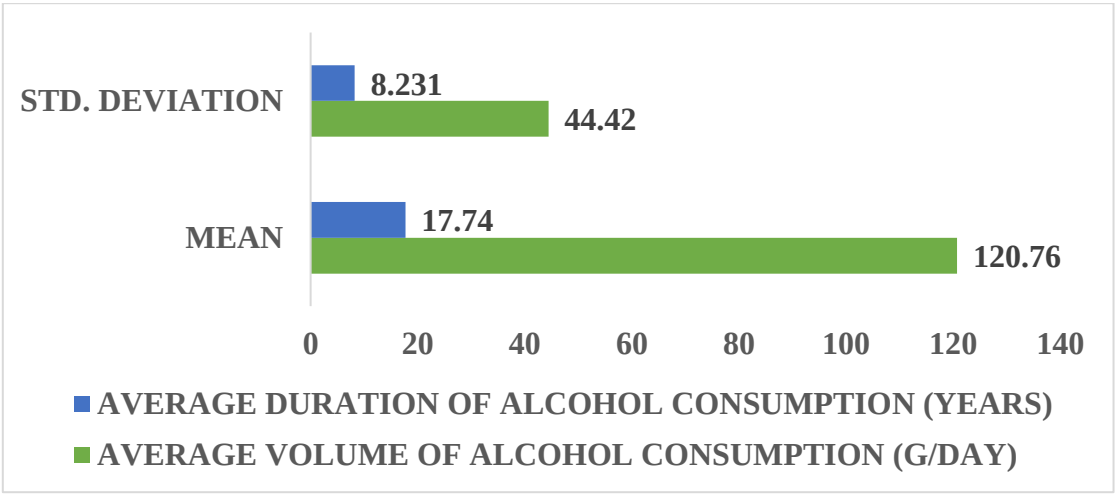


TABLE 23 : OTHER HABITS IN OBSERVED SUBJECTS

OTHER HABITS	NO.OF PATIENTS	PERCENTAGE
BD SMOKER	8	16.0
CIGARETTE SMOKER	6	12.0
TOBACCO CHEWER	10	20.0
GUTKA CHEWER	3	6.0
NIL	23	46.0
TOTAL	50	100.0

- 4 patients had neither drinking habit nor any other habit.
- 42 patients had only drinking habit without any other habit.
- Table 23 and figure 29 depict the percentages of patients with other habits like smoking bds in 16%, cigarettes in 12%, tobacco chewing in 20% and gutka chewing in 6%

FIGURE 29 : OTHER HABITS IN OBSERVED SUBJECTS

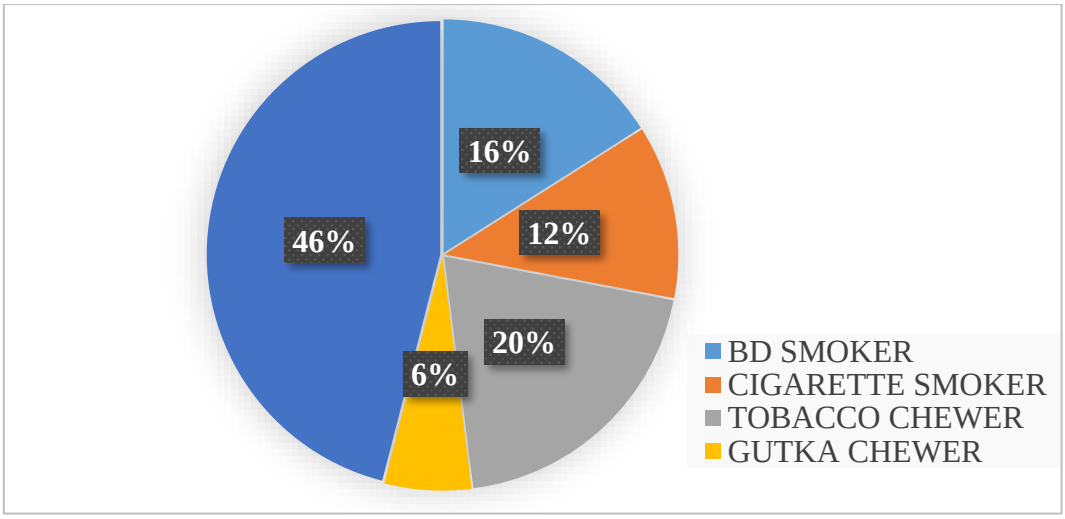


TABLE 24 : PERCENTAGE OF INDIVIDUALS WITH FEVER

FEVER	NO. OF PATIENTS	PERCENTAGE
YES	8	16.0
NO	42	84.0
TOTAL	50	100.0

Table 24 and figure 30 depict that 16% of the subjects had history of fever indicating the possibility of ascitic infection.

FIGURE 30 : PERCENTAGE OF INDIVIDUALS WITH FEVER

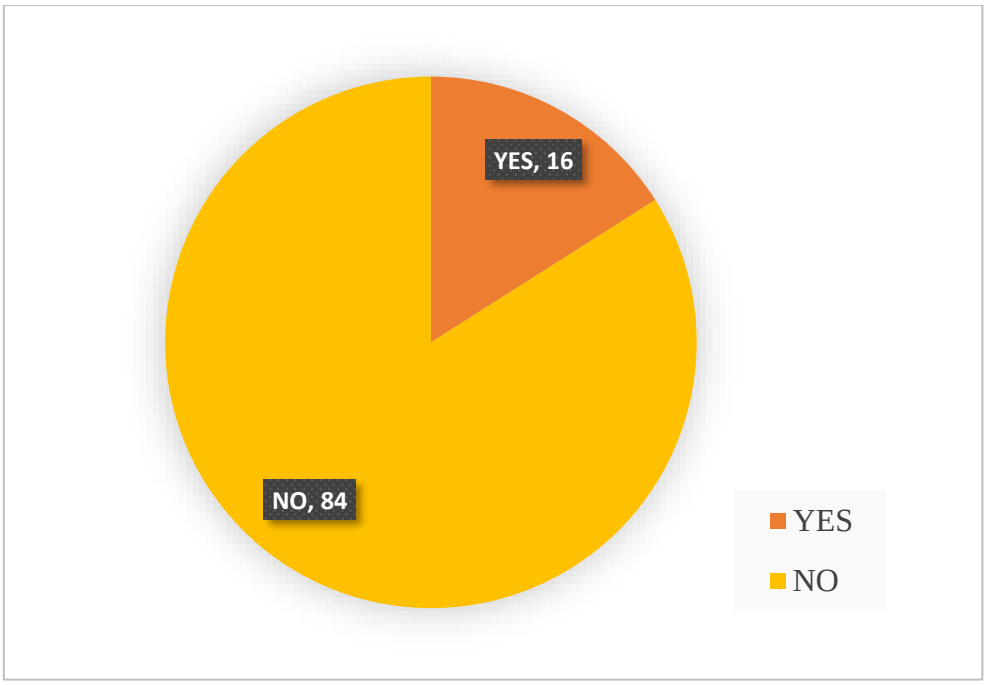


TABLE 25 : PERCENTAGE OF INDIVIDUALS WITH DECREASED URINARY OUTPUT

URINARY OUTPUT	NO. OF PATIENTS	PERCENT
DECREASED OUTPUT	10	20.0
NORMAL	40	80.0
TOTAL	50	100.0

Table 25 and figure 31 demonstrate that 10 patients among 50 had decreased urinary output indicating the possibility of hepatorenal syndrome in 20% of the patients.

FIGURE 31 : PERCENTAGE OF INDIVIDUALS WITH DECREASED URINARY OUTPUT

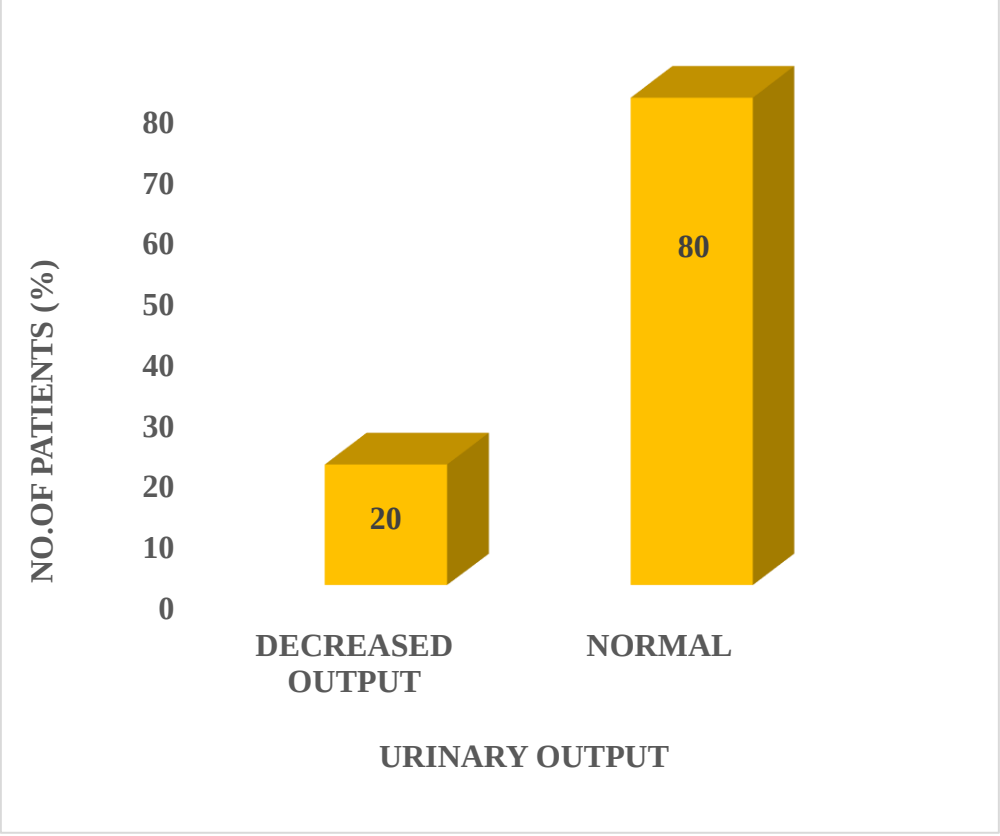


TABLE 26 : PERCENTAGE OF CLINICALLY DETECTABLE ALTERED SENSORIUM

CLINICAL ALTERED SENSORIUM	NO. OF PATIENTS	PERCENTAGE
PRESENT	43	86.0
ABSENT	7	14.0
TOTAL	50	100.0

Table 26 and figure 32 demonstrate that 43 patients among 50 show some deficits in their sensorium indicating overt hepatic encephalopathy but 7 patients among 50 showed no change in their sensorium indicating covert hepatic encephalopathy.

FIGURE 32 : PERCENTAGE OF CLINICALLY DETECTABLE ALTERED SENSORIUM

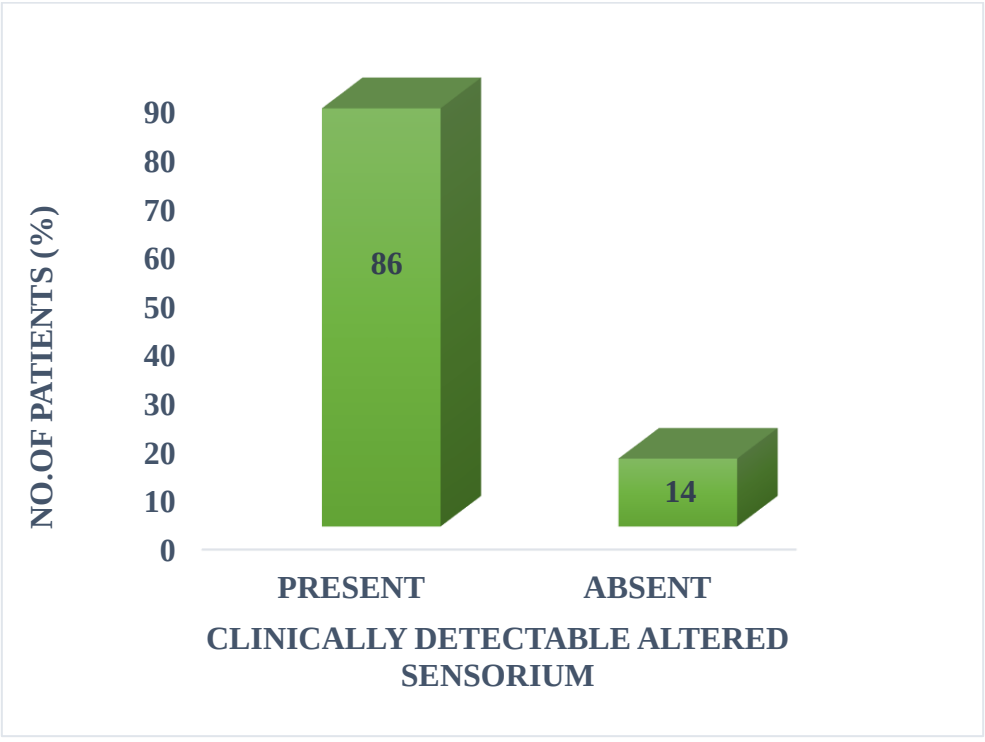


TABLE 27 : PERCENTAGE OF DIFFERENT SENSORIA OBSERVED IN SUBJECTS

SENSORIUM	NO. OF PATIENTS	PERCENTAGE
NORMAL BEHAVIOUR (WHC GRADE 0)	7	14.0
SHORT ATTENTION SPAN (WHC GRADE 1)	18	36.0
DISORIENTED (WHC GRADE 2)	11	22.0
STUPOROUS (WHC GRADE 3)	14	28.0
TOTAL	50	100.0

36% of the patients studied had short attention span, 28% had stupor, 22% had disorientation and 7 were in their normal behavior when presented to our hospital as shown in table 27 and figure 33.

FIGURE 33 : PERCENTAGE OF DIFFERENT SENSORIA OBSERVED IN SUBJECTS

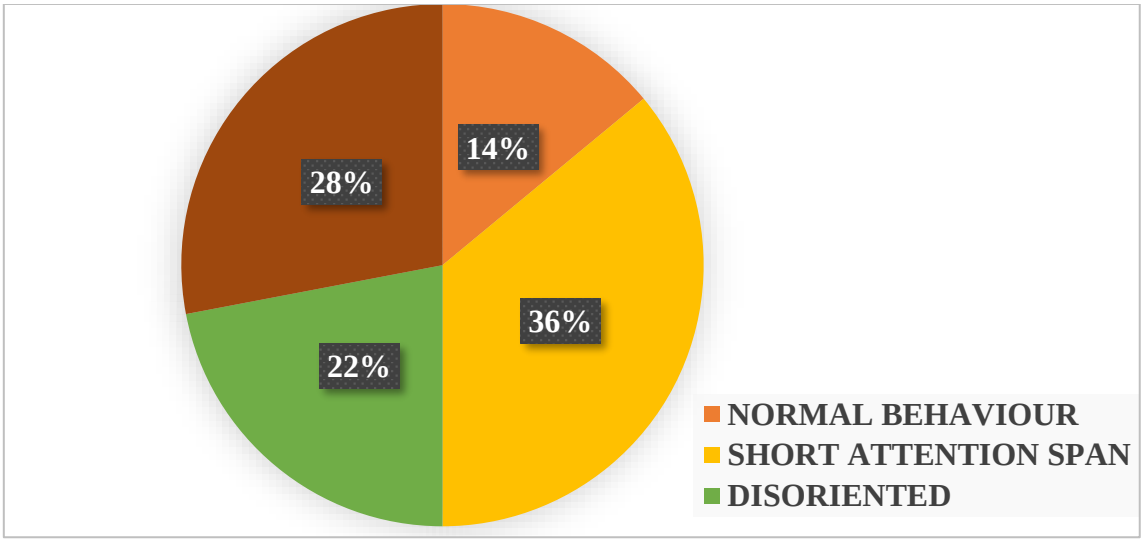


TABLE 28: PERCENTAGE OF INDIVIDUALS WITH PALLOR

PALLOR	NO. OF PATIENTS	PERCENTAGE
PRESENT	9	18
SEVERE	16	32
ABSENT	25	50
TOTAL	50	100

Half of the observed individuals had pallor and out of which 16 were severely pale as shown in table 28 and figure 34.

FIGURE 34 : PERCENTAGE OF INDIVIDUALS WITH PALLOR

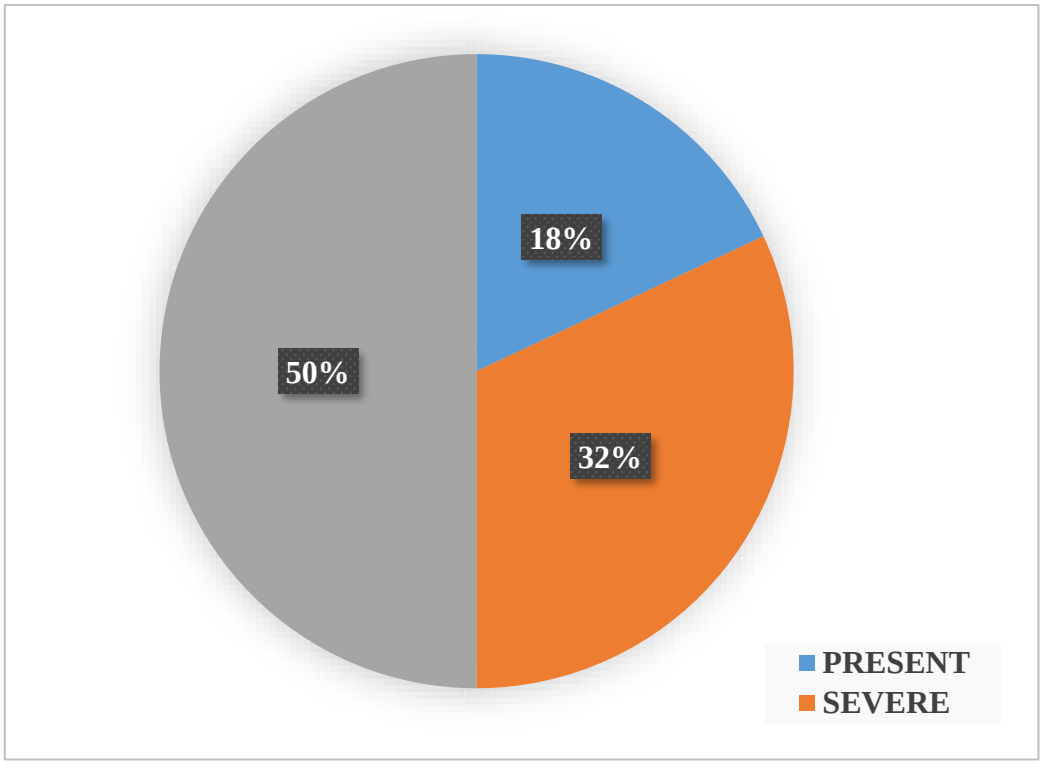


TABLE 29 : NAILS CHANGES OBSERVED IN SUBJECTS

NAIL CHANGES	NO. OF PATIENTS	PERCENTAGE
LEUKONYCHIA	12	24
CLUBBING	4	8
PALLOR	9	18
PLATYNYCHIA	1	2
LEUKONYCHIA, CLUBBING	2	4
KOILONYCHIA, PLATYNYCHIA, CLUBBING	1	2
NORMAL	21	42
TOTAL	50	100

14 patients had leukonychia and other nail changes were observed in subjects as shown in table 29 and figure 35.

Figure 35 : NAILS CHANGES OBSERVED IN SUBJECTS

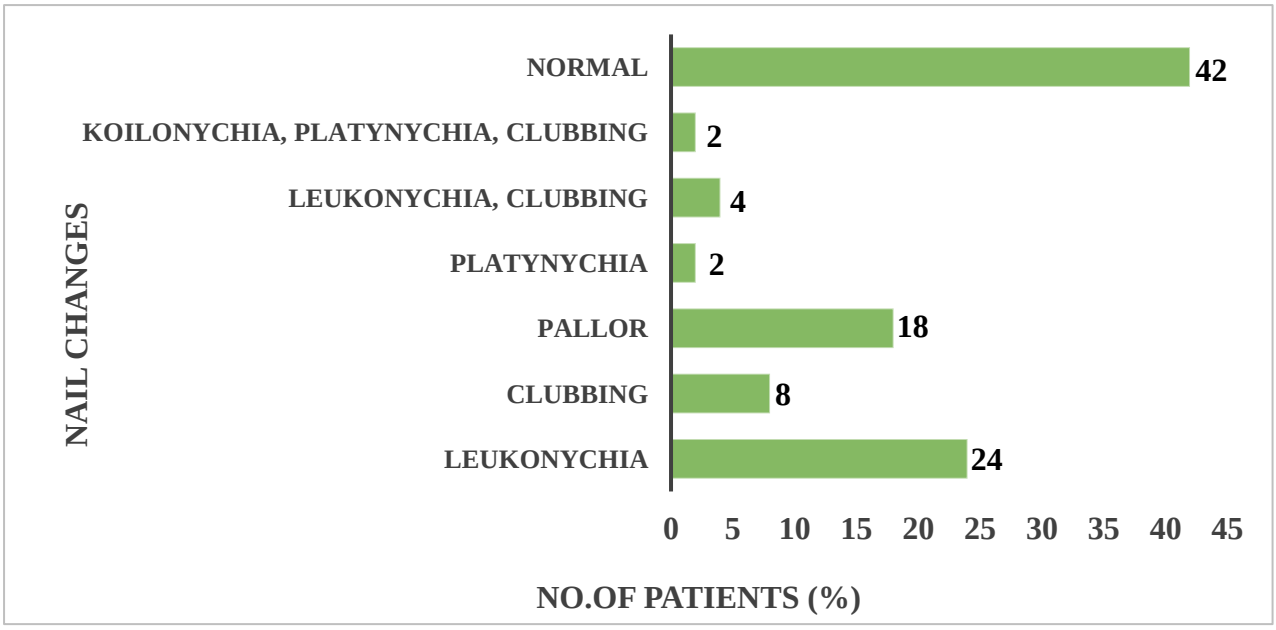


TABLE 30 : ASTEREXIS IN OBSERVED INDIVIDUALS

ASTEREXIS	NO. OF PATIENTS	PERCENT
RARE FLAPS	13	26.0
OCCASIONAL FLAPS	9	18.0
FREQUENT FLAPS	11	22.0
CONTINUOUS FLAPS	4	8.0
ABSENT	13	26.0
TOTAL	50	100.0

Table 30 and figure 36 depict the observation of rare flaps in 13 patients indicating intial end of disease spectrum to continuous flaps in 4 patients indicating the other extreme of disease spectrum.

FIGURE 36 : ASTEREXIS IN OBSERVED INDIVIDUALS

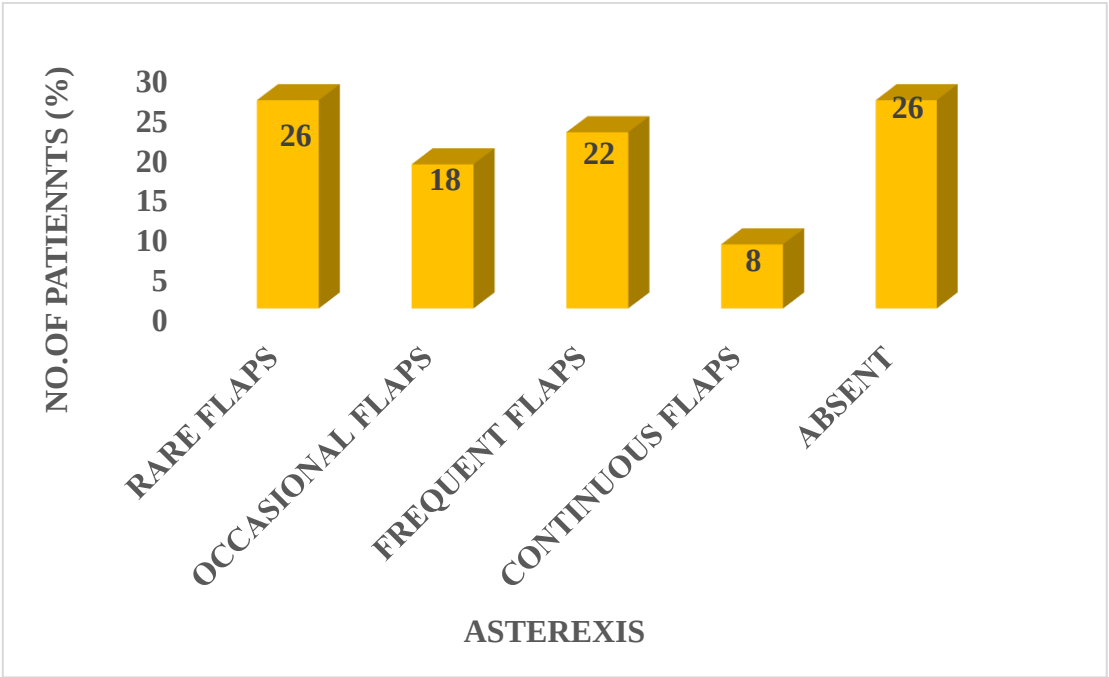


TABLE 31 : ARTERIAL SPIDERS IN OBSERVED INDIVIDUALS

ARTERIAL SPIDERS	NO. OF PATIENTS	PERCENT
PRESENT	31	62.0
ABSENT	19	38.0
TOTAL	50	100.0

Arterial spiders were found to be present in 31 patients among 50 as shown in table 31 and figure 37.

FIGURE 37 : ARTERIAL SPIDERS IN OBSERVED INDIVIDUALS

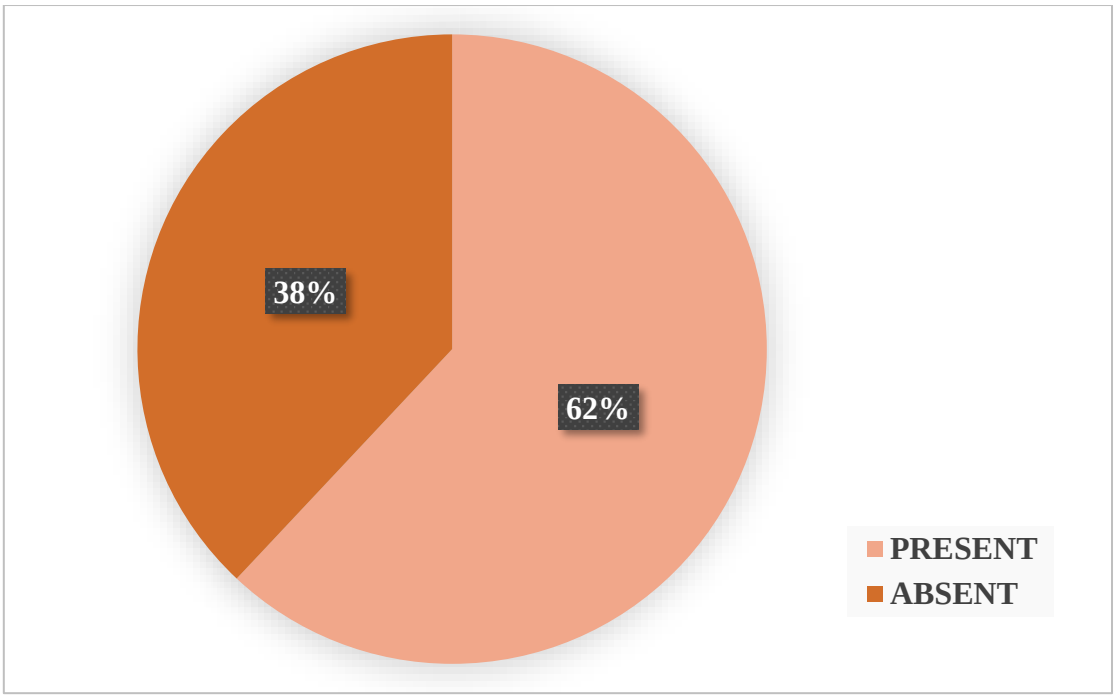


TABLE 32 : ETIOLOGY OF CIRRHOSIS AMONG CASES

ETIOLOGY OF CIRRHOSIS	NO. OF PATIENTS	PERCENTAGE
ALCOHOL	46	92.0
HBV	1	2.0
HCV	1	2.0
UNKNOWN	2	4.0
TOTAL	50	100.0

92% of the patients had alcohol as the cause of cirrhosis and the rest had viral or unknown etiology as depicted in table 32 and figure 38.

FIGURE 38 : ETIOLOGY OF CIRRHOSIS AMONG CASES

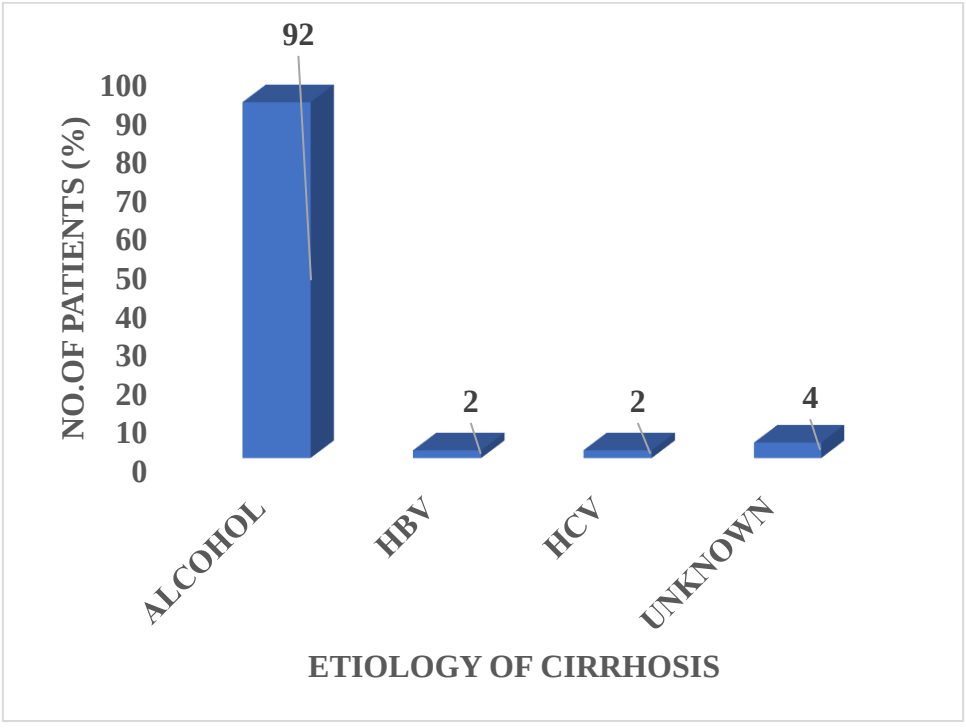


TABLE 33 : UPPER GI ENDOSCOPY FINDINGS AMONG CASES

UPPER GI ENDOSCOPY	NO. OF PATIENTS	PERCENTAGE
GRADE 1 ESOPHAGEAL VARICES	5	10.0
GRADE 2 ESOPHAGEAL VARICES	5	10.0
GRADE 3 ESOPHAGEAL VARICES	4	8.0
EARLY ESOPHAGEAL VARICES	1	2.0
PORTAL HYPERTENSIVE GASTROPATHY	2	4.0
GRADE 1 ESOPHAGITIS	1	2.0
ESOPHAGEAL CANDIDIASIS	1	2.0
GASTRIC EROSIONS	1	2.0
GASTRITIS	3	6.0
PREPYLORIC ULCERS	1	2.0
NORMAL	5	10.0
NOT DONE	21	42.0
TOTAL	50	100.0

Table 33 and figure 39 depict the various upper gastrointestinal findings, the most common finding being esophageal varices of 30%.

FIGURE 39 : UPPER GI ENDOSCOPY FINDINGS AMONG CASES

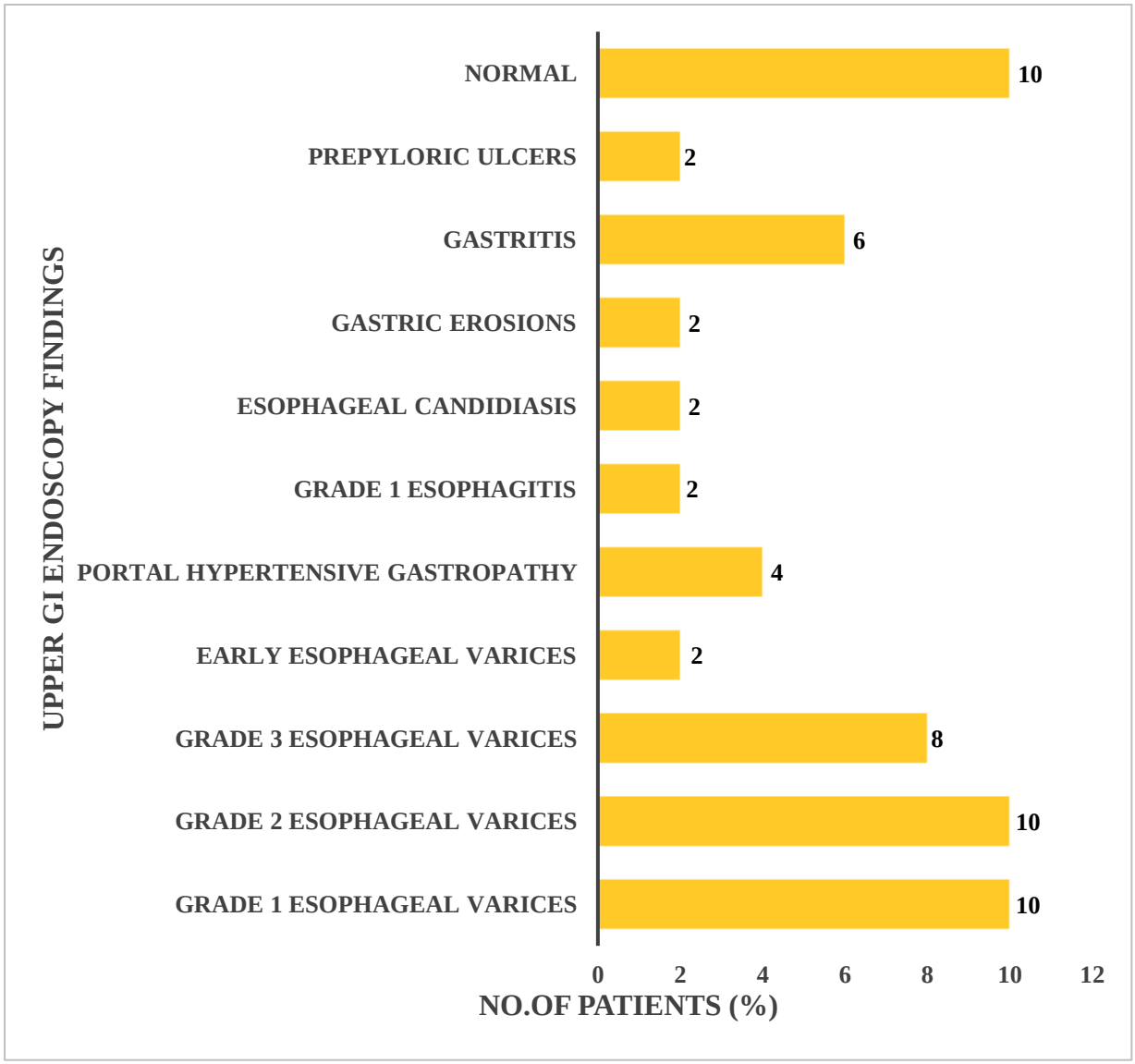


TABLE 34 : BLOOD PARAMETERS IN THE SUBJECTS OBSERVED

BLOOD PARAMETERS	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
RBC	1.23	5.29	3.02	0.82
HEMOGLOBIN	3.4	15.6	9.16	2.69
MCV	63.6	124.7	91.47	11.33
MCH	15.8	37.9	31.19	4.34
MCHC	24.2	39.2	33.89	2.43
TOTAL LEUCOCYTE COUNT	1870	35990	10659.6	7459.33
NEUTROPHILS	45.6	94	75.85	12.7
LYMPHOCYTES	2.9	40.1	15.63	10
EOSINOPHILS	0	15	2.43	3.03
MONOCYTES	0	9.6	4.68	2.65
BASOPHILS	0	1	0.24	0.33
PLATELET COUNT	0.16	4.4	1.27	0.89

- Table 34 and figure 40 show the minimum, maximum, mean and standard deviations of liver parameters observed in our study.
- In this study, RBC count ranged from a minimum of 1.23 million/mm^3 to a maximum of 5.29 million/mm^3 with a mean of 3.02million/mm^3 which was lower than normal range indicating the presence of anemia in majority of the subjects.

- Hemoglobin ranged from a minimum of 3.4mg/dL to a maximum of 15.6mg/dL with a mean of 9.1mg/dL which was also lower than the normal range.
- Mean values of MCV and MCH are towards the upper limit of normal range whereas the mean of MCHC was well within the normal range indicating macrocytic type of anemia.
- WBC count ranged well within the normal limits but mean percentage of neutrophils was found to be towards the upper limit of normal range.
- Platelet count ranged from a minimum of 16000 cells/mm^3 to 4.4 lakh cells/mm^3 with a mean of 1.27 lakh cells/mm^3 which was on the lower side of normal range.

FIGURE 40 : BLOOD PARAMETERS IN THE SUBJECTS OBSERVED

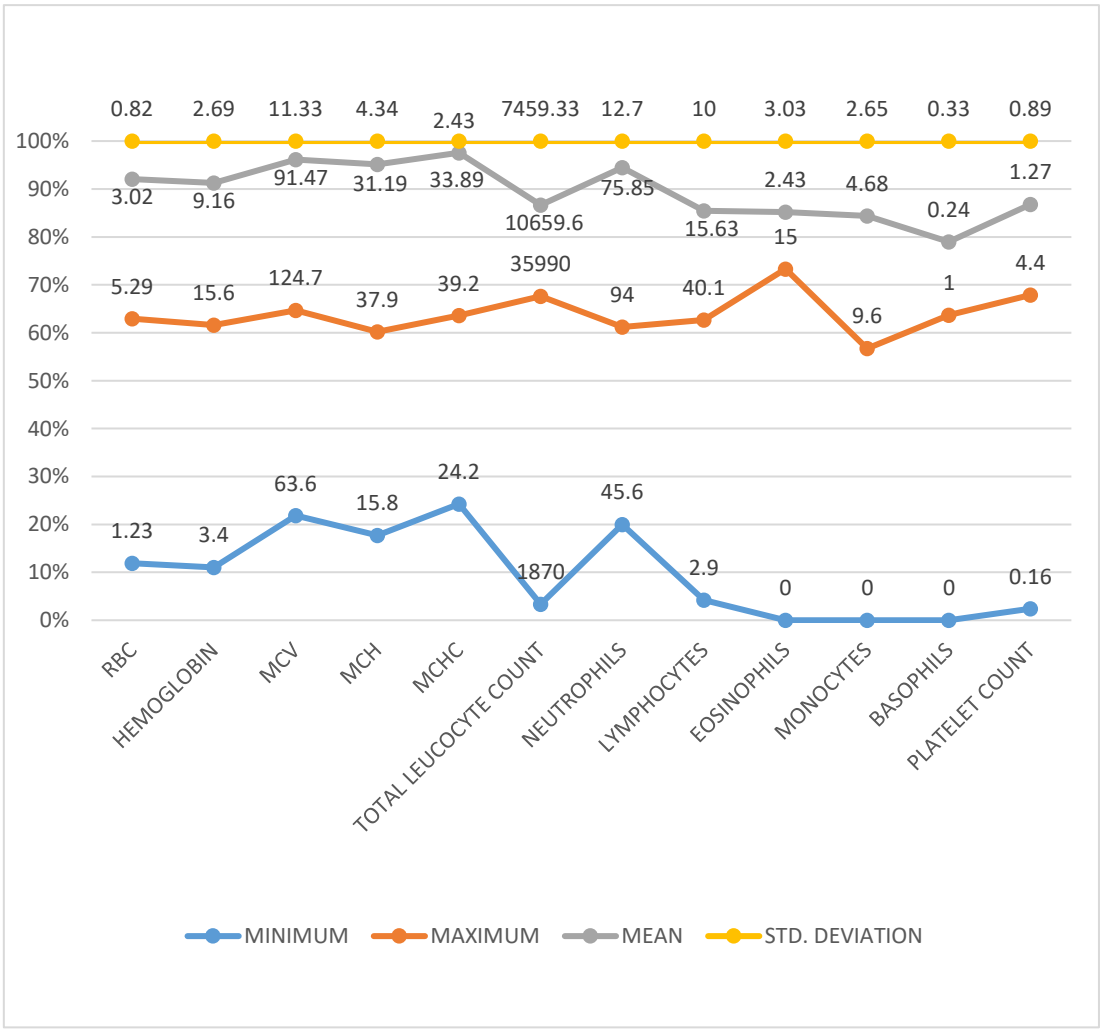


TABLE 35 : LIVER PARAMETERS IN THE SUBJECTS OBSERVED

LIVER PARAMETERS	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
TOTAL BILIRUBIN	0.7	27	8.1	7.7
UNCONJUGATED BILIRUBIN	0.3	8	2.9	2.3
CONJUGATED BILIRUBIN	0.2	23	5.1	5.8
ALBUMIN	1.3	4	2.4	0.5
SGOT	7.0	1500	137.3	243.5
SGPT	1.34	1462	96.1	235.8
ALP	58	285	137.5	54.0

- Table 35 and figure 41 show the minimum, maximum, mean and standard deviations of liver parameters observed in our study.
- In this study, total bilirubin ranged from a minimum of 0.7mg/dL to as high as 27mg/dL.
- Mean albumin as expected was lower than the normal range with a mean of 2.4g/dL and the minimum value observed being 1.3g/dL.
- Mean SGOT was more than twice the normal range and mean SGPT was almost one and half times elevated than the normal range where as mean ALP was within normal limits.

FIGURE 41 : MEAN AND STANDARD DEVIATION OF LIVER PARAMETERS IN THE SUBJECTS OBSERVED

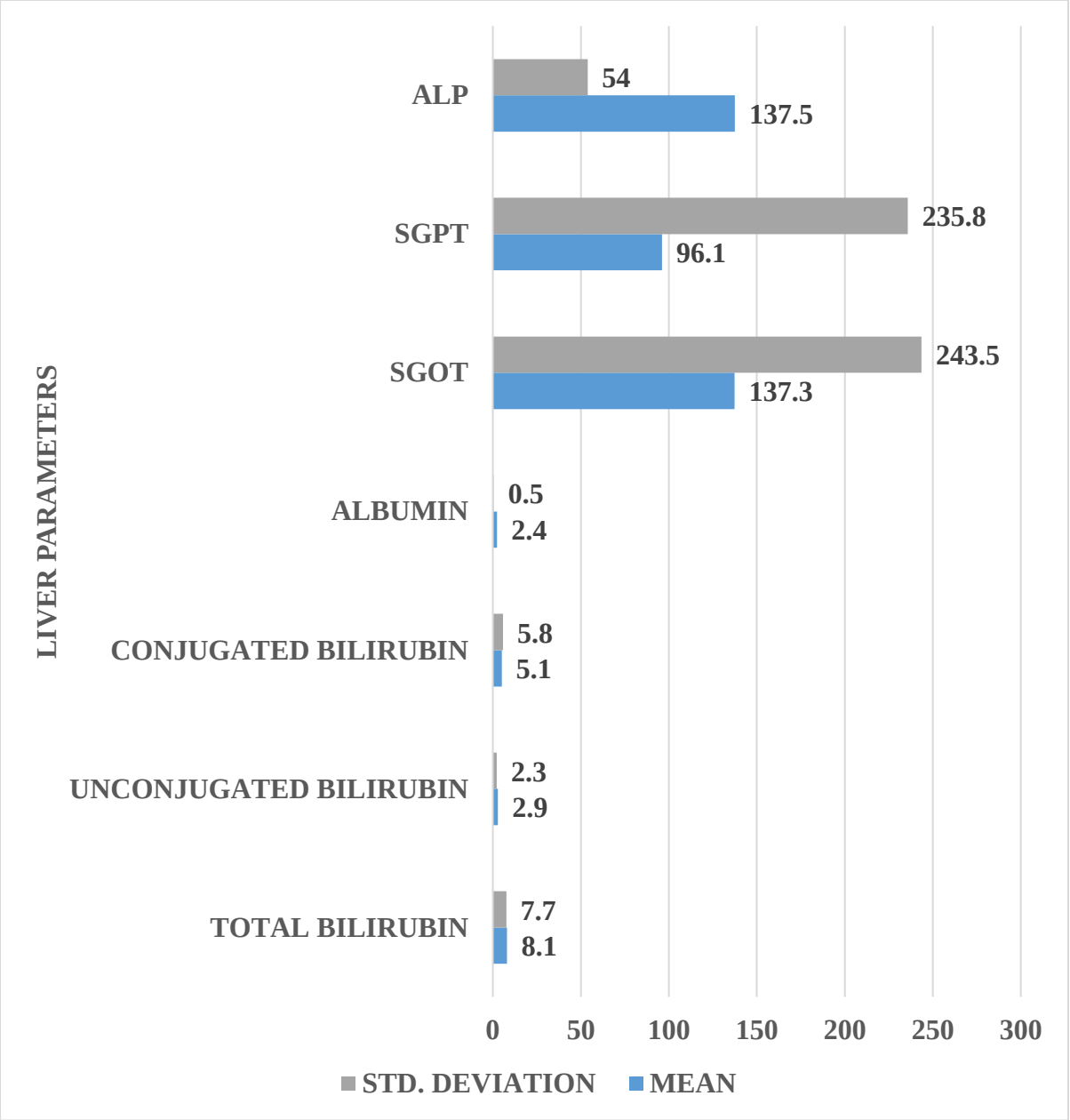


TABLE 36 : RENAL PARAMETERS IN THE SUBJECTS OBSERVED

RENAL PARAMETERS	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
CREATININE	0.5	6	1.3	1.01
POTASSIUM	3.2	5.2	4.1	0.5
SODIUM	130	148	136.2	3.8

In this study, creatinine ranged from a minimum of 0.5 to as high as 6 with a mean value of 1.3 ± 1.01, potassium ranged from 3.2 to 5.2 with a mean value of 4.1± 0.5, sodium ranged from 120 to 148 with a mean of 136.2 ± 3.8 as shown in table 36 and figure 42.

FIGURE 42 : MEAN AND STANDARD DEVIATION OF RENAL PARAMETERS IN THE SUBJECTS OBSERVED

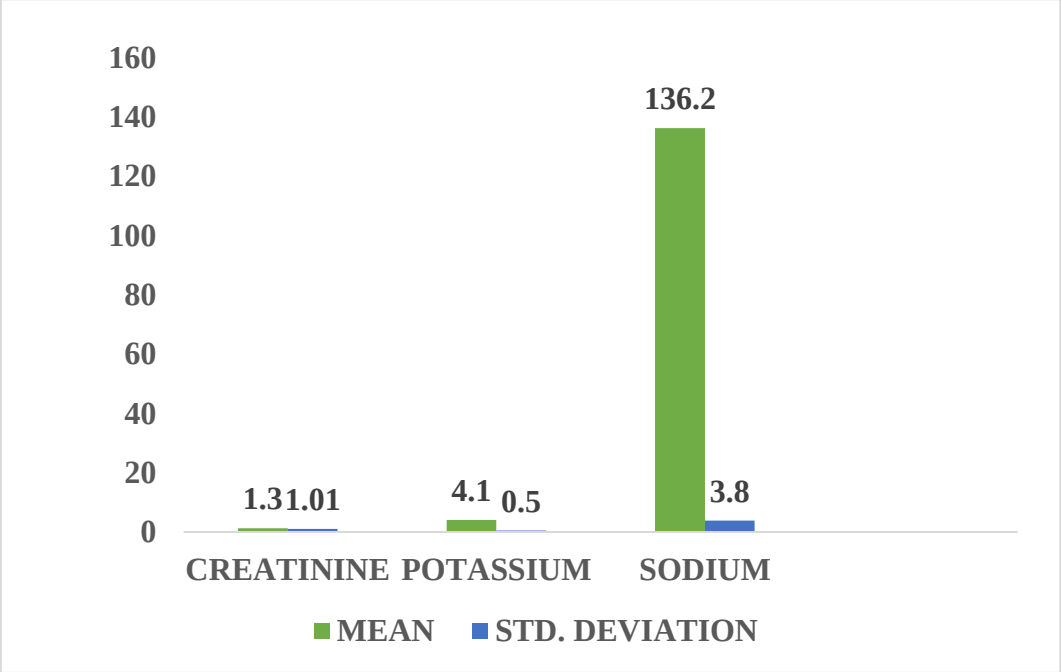


TABLE 37 : RANGE OF AMMONIA AND SPLEEN MEASUREMENTS IN THE SUBJECTS OBSERVED

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
AMMONIA	39	168	95.6	27.32
SPLEEN MEASUREMENTS	9.5	18	13.3	1.92

- Ammonia ranged from a minimum of 39 micromole/L to a maximum of 168 micromole/L which had even the minimum value more than the normal range.
- Spleen measurements ranged from 9.5 cms to 18 cms with a mean range of 13.3 ± 1.92 cms.
- Table 37 and figure 43 depict the above said.

FIGURE 43 : MEAN AND STANDARD DEVIATION OF AMMONIA AND SPLEEN MEASUREMENTS IN THE SUBJECTS OBSERVED

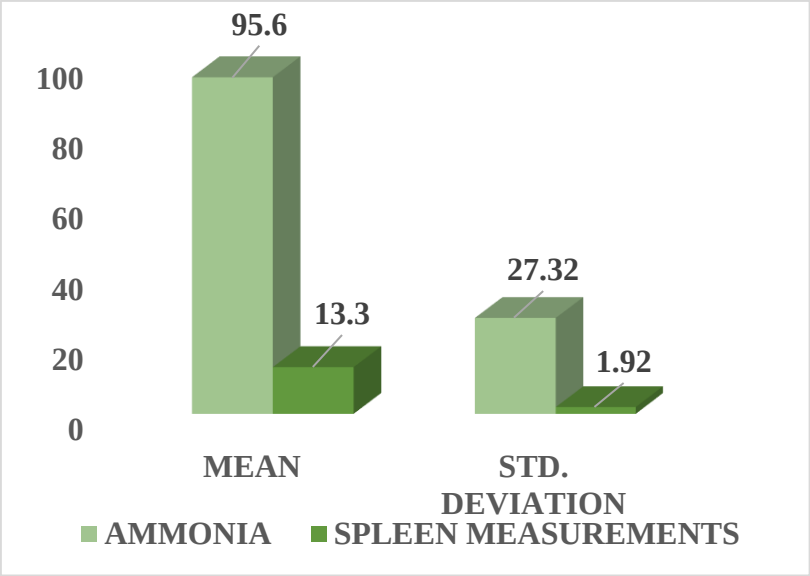


TABLE 38 : RANGE OF PSE SUM AND PSEI IN THE SUBJECTS OBSERVED

	MINIMUM	MAXIMUM	MEAN	STD. DEVIATION
PSE SUM	1	20	10.82	5.975
PSEI	0.04	0.95	0.51	0.28

- In this study, the minimum value of PSE sum was 1 and the maximum was 20.
- PSEI ranged from 0.04 to 0.95 with a mean of 0.51 $\pm$ 0.28.
- Table 38 and figure 44 depict the above said.

FIGURE 44 : MEAN AND STANDARD DEVIATION OF PSE SUM AND PSEI IN THE SUBJECTS OBSERVED

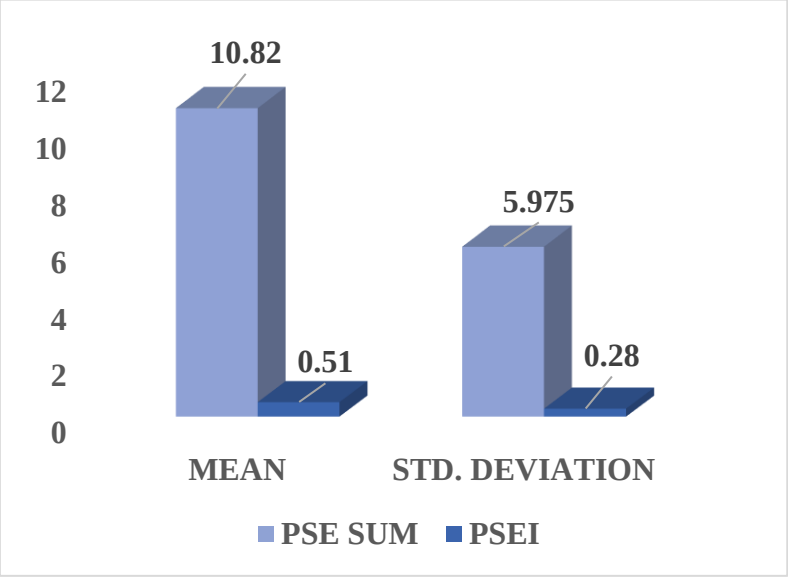


TABLE 39 : CORRELATION BETWEEN THE TOTAL BILIRUBIN AND AMMONIA

CORRELATION BETWEEN	SPEARMAN'S RHO CORRELATION COEFFICIENT	p VALUE	REMARK
Total Bilirubin and Ammonia	r = 0.642	p = 0.001*	Moderate Positive Correlation
*: CORRELATION IS SIGNIFICANT			

Table 39 and figure 45 show moderately positive correlation (r = 0.642) between total bilirubin and ammonia which is statistically significant (P = 0.001).

FIGURE 45 : CORRELATION BETWEEN THE TOTAL BILIRUBIN AND AMMONIA

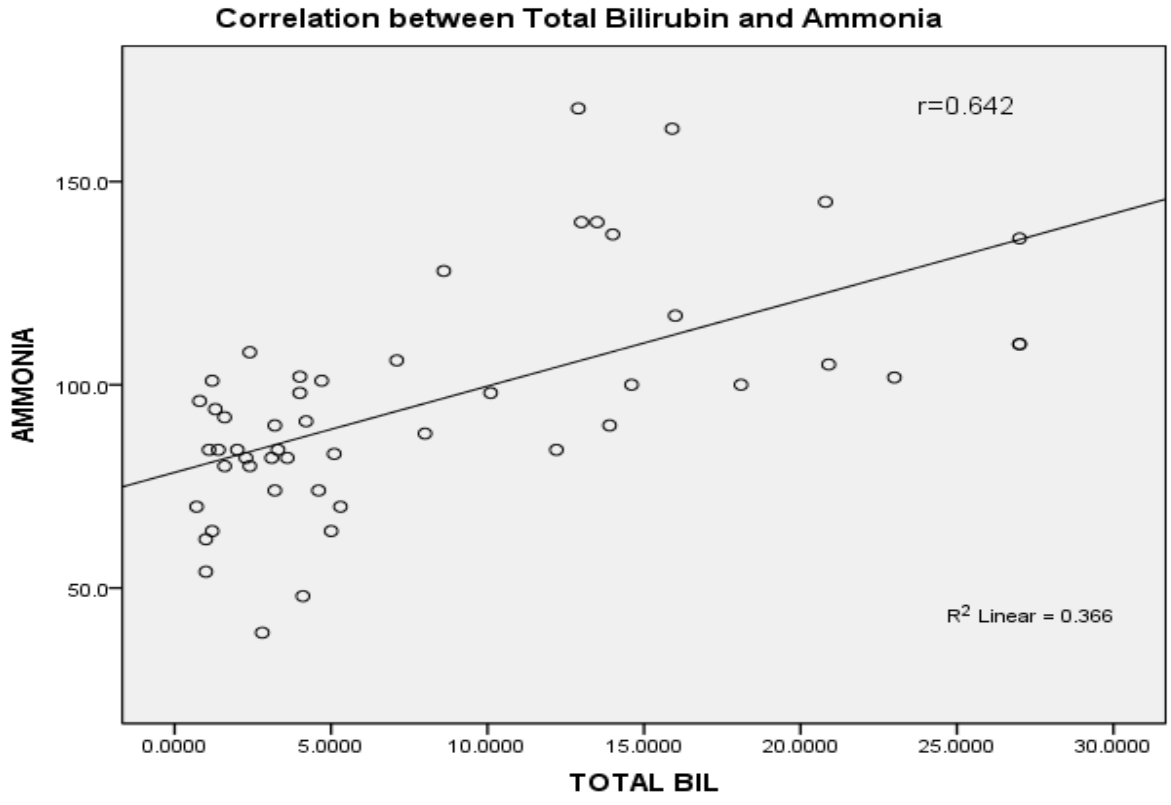


TABLE 40 : CORRELATION BETWEEN AMMONIA AND CHILD-TURCOTTE-PUGH SCORE

CORRELATION BETWEEN	SPEARMAN'S RHO CORRELATION COEFFICIENT	p VALUE	REMARK
Ammonia and Child-Turcotte-Pugh Score	r = 0.599	p = 0.001*	Moderate positive correlation
*:Correlation is significant			

Table 40 and figure 46 show moderately positive correlation (r = 0.599) between total bilirubin and ammonia which is statistically significant (p = 0.001).

FIGURE 46 : CORRELATION BETWEEN AMMONIA AND CHILD-TURCOTTE-PUGH SCORE

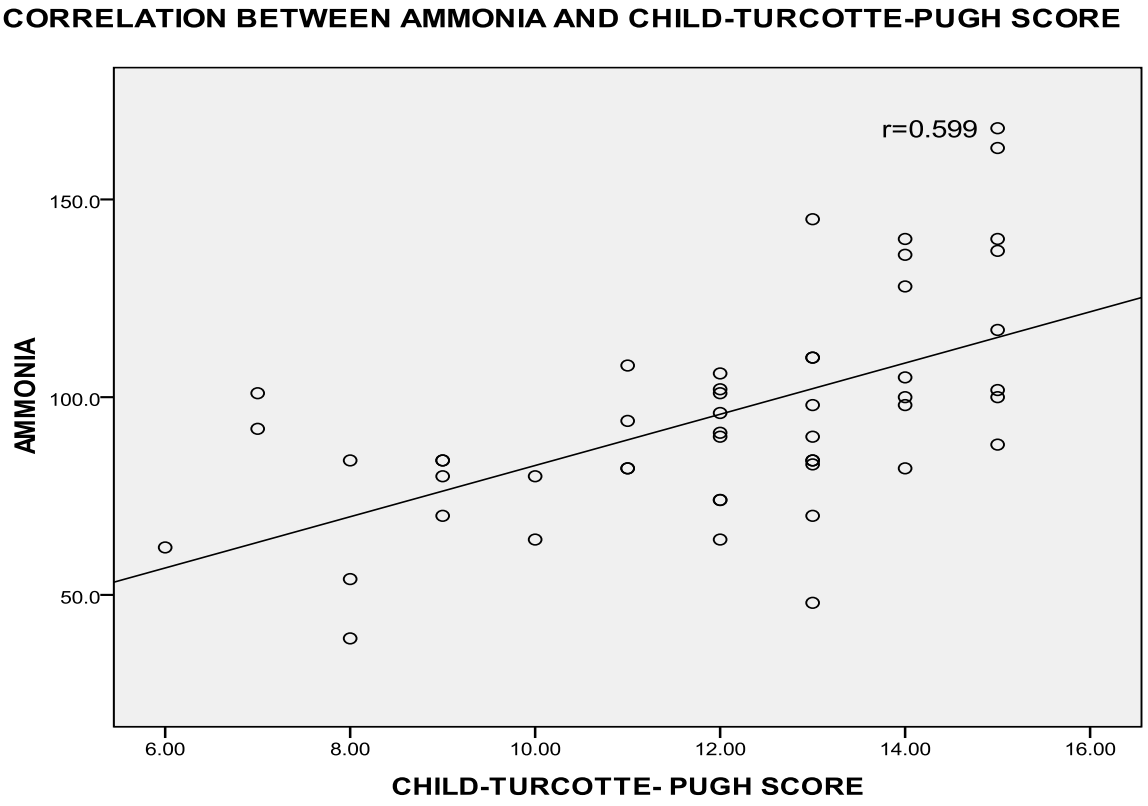


TABLE 41 : ASSOCIATION BETWEEN AMMONIA AND DIFFERENT SENSORIA OBSERVED (SEVERITY OF HEPATIC ENCEPHALOPATHY)

AMMONIA	DIFFERENT SENSORIA					CHI SQUARE TEST	p VALUE
	NORMAL BEHAVIOUR	SHORT ATTENTION SPAN	DISORI-ENTED	STUPO-ROUS	TOTAL		
<80	6	6	0	0	12		
%	85.7%	33.3%	0.0%	0.0%	24.0%		
81-105	1	11	10	3	25		
%	14.3%	61.1%	90.9%	21.4%	50.0%		
106-135	0	0	1	4	6	X^2=48.70	p=0.001 *
%	0.0%	5.6%	9.1%	28.6%	12.0%		
136-160	0	0	0	5	5		
%	0.0%	0.0%	0.0%	35.7%	10.0%		
>160	0	0	0	2	2		
%	0.0%	0.0%	0.0%	14.3%	4.0%		
TOTAL	7	18	11	14	50		

* : HIGHLY SIGNIFICANT

- Cirrhotics with normal behaviour had ammonia values of less than 80 micromole/L except for one patient.
- 61.1% of the cirrhostics with short attention span had ammonia values ranging from 81-105 micromoles/L, 33.3% had ammonia values less than 80 and 5.6% had ammonia values ranging from 106-135.
- Cirrhotics with disorientation had ammonia values ranging from 81-105 except for one patient.
- Majority of the cirrhotics with stupor had ammonia values ranging from 136-160 micromole/L.
- This study showed statistically significant association between ammonia and different sensoria (p = 0.001) and table 37and figure 47 depict the same.

FIGURE 47 : ASSOCIATION BETWEEN AMMONIA AND DIFFERENT SENSORIA OBSERVED (SEVERITY OF HEPATIC ENCEPHALOPATHY)

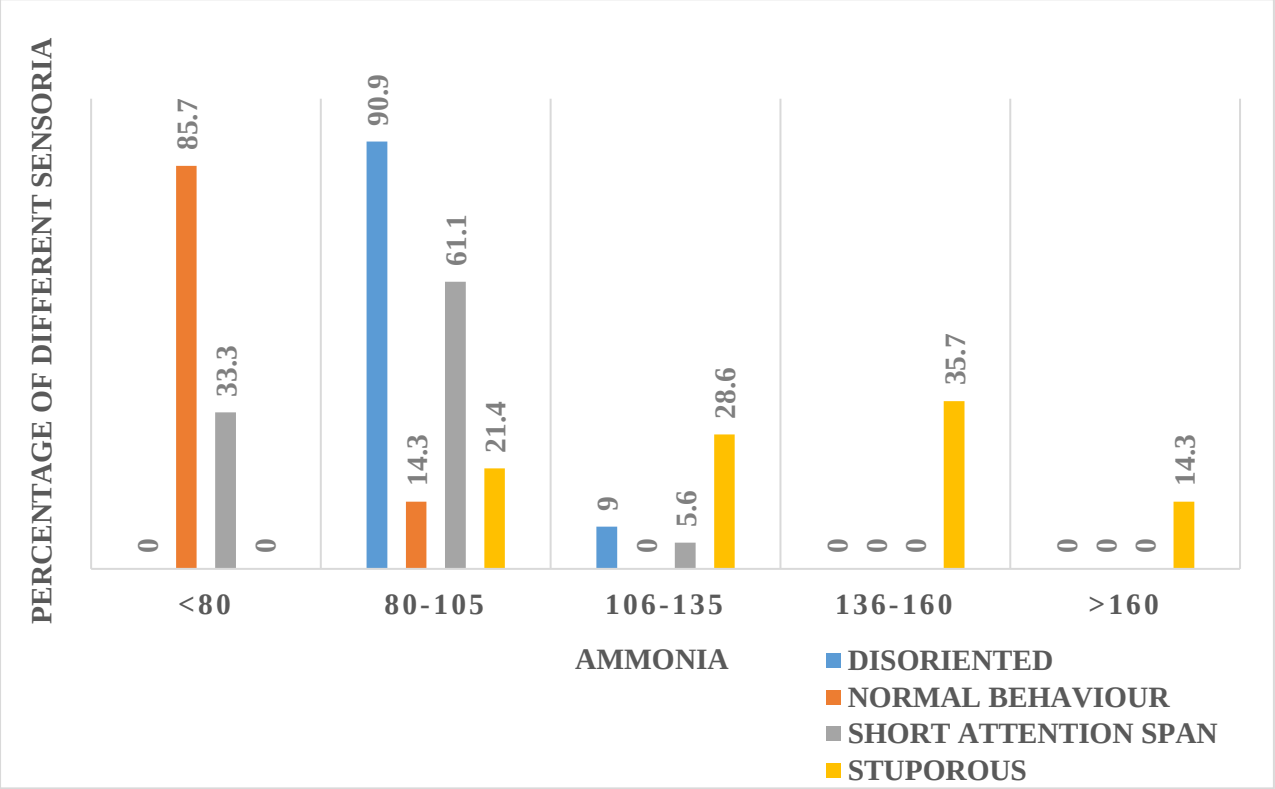
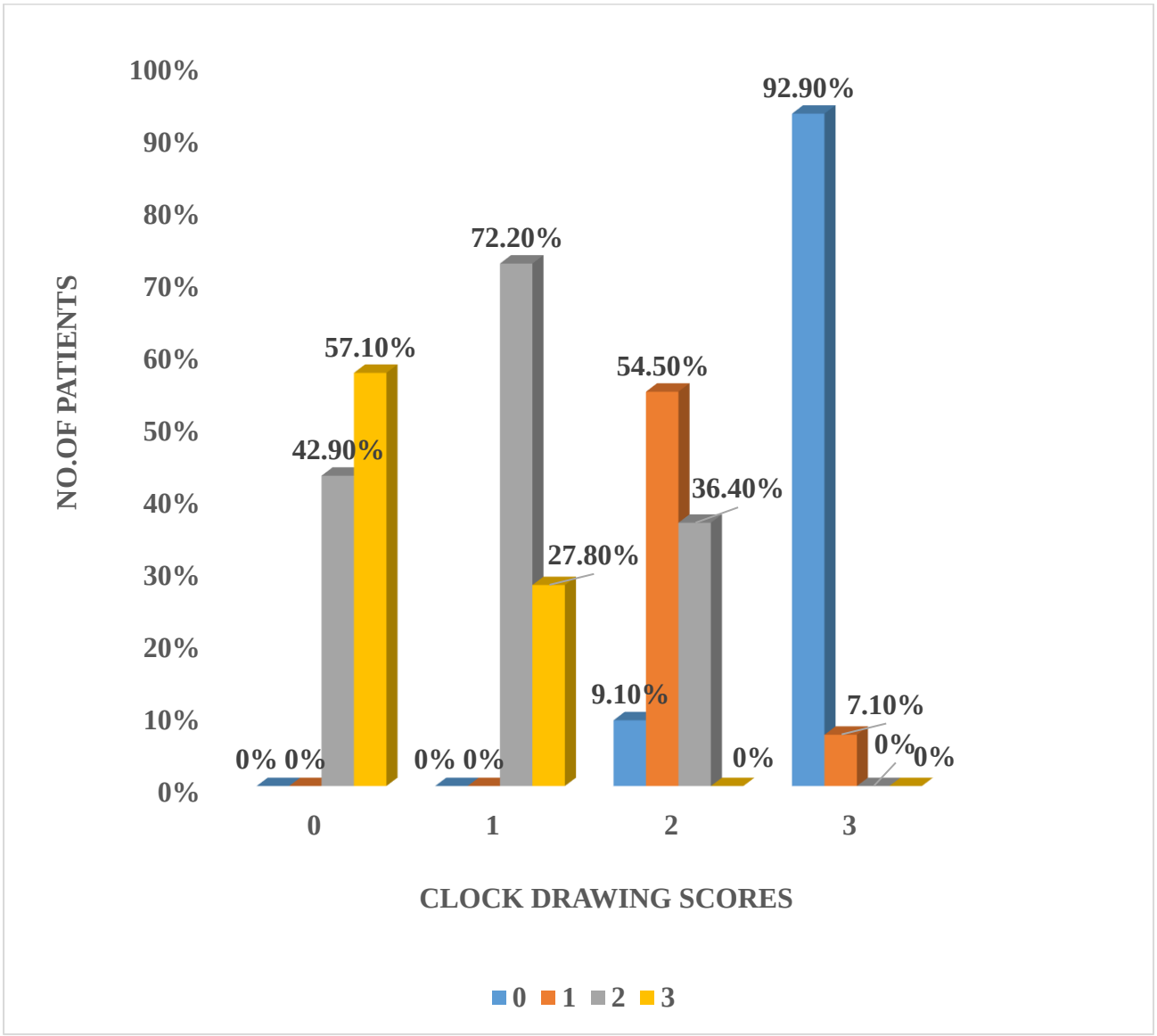


TABLE 42 : ASSOCIATION BETWEEN CLOCK DRAWING AND WHC GRADES

CLOCK	WHC GRADE					CHI SQUARE TEST	p VALUE
	0	1	2	3	TOTAL		
0	0	0	1	13	14		
%	0%	0%	9.1%	92.9%	28%		
1	0	0	6	1	7		
%	0%	0%	54.5%	7.1%	14%	X^2=68.061	p=0.001*
2	3	13	4	0	20		
%	42.9%	72.2%	36.4%	0%	40%		
3	4	5	0	0	9		
%	57.1%	27.8%	0%	0%	18%		
TOTAL	7	18	11	14	50		
* : HIGHLY SIGNIFICANT							

- 57.1% of the cirrhotics with WHC grade 0 had clock drawing score of 3 and 42.9% of them had clock score of 2.
- 72.2% of the cirrhotics with WHC grade 1 had clock drawing score of 2 and 27.8% of them had clock drawing score of 3.
- 54.5% of the cirrhotics with WHC grade 2 had clock drawing score of 1, 36.4% of them had score of 2.
- 92.9% of the cirrhotics with WHC grade 3 had clock drawing score of 0, 7.1% of them had clock score 0.
- Table 42 and figure 48 thus shows that there is statistically significant association between clock drawing and WHC grades (p=0.001).

FIGURE 48 : ASSOCIATION BETWEEN CLOCK DRAWING AND WHC GRADES



Colours represent different grades of WHC.

TABLE 43 : ASSOCIATION BETWEEN CLOCK DRAWING AND PSEI

CLOCK	PSEI			CHI SQUARE TEST	p VALUE
	< .3300	0.3300+	TOTAL		
0	0	14	14		
%	0%	36.8%	28%	X^2=12.872	p=0.004*
1	0	7	7		
%	0%	18.4%	14%		
2	7	13	20		
%	58.3%	34.2%	40%		
3	5	4	9		
%	41.7%	10.5%	18%		
TOTAL	12	38	50		
* : HIGHLY SIGNIFICANT					

- 58.3% of the cirrhotics with PSEI less than 0.33 had clock drawing score of 2 and 41.7% had a score of 3.
- 34.2% of the cirrhotics with PSEI more than or equal to 0.33 had clock drawing score of 2, 36.8% had a score of 0, 18.4% had a score of 1.
- Table 43 and figure 49 shows that the clock drawing and PSEI had statistically significant association (p=0.004).

FIGURE 49 : ASSOCIATION BETWEEN CLOCK DRAWING AND PSEI

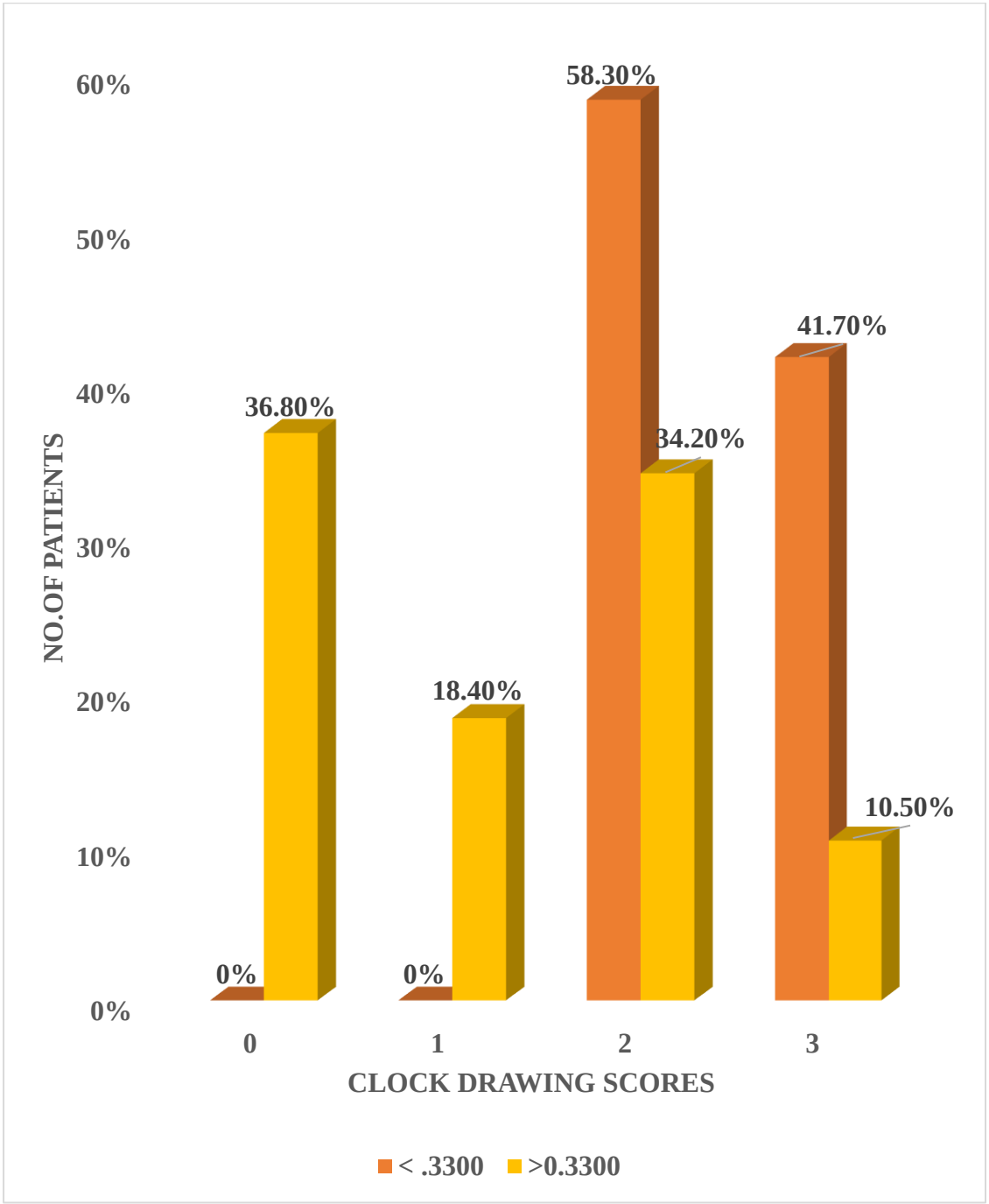


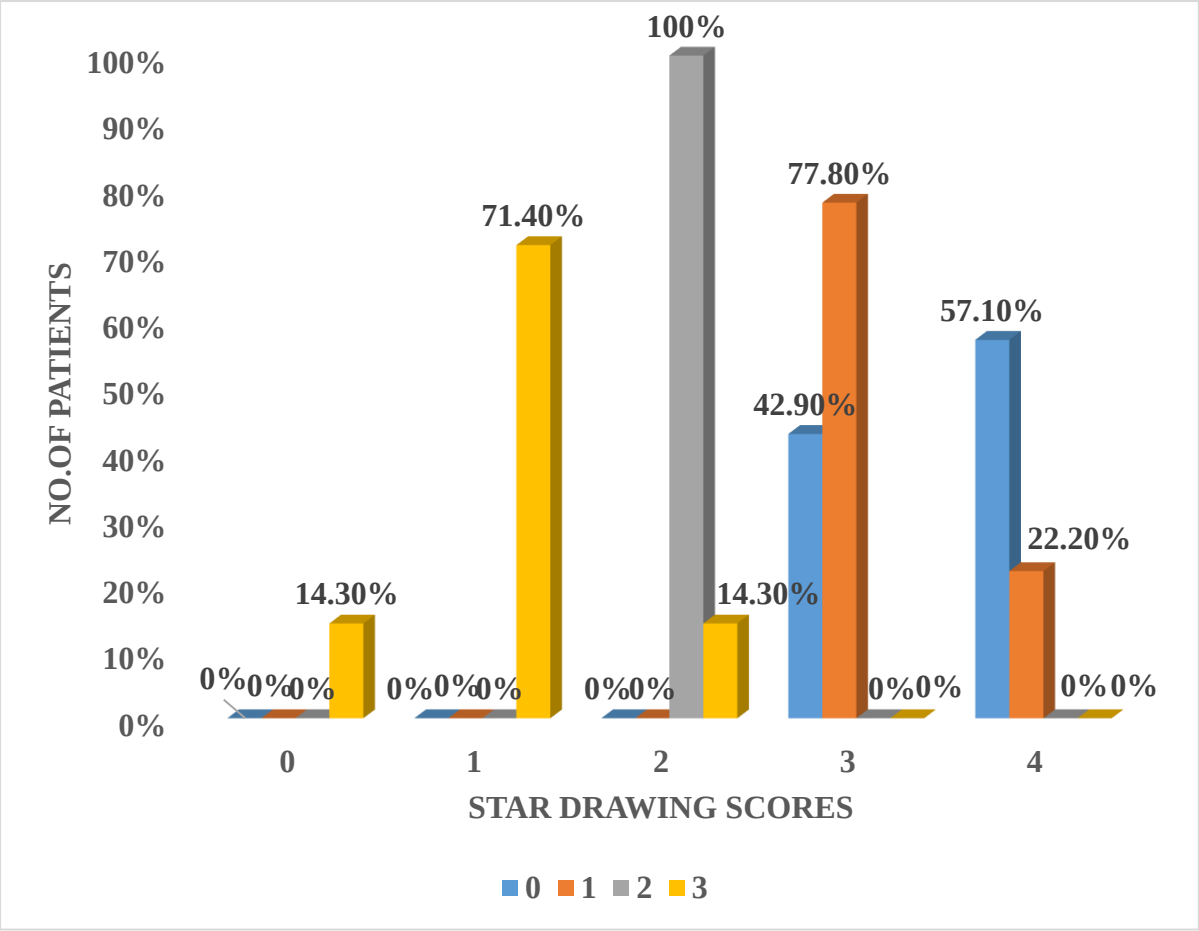
TABLE 44 : ASSOCIATION BETWEEN STAR DRAWING AND WHC GRADES

STAR	WHC GRADE					CHI SQUARE TEST	p VALUE
	0	1	2	3	TOTAL		
0	0	0	0	2	2	X^2=91.913	p=0.001*
%	0%	0%	0%	14.3%	4%		
1	0	0	0	10	10		
%	0%	0%	0%	71.4%	20%		
2	0	0	11	2	13		
%	0%	0%	100%	14.3%	26%		
3	3	14	0	0	17		
%	42.9%	77.8%	0%	0%	34%		
4	4	4	0	0	8		
%	57.1%	22.2%	0%	0%	16%		
TOTAL	7	18	11	14	50		
* : HIGHLY SIGNIFICANT							

- 57.1% of the cirrhotics with WHC grade 0 had star drawing score of 4 and 42.9% of them had star score of 3.
- 77.8% of the cirrhotics with WHC grade 1 had star drawing score of 3 and 22.2% of them had star drawing score of 4.
- 100% of the cirrhotics with WHC grade 2 had star drawing score of 2.

- 71.4% of the cirrhotics with WHC grade 3 had star drawing score of 1, 28.6% of them had a score of 2 and1 with 14.3% each.
- Table 44 and figure 50 thus shows that there is statistically significant association between clock drawing and WHC grades (p=0.001).

FIGURE 50 : ASSOCIATION BETWEEN STAR DRAWING AND WHC GRADES



Colours represent different grades of WHC.

TABLE 45 : ASSOCIATION BETWEEN STAR DRAWING AND PSEI

STAR	PSEI			CHI SQUARE TEST	p VALUE
	< .3300	.3300+	TOTAL		
0	0	2	2	X^2=17.146	p=0.001*
%	0%	5.3%	4%		
1	0	10	10		
%	0%	26.3%	20%		
2	0	13	13		
%	0%	34.2%	26%		
3	7	10	17		
%	58.3%	26.3%	34%		
4	5	3	8		
%	41.7%	7.9%	16%		
TOTAL	12	38	50		
* : HIGHLY SIGNIFICANT					

- 58.3% of the cirrhotics with PSEI less than 0.33 had star drawing score of 3 and 41.7% of them had a score of 4.
- 32.6% of the cirrhotics with PSEI more than or equal to 0.33 had star drawing score of 1 and 3 with 26.3% each, 32.4% of them had a score of 1, 5.3% had a score of 0.

- Table 45 and figure 51 shows that the star drawing and PSEI had statistically significant association at p=0.001

FIGURE 51 : ASSOCIATION BETWEEN STAR DRAWING AND PSEI

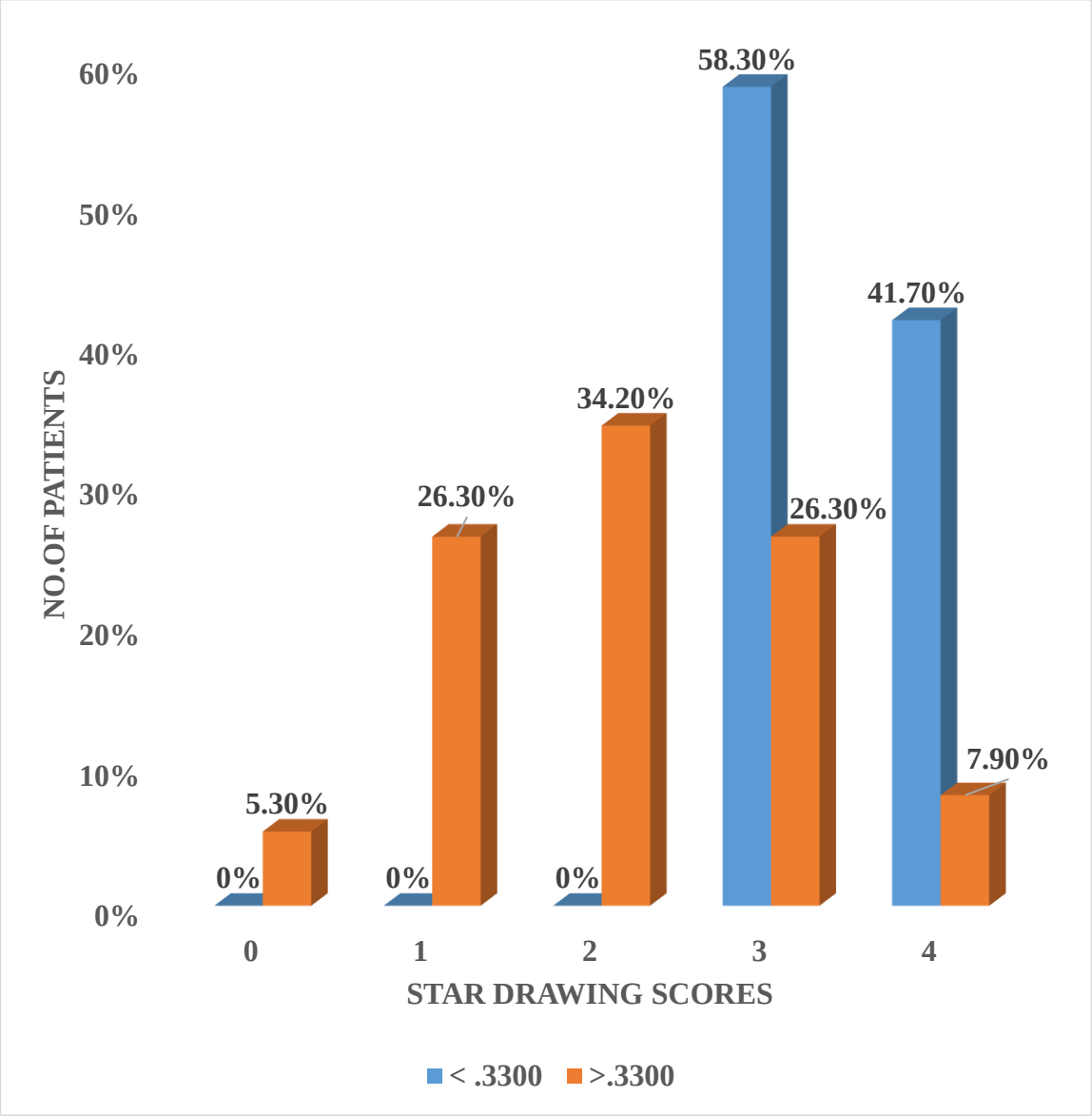


TABLE 46 : KRUSKAL-WALLIS TEST BETWEEN CLOCK SCORES AND PSEI

CLOCK	PSEI			KRUSKAL-WALLIS TEST	p VALUE
	N	MEAN	STD. DEVIATION		
0	14	0.858	0.077	KW=37.472	p=0.0001*
1	7	0.654	0.114		
2	20	0.346	0.167		
3	9	0.223	0.136		
TOTAL	50	0.510	0.284		
* : HIGHLY SIGNIFICANT					

Mean value of PSEI decreases as the clock scoring moves from 0 to 3 as shown in table 46 and figure 52.

FIGURE 52 : MEAN PSEI FOR EACH CLOCK SCORE

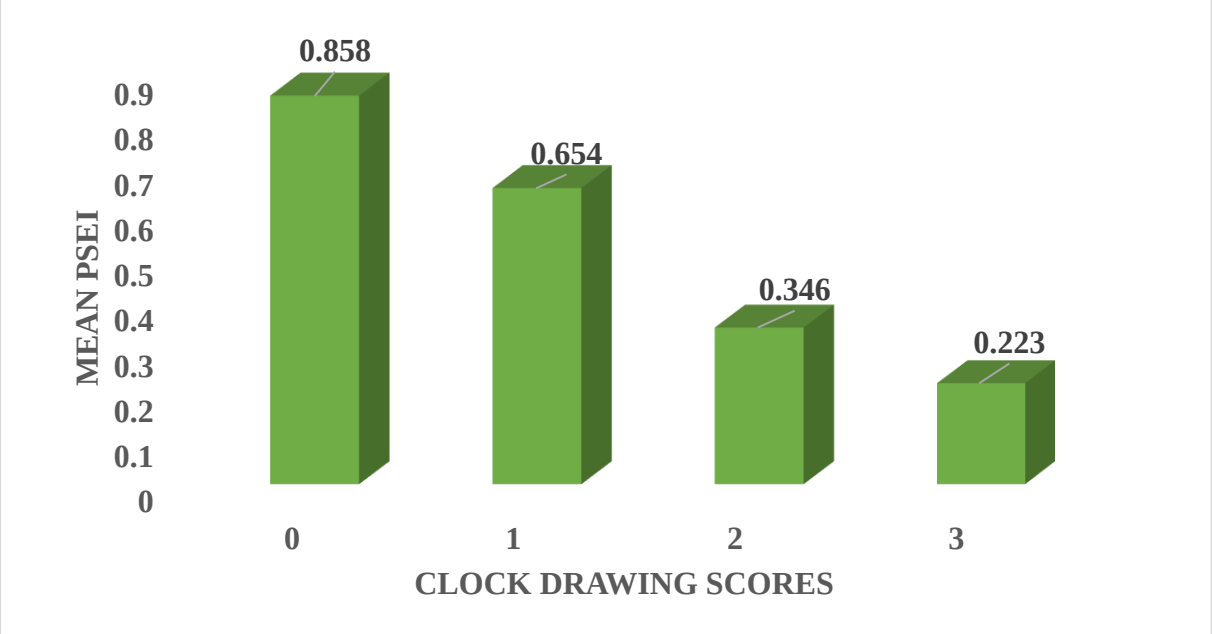


TABLE 47 : TUKEY'S MULTIPLE COMPARISON (POST HOC TESTS) OF VARIOUS CLOCK SCORES

CLOCK	COMPARISON BETWEEN	POST HOC TEST	REMARK
0 VS	1	.011	HS
	2	.000	HS
	3	.000	HS
1 VS	0	.011	HS
	2	.000	HS
	3	.000	HS
2 VS	0	.000	HS
	1	.000	HS
	3	.121	NS
3 VS	0	.000	HS
	1	.000	HS
	2	.121	NS
NS: NOT SIGNIFICANT HS: HIGHLY SIGNIFICANT			

Tukey all pairwise multiple comparisons indicate that the mean PSEI for a clock score of 0 was significantly higher than 1, 2, 3 clock scores as shown in table 47.

TABLE 48 : KRUSKAL-WALLIS TEST BETWEEN STAR SCORES AND PSEI

STAR	PSEI			KRUSKAL-WALLIS TEST	p VALUE
	N	MEAN	STD. DEVIATION		
0	2	0.900	0.000	KW=41.327	p=0.0001*
1	10	0.866	0.082		
2	13	0.654	0.105		
3	17	0.290	0.120		
4	8	0.203	0.131		
TOTAL	50	0.510	0.284		
* : HIGHLY SIGNIFICANT					

Mean value of PSEI decreases as the star scoring moves from 0 to 4 as shown in table 48 and figure 53.

FIGURE 53 : MEAN PSEI FOR EACH STAR SCORE

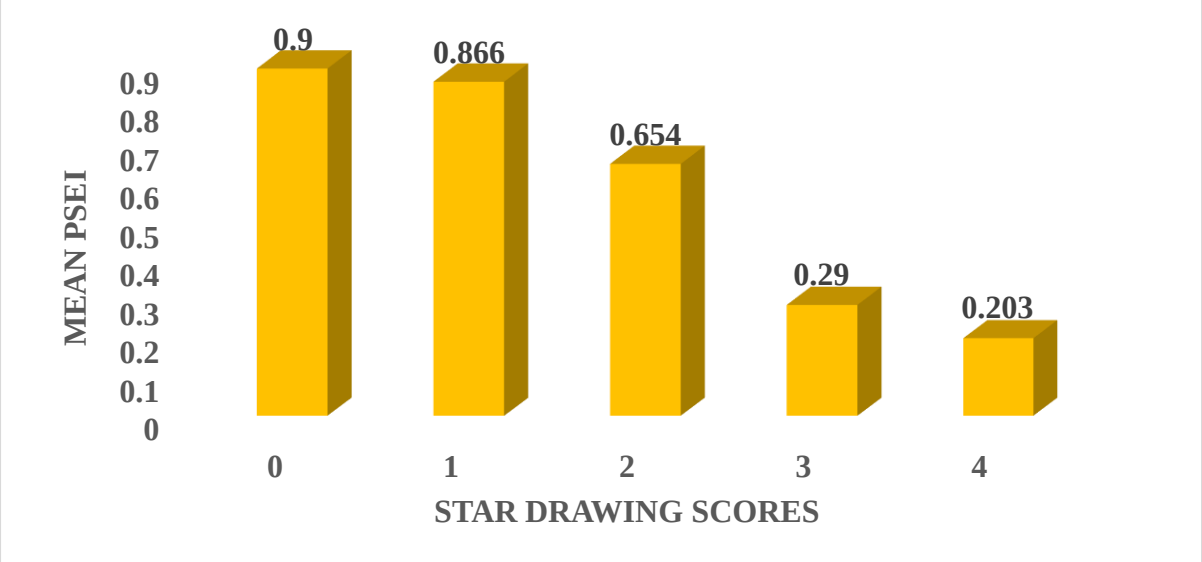


TABLE 49 : TUKEY'S MULTIPLE COMPARISON (POST HOC TESTS) OF VARIOUS STAR SCORES

STAR	COMPARISON BETWEEN	POST HOC TEST	REMARK
0 VS	1	.994	NS
	2	.040	S
	3	.000	HS
	4	.000	HS
1 VS	0	.994	NS
	2	.000	HS
	3	.000	HS
	4	.000	HS
2 VS	0	.040	S
	1	.000	HS
	3	.000	HS
	4	.000	HS
3 VS	0	.000	HS
	1	.000	HS
	2	.000	HS
	4	.370	NS
4 VS	0	.000	HS
	1	.000	HS
	2	.000	HS
	3	.370	NS
NS: NOT SIGNIFICANT HS: HIGHLY SIGNIFICANT S: SIGNIFICANT			

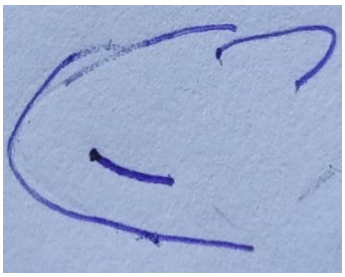
Tukey all pairwise multiple comparisons indicate that the mean PSEI for a star score of 0 was significantly higher than the 2,3,4 star scores as shown in table 49.

TABLE 50 : SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE, NEGATIVE PREDICTIVE VALUES OF CLOCK AND STAR DRAWING TESTS FOR THE DIAGNOSIS OF HEPATIC ENCEPHALOPATHY

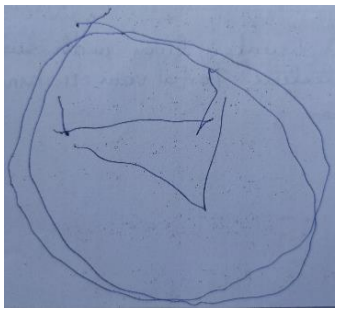
	CLOCK	STAR	CLOCK AND STAR
SENSITIVITY	88.37%	90.70%	76.74%
SPECIFICITY	57.14%	57.14%	71.43%
POSITIVE PREDICTIVE VALUE	92.68%	92.86%	94.29%
NEGATIVE PREDICTIVE VALUE	44.44%	50.00%	33.33%

Our study had shown drawings of clock and star as follows :

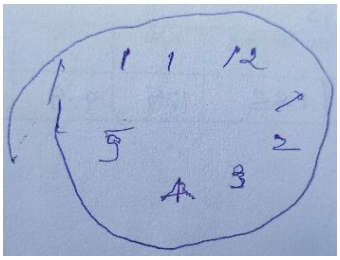
0 Poor Non-recognisable drawing or gross distortion of the basic gestalt



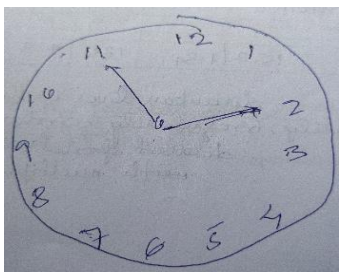
1 Fair Clock should contain an approximately circular face or the numbers 1 through 12.



2 Good Clock should contain 2 of the following circular face numbers 1 through 12 symmetric number placement

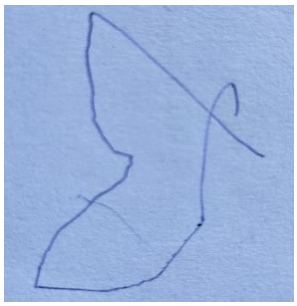


3 Excellent Near perfect representation of the items with all appropriate components placement and perspective

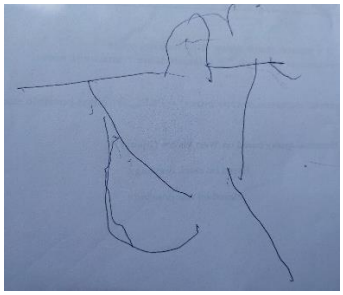


0 Unable to draw

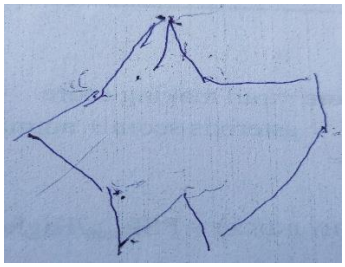
1 Scribble



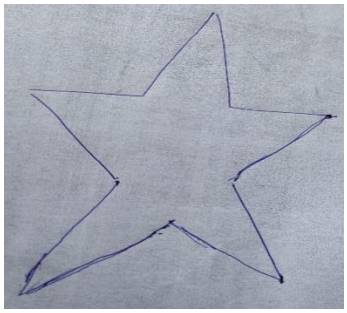
2 Able to draw lines but unable to connect sensibly to form the desired figure



3 Able to draw but imperfect



4. Perfect



DISCUSSION :

In our study, we observed cirrhotic patients admitted to Shri B M Patil medical college, Vijayapura with a spectrum of neurological manifestations ranging from being normal, short attention span and disorientation to stupor. Those presented with coma were excluded from our study. Our study parameters were compared with the parameters in different studies as shown.

TABLE 51 : COMPARISION OF MEAN AGE AMONG DIFFERENT STUDIES

DIFFERENT STUDIES	MEAN AGE (YEARS)
OUR STUDY	45.36±11.972
Mukherjee PS et al[93]	42.8±14.4
Suthar H et al[94]	41
Luca A et al[95]	55.3±9.8
Sajja KC et al[96]	52 ± 11

In our study mean age of the cirrhotics was 45.36±11.972 years of age which was comparable with studies done in India by Mukherjee PS et al[93] which depicted mean age of 42·8±14.4 years and Suthar H et al[94] which had shown a mean age of 41 years where as higher mean age of 55.3±9.8 years and 52 ±11 years were found in studies done by Luca A et al (Austria, Europe)[95] and Sajja KC et al (Texas, USA)[96].

Lower mean age among Indian studies may suggest higher burden of cirrhosis in our country.

TABLE 52 : COMPARISION OF GENDER FREQUENCY AMONG DIFFERENT STUDIES

DIFFERENT STUDIES	FEMALE	MALE
OUR STUDY	2	48
Maskey R et al[97]	33	72
Scaglione Set al[98]	27	72
Wang X et al[99]	1361	6719

Studies done across the world like in Nepal by Maskey R et al[97], in USA by Scaglione et al[98], in China by Wang X et al[99] had shown male preponderance in cirrhotics but the ratio of female to male doesn't match because of the smaller sample size and duration of our study.

Most common etiology of cirrhosis in our study was alcohol related followed by viral etiology. The same pattern of alcohol being the most common cause of cirrhosis was observed in studies done by Baki JA et al[100], Mukherjee PS et al[93], Ahmed S et al[101] . Though there is a recent incline in trend towards non alcoholic fatty liver disease as the cause of cirrhosis, mortality due to alcohol related liver disease too remains on the race when studied from 2007-2016[102].

Mean volume of alcohol consumption in our study was 120.76 ± 44.42 grams/day and mean duration of alcohol consumption was 17.74 ± 8.231 as comparable to a study done by Maskey R et al[97] which had shown mean duration of alcohol consumption in alcohol related diseases as 16.25 years. Alcoholic cirrhosis can be diagnosed with history of alcohol consumption of more than 80g/day in males and 40g/day in females[97].

TABLE 53 : COMPARISION OF CLINICAL FINDINGS AMONG DIFFERENT STUDIES

	OUR STUDY	**Pathak OK et al[103]**	**Rishi AK et al[104]**
Pallor	50	33	10.5
Fever	16	19	16
Hematemesis	10	20	17.1
Malena	14	37	26
Other bleeding manifestations	36		6.1
Spider nevi	62	30	8.8

In our study, pallor was present in 50% of the patients but severe in 32% of the patients as comparable to study done by Pathak OK et al[103]. Fever was present in 16% of the patients as comparable with studies done by Pathak OK et al[103] and Rishi AK et al[104]. Hematemesis and malena were present in 10% and 14% respectively in our study.

TABLE 54 : COMPARISION OF LAB PARAMETERS AMONG DIFFERENT STUDIES

LAB PARAMETERS	OUR STUDY	Behera BP et al[105]	Pathak OK et al[103]
RBC (million cells/mm3)	3.02±0.82	3.15±0.90	
HEMOGLOBIN (mg/dL)	9.16±2.69	7.99±2.18	11.85 ± 3.45
MCV (fL)	91.47±11.33	76.12±12.01	96.42 ± 9.09
MCH (pg)	31.19±4.34	25.38±3.74	-
MCHC (%)	33.89±2.43	33.49±6.24	-
TOTAL LEUCOCYTE COUNT (cells/mm3)	10659.6±7459.33	-	9303.89 ± 4718.38
PLATELET COUNT (lakh cells/mm3)	1.27±0.89	1.38±0.79	1.62 ± 0.89
TOTAL BILIRUBIN (mg/dL)	8.1±7.7	3.78±5.74	4.05±4.5
UNCONJUGATED BILIRUBIN (mg/dL)	2.9±2.3	-	2.53±3.56
CONJUGATED BILIRUBIN (mg/dL)	5.1±5.8	1.86±2.62	1.47±1.44
ALBUMIN (g/dL)	2.4±0.8	-	3.22±0.86
SGOT (U/L)	137.3±243.5	99.49±115.93	142.95±158.85
SGPT (U/L)	96.1±235.8	75.45±79.68	81.56±133.7
ALP (U/L)	137.5±54	128.66±80.80	-
CREATININE (mg/dL)	1.3±1.01	1.53±1.51	-

Abnormal hematological parameters in cirrhotics are due to[106] :

- Increased splenic sequestration due to portal hypertension.
- Decline in thrombopoietin, erythropoietin, hematopoietic stimulating factor.
- Suppression of bone marrow mediated by toxins like alcohol, hepatitis B and C.
- Increased blood loss with gastro intestinal bleeds or hemolysis.

In our study, anemia is observed with a mean Hb of 9.16±2.69 whereas much lower value of Hb was seen in study done by Behera BP et al[105] in Orissa which can be attributed to much lower socioeconomic condition of their state and higher value of mean Hb was seen in study by Pathak OK et al[103] as their study included milder forms of alcoholic liver diseases and not only cirrhosis. But overall in all the studies, anemia is significantly observed.

Macrocytic type of anemia was seen in our study inferring from the fact that the MCV values were higher and MCH and MCHC were on their lower side of normal range. In study done by Behera BP et al[105] in Orissa, microcytic anemia was seen which can be attributed to much lower socioeconomic condition of their state.

Not much leucopenia was observed in our study as well as study done by Pathak OK et al[103].

Thrombocytopenia was observed in our study with a mean platelet count of 1.27±0.89 as comparible with Behera BP et al[105] study but Pathak OK et al[103] study had shown lower normal platelet count as their study included milder forms of alcoholic liver diseases and not just cirrhosis.

Obviously elevated levels of bilirubin, hypoalbuminemia, SGOT levels very much higher than SGPT were observed in our study as well as in Behera BP et al[105] study and Pathak OK et al[103] study.

Creatinine was found to be on the higher side of normal with a mean of 1.3±1.01 as similar to Behera BP et al[105]

TABLE 55 : COMPARISION OF UPPER GI FINDINGS AMONG DIFFERENT STUDIES

UPPER GI FINDINGS	OUR STUDY	Svoboda P et al[107]	Hadayat R et al[108]
Esophageal varices	30%	64.90%	92.90%
Portal hypertensive gastropathy	4%	45.70%	38.90%
Gastric erosions/ulcers	4%	4.60%	10.30%
Acid reflux changes in esophagus	8%	13.20%	3.20%

Most common upper gastrointestinal endoscopic findings were esophageal varices followed by acid reflux changes in esophagus in our study, whereas studies done by Svoboda P et al[107] and Hadayat R et al[108] though had shown esophageal varices as the most common finding, it is followed by portal hypertensive gastropathy. Higher incidence of acid peptic disease in cirrhotics was observed as compared to the general population[107].

TABLE 56 : COMPARISION OF PERCENT OF SEVERITY OF HEPATIC ENCEPHALOPATHY AMONG DIFFERENT STUDIES

GRADES OF HEPATIC ENCEPHALOPATHY	OUR STUDY	Khan A et al[109]	Ong JP et al[110]
Grade 0 WHC	14%	13.50%	25%
Grade 1 WHC	36.00%	34%	22%
Grade 2 WHC	22.00%	22.20%	19%
Grade 3 WHC	28.00%	23.40%	23%

Percentages of patients in various WHC grades in our study are very similar to those in the study done by Khan A et al[109] but higher percent of grade 0 hepatic encephalopathy seen in study done by Ong JP et al[110] in USA may be explained by higher level of identification of covert hepatic encephalopathy there.

In our study, clock and star each had shown statistically significant associations with WHC grades and PSEI (p=0.001*) similar to the study done by Edwin N et al[111], WHC grades and PSEI were comparable with the star and clock drawings. The sensitivity and specificity of star and clock in our study was 90.7%, 88.37% and 57.14%, 57.14% respectively whereas sensitivity and specificity of star and clock in the study done by Edwin N et al[111] was 77%, 85% and 70%, 80% respectively. This may be explained by smaller sample size in our study.

SUMMARY

- The present study was a hospital based cross sectional observational study of 50 patients with sonological diagnosis of cirrhosis admitted in Shri B M Patil medical college, Vijayapura between the period of November 2018 to June 2020 were tested for the degree of hepatic encephalopathy by using tests of constructional apraxia that were star and clock drawings.
- The clinical profile of cirrhotics were studied which had shown alcohol as the most common etiology of cirrhosis with mean volume of alcohol being 120.76 ± 44.42 grams/day and mean duration of alcohol being 17.74 ± 8.231.
- Laboratory evaluation had shown macrocytic anemia and thrombocytopenia and also SGOT levels much higher than SGPT.
- Most common finding in upper gastrointestinal endoscopy was esophageal varices (30%).
- Statistically significant correlation was observed between ammonia and Child Pugh score.
- Statistically significant association was observed between ammonia and severity of hepatic encephalopathy.
- Statistically significant association was present between clock drawing and WHC grades and PSEI as well as star drawing and WHC grades and PSEI. The sensitivity and specificity of star and clock in our study was 90.7%, 88.37% and 57.14%, 57.14% respectively

CONCLUSION

- As there is statistically significant association between standard evaluation methods of hepatic encephalopathy like WHC grades and portosystemic encephalopathy scoring and clock and star drawings which are simple, bedside, less time consuming tests of constructional apraxia could be recommended to assess the severity of hepatic encephalopathy on a routine basis.

LIMITATIONS OF OUR STUDY

- In the absence of the gold standard method of diagnosing hepatic encephalopathy, a combination of West Haven Criteria (WHC) and Porto Systemic Encephalopathy Index (PSEI) was used as : No encephalopathy if the WHC grade was 0 and the PSEI was < 0.33 and as having encephalopathy if WHC grade > 0 or a PSEI $\geq$ 0.33
- Reliability of the tests applied could not be assessed.

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ANNEXURE -I

ETHICAL CLEARENCE CERTIFICATE

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC. NO. 286/18
17/11/2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Use of clock & star drawing , as a marker of neuropsychological assessment in the grading of hepatic encephalopathy and compare with west haven criteria and portosystemic encephalopathy score & index.

Name of P.G. Student : Dr Nimmagadda Viraja
Department of General Medicine.

Name of Guide/Co-investigator: Dr. Mallanna S.Mulimani, Professor & HOD of General Medicine.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDE(D)'s Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURE II

INFORMED CONSENT FORM:

TITLE OF RESEARCH: **"USE OF CLOCK AND STAR DRAWING, AS A MARKER OF NEUROPSYCHOLOGICAL ASSESSMENT IN THE GRADING OF HEPATIC ENCEPHALOPATHY AND COMPARE WITH WEST HAVEN CRITERIA AND PORTOSYSTEMIC ENCEPHALOPATHY SCORE"**

GUIDE : **Dr. MALLANNA S. MULIMANI**

MD MEDICINE

P.G. STUDENT: **Dr. NIMMAGADDA VIRAJA**

All aspects of this consent form are explained to the patient in the language understood by him or her.

PURPOSE OF STUDY:

I have been informed that the purpose of this study is to study diagnostic importance of platelet volume indices in patients with acute chest pain suggesting acute coronary syndrome.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations

BENEFITS:

I understand that my participation in this study will have no direct benefit to me other than the potential benefit of treatment which is planned to prevent further morbidity and mortality in me.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

(Signature of Guardian) (Signature of patient)

STUDY SUBJECT CONSENT FORM:

I confirm that **Dr. NIMMAGADDA VIRAJA** has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

DATE SIGNATURE OF PARTICIPANT

DATE SIGNATURE OF WITNESS

ANNEXURE III

PROFORMA OF CASE TAKING

Identification Details :

Name/ Age/ Sex	
Education	
Address	
Date/ IP No	

Presenting Complaints :

Personal Habits :

Diet	
Sleep	
Appetite	
Bowel	
Bladder	
Habits: Alcoholism Smoking Others	

General Physical Examination :

Vitals:

Pulse (bpm)	Blood Pressure (mm hg)	Respiratory Rate (cpm)	Temperature (degree celcius)

Others:

Systemic Examination :

Per Abdomen:

Central Nervous System:

Respiratory System:

Cardio Vascular System:

Investigations:

Complete Blood Count:

Urine Routine:

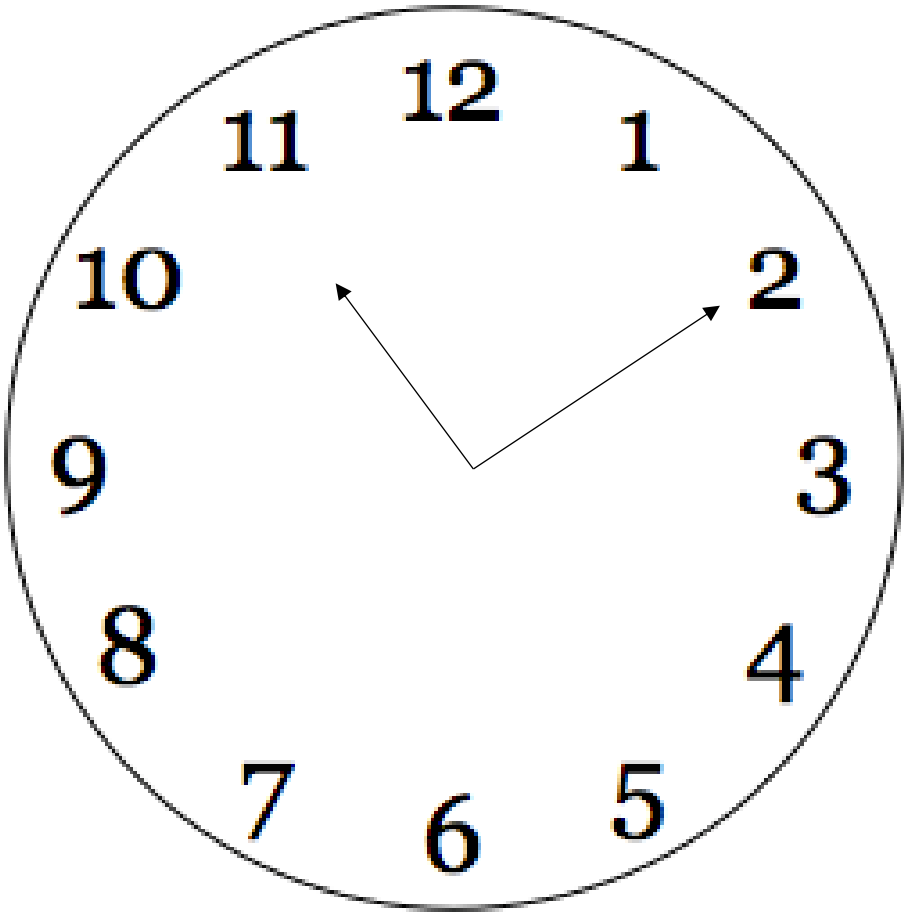
Liver Function Test:

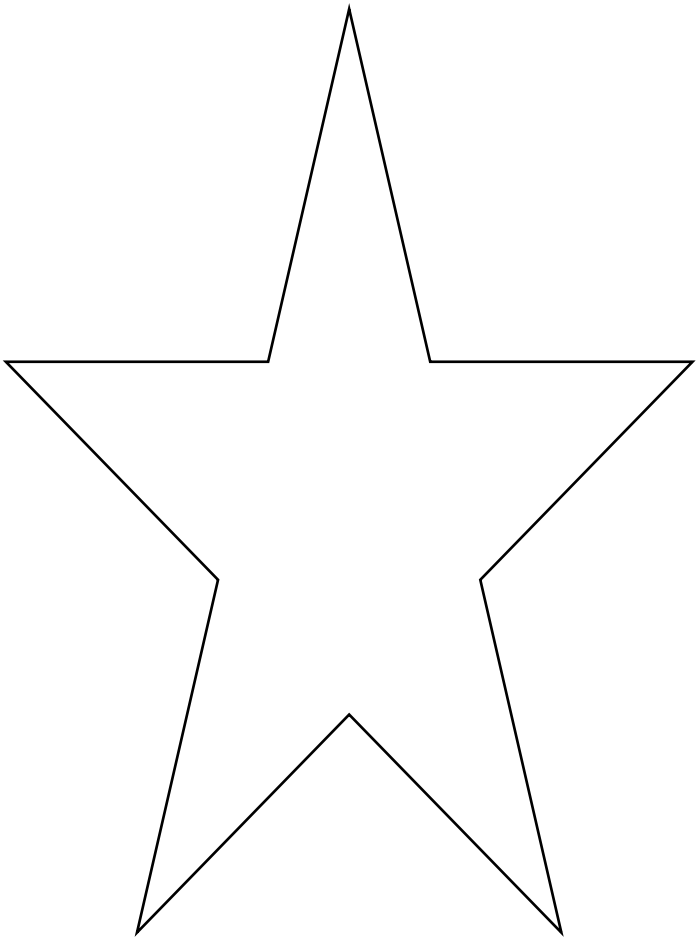
Bleeding time	Clotting time	Prothrombin time/INR	$S.Na^+$	$S.K^+$	S.Creatinine	S.Ammonia

Ultrasonography of abdomen:

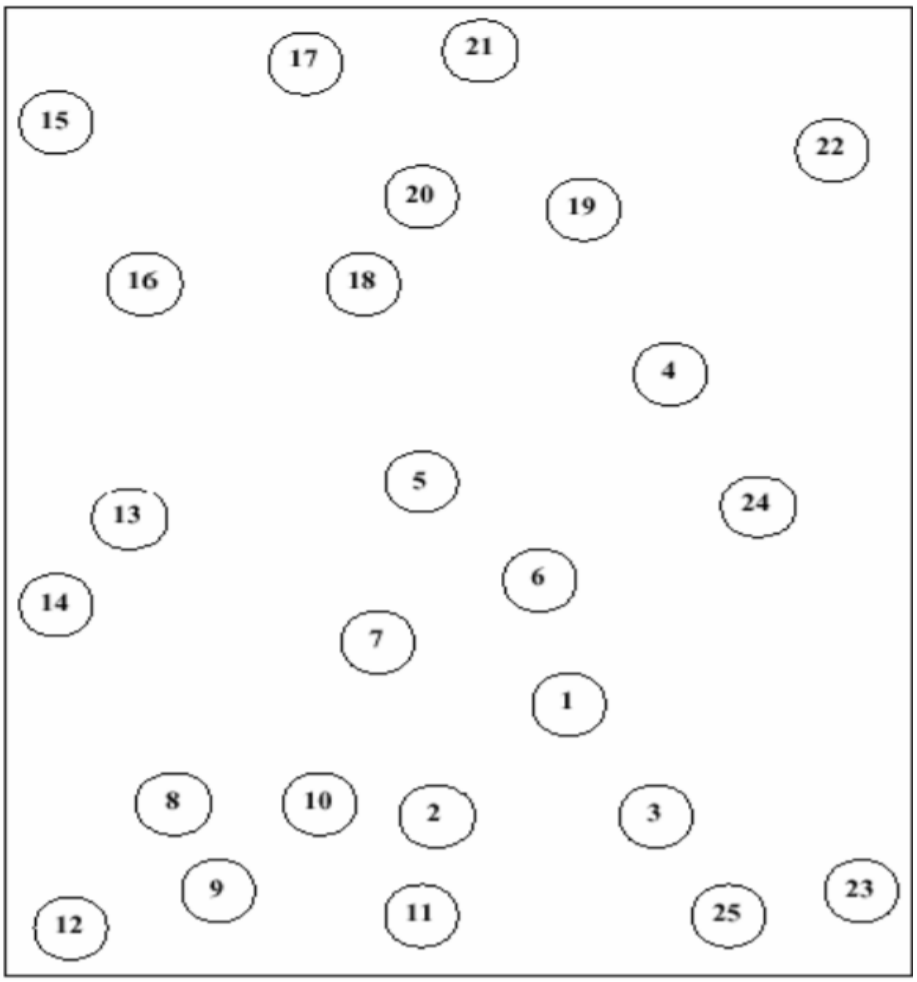
Upper Gastrointestinal Endoscopy:

Drawings of Clock And Star :





Time taken for Trail Making :



PSE_{sum} = 3 x mental status score + trail making score (PORTO SYSTEMIC ENCEPHALOPATHY SUM) + asterixis score + ammonia score =

PSEI(PORTO SYSTEMIC ENCEPHALOPATHY INDEX) = PSE_{sum}/Highest possible sum. =

Grade of Hepatic Encephalopathy based on West Haven Criteria :

Based on clock drawing :

Based on star drawing :

ANNEXURE IV
MASTER CHART

SNO	NAME	AGE	SEX	DURATION OF SYMPTOMS	CLINICAL ALTERED SENSORIUM	FEVER	PAST H/O	BLADDER	AVERAGE VOL OF ALCOHOL CONSUMPTION	AVERAGE DURATION OF ALCOHOL CONSUMPTION	OTHER HABITS	PALLOR	NAILS	ASTEREXIS	ARTERIAL SPIDERS	BLEEDING MANIFESTATIONS	PA	CNS
1	LOKAPPA	43	M	3 TO 6 MONTHS	PRESENT	NO	CIRRHOSIS MORE THAN 6 MONTHS	N	125	35 YRS	NIL	PRESENT	LEUKONYCHIA	CONTINUOUS FLAPS	PRESENT	ECCHYMOSIS ON BODY, MALENA	FLUID THRILL PRESENT	STUPOROUS
2	SHRIKANTH	50	M	3 TO 6 MONTHS	PRESENT	NO	CIRRHOSIS MORE THAN 6 MONTHS	DECREASED OUTPUT	200	35 YRS	BD SMOKER FOR 35 YRS	SEVERE	LEUKONYCHIA	FREQUENT FLAPS	PRESENT	BLEEDING PER RECTUM	FLUID THRILL PRESENT	DISORIENTED
3	VIJAY PATRE	42	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	178	28 YRS	GUTKA CHEWER FOR 28 YRS	SEVERE	PALLOR	OCCASIONAL FLAPS	ABSENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
4	PRASANNA	38	M	1 TO 3 MONTHS	PRESENT	NO	CIRRHOSIS 3 TO 6 MONTHS	N	231	20 YRS	NIL	SEVERE	KOILONYCHIA, PLATYNYCHIA, CLUBBING	FREQUENT FLAPS	ABSENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	STUPOROUS
5	GOUDAPPA	40	M	LESS THAN 1 MONTH	PRESENT	YES	NIL	N	66	20 YRS	BD SMOKER FOR 10 YRS	PRESENT	LEUKONYCHIA, CLUBBING	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
6	SOMANING	37	M	LESS THAN 1 MONTH	PRESENT	YES	CIRRHOSIS MORE THAN 6 MONTHS	N	60	10 YRS	TOBACCO CHEWER FOR 5 YRS	PRESENT	PALLOR	CONTINUOUS FLAPS	PRESENT	ECCHYMOSIS ON BODY	SHIFTING DULLNESS PRESENT	STUPOROUS
7	AKBAR	38	M	1 TO 3 MONTHS	PRESENT	YES	NIL	N	125	10 YRS	GUTKA CHEWER FOR 4 YRS	SEVERE	PALLOR, LEUKONYCHIA	FREQUENT FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	DISORIENTED
8	SHRIKANTH	40	M	LESS THAN 1 MONTH	ABSENT	NO	NIL	N	90	15 YRS	BD SMOKER FOR 5 YRS	SEVERE	PALLOR, LEUKONYCHIA	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
9	RAJU PANDURANGARAO	39	M	LESS THAN 1 MONTH	ABSENT	NO	NIL	N	125	20 YRS	CIGARETTE SMOKER FOR 45 YRS	ABSENT	N	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
10	LAXMAN KASE	42	M	MORE THAN 6 MONTHS	PRESENT	NO	NIL	N	160	25 YRS	NIL	SEVERE	PALLOR, LEUKONYCHIA	FREQUENT FLAPS	PRESENT	ORAL MUCOSAL BLEEDING	SHIFTING DULLNESS PRESENT	STUPOROUS
11	UMESH WALI	28	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	125	6 YRS	TOBACCO CHEWER SINCE 15 YRS	ABSENT	LEUKONYCHIA	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
12	ARUN MOHANRAO	25	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS 3 TO 6 MONTHS	N	60	4 YRS	CIGARETTE SMOKER FOR 4 YRS	SEVERE	LEUKONYCHIA, PALLOR	OCCASIONAL FLAPS	PRESENT	NIL	FLUID THRILL PRESENT	DISORIENTED
13	SHIVANAND MURANAL	51	M	1 TO 3 MONTHS	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	N	60	20 YRS	TOBACCO CHEWER FOR 25 YRS	ABSENT	N	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
14	RUDRAPPA ZENDED	40	M	1 TO 3 MONTHS	PRESENT	NO	NIL	DECREASED OUTPUT	178	5 YRS	TOBACCO CHEWER FOR 5 YRS	SEVERE	LEUKONYCHIA	FREQUENT FLAPS	PRESENT	MALENA	FLUID THRILL PRESENT	STUPOROUS
15	SHRISHAIL IMADI	51	M	1 TO 3 MONTHS	PRESENT	YES	CIRRHOSIS MORE THAN 1 YEAR	N	125	25 YRS	NIL	ABSENT	N	RARE FLAPS	ABSENT	NIL	FLUID THRILL PRESENT	SHORT ATTENTION SPAN
16	SHIVANAND MALGAR	62	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	125	30 YRS	CIGARETTE SMOKER FOR 8 YRS	ABSENT	N	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
17	CHAMPABAI MASALI	38	F	1 TO 3 MONTHS	PRESENT	YES	NIL	N	NIL	NIL	NIL	SEVERE	PLATYNYCHIA	FREQUENT FLAPS	PRESENT	BLEEDING PER RECTUM	FLUID THRILL PRESENT	STUPOROUS
18	YALLAPPA	30	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	90	10 YRS	TOBACCO CHEWER FOR 5 YRS	ABSENT	N	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
19	GANGAPPA PUJARI	65	M	1 TO 3 MONTHS	PRESENT	NO	NIL	N	NIL	NIL	NIL	PRESENT	N	FREQUENT FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	STUPOROUS
20	ASHFAQ TIKOTI	40	M	LESS THAN 1 MONTH	PRESENT	YES	CIRRHOSIS 1 TO 3 MONTHS	N	60	25 YRS	GUTKA CHEWER FOR 10 YRS	ABSENT	N	FREQUENT FLAPS	PRESENT	ECCHYMOSIS ON BODY	FLUID THRILL PRESENT	STUPOROUS
21	AMAR KHANSE	42	M	LESS THAN 1 MONTH	PRESENT	NO	TZDM, HTN, CIRRHOSIS 3 TO 6 MONTHS	N	178	20 YRS	NIL	ABSENT	N	CONTINUOUS FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	STUPOROUS
22	KESHUNAIK	54	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	N	125	20 YRS	NIL	PRESENT	PALLOR	OCCASIONAL FLAPS	PRESENT	NIL	FLUID THRILL PRESENT	DISORIENTED
23	BABAGOUDA	61	M	3 TO 6 MONTHS	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	N	90	20 YRS	NIL	PRESENT	LEUKONYCHIA	OCCASIONAL FLAPS	PRESENT	MALENA	FLUID THRILL PRESENT	DISORIENTED
24	SURESH	43	M	LESS THAN 1 MONTH	ABSENT	YES	NIL	N	90	15 YRS	CIGARETTE SMOKER FOR 10 YRS	PRESENT	N	RARE FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
25	SIDDAPPA PUJARI	24	M	LESS THAN 1 MONTH	ABSENT	YES	CIRRHOSIS 3 TO 6 MONTHS	DECREASED OUTPUT	90	6 YRS	NIL	SEVERE	PALLOR	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR

SNO	RBC	HB	MCV	MCH	MCHC	TLC	NEUTRO	LYMPHO	EOSINO	MONO	BASO	PLT	TOTAL BIL	UNCONJ BIL	CONJ BIL	ALBUMIN	SGOT	SGPT	ALP	INR	SODIUM	POTASSIUM	CREAT	AMMONIA	ETIOLOGY OF CIRRHOSIS	SONOLOGICAL ASCITES	SPLENOMEGALY	UGI ENDOSCOPY	CLOCK	STAR	TRAIL	WHC GR	PSE SUM	PSEI	CP SCORE	CHILD CLASS
1	2.79	9.9	104.3	35.4	34.02	35990	94	4	2	0	0	1	0.84	13.5	5.9	7.53	2	56.5	19.5	65	3.78	144	3.5	0.6	140	ALCOHOL	GROSS ASCITES	15 CMS	ND	0	0	INCOMPLETE	3	19	0.9	15	C
2	2.22	7.4	102.7	33.3	32.5	21560	91.6	3.6	0.4	4.3	0.1	0.84	4	13.5	5.9	7.53	3	56.5	19.5	107	2.27	136	5.2	3	98	ALCOHOL	GROSS ASCITES	12.6 CMS	ND	0	2	INCOMPLETE	2	17	0.8	14	C
3	3	7.8	85.4	25.9	30.4	9920	72.4	15.6	4	2	1	0.92	3.2	1	2.2	2	34	40	260	1.5	132	4.7	1.9	74	ALCOHOL	MODERATE ASCITES	12 CMS	PREPYLORIC ULCERS	3	3	78	1	8	0.38	12	C
4	2.6	7	84.8	31.3	36.8	11690	91.5	3	3	2	1	0.88	8.6	5.2	3.4	2.3	54	46	111	1.86	132	3.2	0.7	128	ALCOHOL	MODERATE ASCITES	14 CMS	ND	0	1	INCOMPLETE	3	18	0.85	14	C
5	3	8.3	81	26	32	16300	86	6.8	6	4	1	0.43	0.7	0.3	0.4	1.6	16	16	125	1.68	140	4	0.5	70	ALCOHOL	MILD ASCITES	11.5 CMS	ND	2	4	80	1	6	0.28	9	B
6	3	8.1	109.3	37.9	34.6	23630	91.2	2.9	1.2	3	0	0.35	23	4	19	2.5	160	37	114	2.36	136	4	1.6	101.8	ALCOHOL	MODERATE ASCITES	12.3 CMS	ND	0	1	INCOMPLETE	3	19	0.9	15	C
7	2.5	6.9	111.9	35.8	31.9	31960	87.9	6.9	0.8	2	1	2	12.2	4.8	7.4	2.3	72	17	224	1.83	139	4.9	1.5	84	ALCOHOL	MODERATE ASCITES	16 CMS	ND	2	2	>120	2	14	0.66	13	C
8	2.4	6.6	80.3	27	33.7	5590	91.6	5.9	0	2.5	0	0.37	2	1	1	2.6	15.7	1.34	141	1.34	135	4.3	1.7	84	ALCOHOL	MODERATE ASCITES	12 CMS	ND	3	4	84	0	4	0.19	8	B
9	3.75	10	79.2	26.7	33.7	6520	60.3	28.5	1.7	9	0.5	1.47	2.4	1.3	1.1	2.7	153	64	171	1.5	135	3.4	0.9	80	ALCOHOL	MILD ASCITES	10 CMS	ND	2	3	90	0	3	0.14	9	B
10	1.78	6.7	124.7	37.6	30.2	12180	91	6.6	0.8	1.4	0	0.7	12.9	6	6.9	2.3	74	36	151	4.74	131	5.1	1.6	168	ALCOHOL	GROSS ASCITES	14 CMS	ND	0	1	INCOMPLETE	3	19	0.9	15	C
11	3.8	10.9	83.6	29	34.9	8890	71	19	0.1	8.2	0	3.24	3.3	1.5	1.8	2.7	69	21	168	2.03	132	3.5	0.5	84	ALCOHOL	MODERATE ASCITES	12 CMS	ND	3	4	60	1	7	0.33	13	C
12	1.23	4.6	104.1	37	35.9	8240	78	13	1.2	7.5	0.1	1.25	14.6	2.9	11.7	2.2	66	32	99	2.26	131	4.4	0.8	100	ALCOHOL	MODERATE ASCITES	14.5 CMS	ND	2	2	80	2	12	0.57	14	C
13	3.39	10.5	91	31	34.1	10030	77	14	9	0	0	1.14	1.4	0.8	0.6	2.2	78	21	90	1.33	133	4.1	0.8	84	ALCOHOL	MILD ASCITES	13.5 CMS	GASTRITIS	2	3	70	1	7	0.33	9	B
14	2	5.9	91.5	29	32	2930	87	10	0	1.7	0	0.71	0.8	0.4	0.4	1.3	42	32	72	3.49	136	4.1	3	96	ALCOHOL	MILD ASCITES	15 CMS	GRADE3 ESOPHAGEAL VARICES	0	1	INCOMPLETE	3	14	0.66	12	C
15	3.45	10.3	102	36	35.3	18850	85	7.3	2.2	4.2	0.9	1.08	8	4	4	2.5	48	24	120	2.6	137	4.5	1.7	88	ALCOHOL	GROSS ASCITES	15 CMS	ND	2	3	60	1	7	0.33	15	C
16	4	12.9	103	36.9	35	6420	73	19	1.2	6.2	0.3	0.69	2.4	1.8	0.6	2.5	108	37	99	1.36	130	4	0.6	108	ALCOHOL	MODERATE ASCITES	12 CMS	ND	3	4	50	1	7	0.33	11	C
17	2.5	6.3	86.7	27.9	32.1	3610	73	14	4	7.8	0	0.51	27	4	23	2.3	58	71	138	2.03	139	4	0.9	136	UNKNOWN	GROSS ASCITES	15 CMS	ND	1	2	INCOMPLETE	3	19	0.9	14	C
18	3.5	11.5	92.4	31.3	33.9	3230	88	9.6	0	2.2	0	0.55	5	2	3	2.5	239	250	151	2.01	131	3.7	0.8	64	ALCOHOL	MODERATE ASCITES	13.5 CMS	ND	3	3	80	1	6	0.28	12	C
19	3.29	9.6	84.8	29.2	34.4	5400	74.8	17.4	0.4	7.4	0	1.22	13	5	8	2.3	45	18	88	1.23	135	3.3	0.8	140	UNKNOWN	MODERATE ASCITES	14.5 CMS	ND	0	0	INCOMPLETE	3	19	0.9	14	C
20	3.09	9.9	99	32	32.4	9730	75.7	15.8	1.4	6.9	0.2	1.9	20.8	7.8	13	2.6	139	49	187	1.55	135	4.4	0.8	145	ALCOHOL	GROSS ASCITES	14.8 CMS	ND	0	1	INCOMPLETE	3	19	0.9	13	C
21	3.19	10.5	96.2	32.9	34.2	6220	69	22.5	1.9	6.3	0.3	3.11	27	7	20	2.7	109	22	122	2.01	139	3.4	0.7	110	ALCOHOL	MODERATE ASCITES	18 CMS	ND	0	1	INCOMPLETE	3	19	0.9	13	C
22	2.41	8.4	101.7	34.9	34.3	4660	56.3	19.1	15	9.2	0.4	0.66	3.2	2	1.2	2.4	87	56	188	1.78	142	3.9	0.9	90	ALCOHOL	GROSS ASCITES	16 CMS	PORTAL HYPERTENSIVE GASTROPATHY	2	2	INCOMPLETE	2	12	0.57	13	C
23	2.8	8.2	99.3	29.3	29.5	4600	57	34	6	3	0	1.14	10.1	2.9	7.2	2.7	82	101	105	1.7	138	4	0.6	98	ALCOHOL	MODERATE ASCITES	13.5 CMS	ND	2	2	90	2	12	0.57	13	C
24	2.97	9.1	88.2	30.6	34.7	8320	74.5	17.4	0.8	6.6	0.7	1.76	4	1.9	2.1	2.4	64	20	152	1.7	132	3.2	2.1	102	ALCOHOL	MODERATE ASCITES	11 CMS	NORMAL	2	3	76	1	7	0.33	12	C
25	1.73	4.2	74.6	24.3	32.6	2820	81.2	10.6	1.1	7.1	0	0.68	1	0.5	0.5	3.1	39	32	69	1.3	134	3.9	0.7	54	ALCOHOL	MILD ASCITES	15.3 CMS	PORTAL HYPERTENSIVE GASTROPATHY	3	4	50	0	1	0.04	8	B

26	AJEETH HIREDESAI	50	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS 3 TO 6 MONTHS	N	125	10 YRS	NIL	ABSENT	N	ABSENT	PRESENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
27	BOURAMMA	80	F	3 TO 6 MONTHS	PRESENT	NO	NIL	N	66	12 YRS	NIL	PRESENT	N	RARE FLAPS	PRESENT	NIL	FLUID THRILL PRESENT	DISORIENTED
28	SIDDAPPA ADLI	45	M	LESS THAN 1 MONTH	ABSENT	NO	HIV	N	60	15 YRS	TOBACCO CHWER FOR 5 YRS	ABSENT	N	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
29	BASAVARAJ	66	M	LESS THAN 1 MONTH	PRESENT	NO	T2DM, HTN, HID	DECREASED OUTPUT	125	20 YRS	BD SMOKER FOR 10 YRS	RARE FLAPS	CLUBBING	RARE FLAPS	PRESENT	MALENA	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
30	DYANESHWAR	36	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	N	125	15 YRS	CIGERATTE SMOKER FOR 15 YRS	ABSENT	N	OCCASIONAL FLAPS	PRESENT	HEMATEMESIS	SHIFTING DULLNESS PRESENT	DISORIENTED
31	BALAGOND GOUDAR	51	M	1 TO 3 MONTHS	PRESENT	NO	NIL	N	90	20 YRS	TOBACCO CHEWER FOR 10 YRS	ABSENT	LEUKONYCHIA	OCCASIONAL FLAPS	PRESENT	ECCHYMOSIS ON BODY	SHIFTING DULLNESS PRESENT	DISORIENTED
32	MAHANTESH HITNALLI	56	M	LESS THAN 1 MONTH	ABSENT	NO	NIL	N	66	10 YRS	NIL	SEVERE	PALLOR	ABSENT	ABSENT	BLEEDING PER RECTUM, HEMATEMESIS	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
33	KUTBUDDIN YELAPUR	44	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	90	30 YRS	TOBACCO CHEWER FOR 30 YRS,BD SMOKER FOR 20 YRS	PRESENT	N	ABSENT	PRESENT	ECCHYMOSIS ON BODY	FLUID THRILL PRESENT	SHORT ATTENTION SPAN
34	GURAPPA KUMBAR	42	M	LESS THAN 1 MONTH	PRESENT	NO	T2DM, CIRRHOSIS 3 TO 6 MONTHS	N	125	20 YRS	NIL	ABSENT	CLUBBING	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	DISORIENTED
35	HIRU RATHOD	56	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	125	30 YRS	BD SMOKER FOR 30 YRS	ABSENT	CLUBBING	FREQUENT FLAPS	PRESENT	NIL	FLUID THRILL PRESENT	DISORIENTED
	RAVI HADAPAD	25	M	1 TO 3 MONTHS	PRESENT	YES	NIL	N	160	8 YRS	TOBACCO CHWER FOR 8 YRS	ABSENT	N	OCCASIONAL FLAPS	PRESENT	ECCHYMOSIS ON BODY	FLUID THRILL PRESENT	STUPOROUS
36	SHIVKUMAR KARJOL	41	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	DECREASED OUTPUT	90	20 YRS	NIL	ABSENT	LEUKONYCHIA	OCCASIONAL FLAPS	PRESENT	MALENA, HEMATEMESIS	FLUID THRILL PRESENT	STUPOROUS
37	PANDAPPA	58	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	NIL	NIL	NIL	ABSENT	N	ABSENT	ABSENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
38	SHRISHAIL PATED	50	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS 3 TO 6 MONTHS	DECREASED OUTPUT	90	15 YRS	TOBACCO CHEWER FOR 15 YRS	SEVERE	PALLOR	OCCASIONAL FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	DISORIENTED
39	RAMU KOLI	52	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	N	125	10 YRS	NIL	ABSENT	N	ABSENT	PRESENT	HEMATEMESIS, MALENA	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
40	DUNDAPPA AKKAGOL	32	M	1 TO 3 MONTHS	PRESENT	NO	NIL	N	125	15 YRS	BD SMOKER FOR 10 YRS	SEVERE	PALLOR	RARE FLAPS	PRESENT	HEMATEMESIS	FLUID THRILL PRESENT	SHORT ATTENTION SPAN
41	UMESH NANDI	28	M	LESS THAN 1 MONTH	ABSENT	NO	NIL	DECREASED OUTPUT	90	12 YRS	NIL	SEVERE	PALLOR	ABSENT	PRESENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
42	SHANKARGOUD PATIL	63	M	1 TO 3 MONTHS	PRESENT	NO	CIRRHOSIS MORE THAN 1 YEAR	DECREASED OUTPUT	125	10 YRS	CIGERATTE SMOKER FOR 30 YRS	ABSENT	CLUBBING	RARE FLAPS	PRESENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
43	MALLAPPA	30	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS 1 TO 3 MONTHS	N	231	15 YRS	NIL	SEVERE	PALLOR	RARE FLAPS	ABSENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
44																		
45	SANGAPPA	42	M	3 TO 6 MONTHS	PRESENT	NO	NIL	N	NIL	NIL	NIL	ABSENT	N	FREQUENT FLAPS	PRESENT	ECCHYMOSIS ON BODY	SHIFTING DULLNESS PRESENT	STUPOROUS
46	PRAKASH BAJENTRI	50	M	LESS THAN 1 MONTH	PRESENT	NO	NIL	DECREASED OUTPUT	125	15 YRS	NIL	ABSENT	N	RARE FLAPS	ABSENT	NIL	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
47	LOKESH RATHOD	41	M	LESS THAN 1 MONTH	PRESENT	NO	CIRRHOSIS 1 TO 3 MONTHS	DECREASED OUTPUT	178	10 YRS	NIL	SEVERE	PALLOR, LEUKONYCHIA	RARE FLAPS	ABSENT	BLEEDING PER RECTUM	SHIFTING DULLNESS PRESENT	SHORT ATTENTION SPAN
48	SIDDAPPA MANNAPUR	42	M	1 TO 3 MONTHS	PRESENT	NO	RVD, HTN, CIRRHOSIS MORE THAN 6 MONTHS	DECREASED OUTPUT	160	20 YRS	BD SMOKER FOR 20 YRS	ABSENT	N	CONTINUOUS FLAPS	PRESENT	NIL	FLUID THRILL PRESENT	STUPOROUS
49	PARASAPPA	45	M	1 TO 3 MONTHS	ABSENT	NO	NIL	N	125	25 YRS	NIL	ABSENT	N	ABSENT	ABSENT	NIL	SHIFTING DULLNESS PRESENT	NORMAL BEHAVIOUR
50	PRAKASH	60	M	1 TO 3 MONTHS	PRESENT	NO	CIRRHOSIS 3 TO 6 MONTHS	N	178	35 YRS	BD SMOKER FOR 25 YRS	ABSENT	CLUBBING, LEUKONYCHIA	FREQUENT FLAPS	PRESENT	MALENA, ECCHYMOSIS ON BODY	SHIFTING DULLNESS PRESENT	STUPOROUS

26	3.4	10.9	98	34	35	3590	45.6	40.1	4.2	9.5	0.1	4.4	1.6	0.7	0.9	1.8	92	31	150	1.6	136	4.2	1.2	80	ALCOHOL	MODERATE ASCITES	14 CMS	GRADE 2 ESOPHA GEAL VARICES	2	3	94	1	6	0.28	10	C
27	2.9	9.1	99	33	35	5240	71.1	20.4	3.1	0.2	0.1	0.82	1.1	0.5	0.6	2.6	20	23	72	1.1	138	4.4	0.6	84	ALCOHOL	GROSS ASCITES	12 CMS	GRADE 3 ESOPHA GEAL VARICES	1	2	160	2	12	0.57	9	B
28	4	13.3	88	34.5	35	10680	83.1	14	0	2.8	1	0.95	1	0.4	0.6	3.7	7	14	157	1.04	136	4.8	0.8	62	ALCOHOL	MILD ASCITES	13CMS	ESOPHA GEAL CANDIDI ASIS	3	4	64	0	2	0.09	6	A
29	3.9	11	84	34	34.6	13630	85.1	6.3	0.4	7.9	0.2	1.84	1.6	0.8	0.8	3.6	1500	1462	163	1.2	138	4.6	2.4	92	ALCOHOL	MILD ASCITES	10CMS	GASTRIT IS	2	3	88	1	8	0.38	7	B
30	3	9.8	94	35	33.6	13990	85.4	9.7	0.1	0.3	0.1	1.3	7.1	3.7	3.4	3.3	255	80	151	1.73	140	4	0.8	106	ALCOHOL	MODERATE ASCITES	13CMS	GRADE 3 ESOPHA GEAL VARICES	1	2	300	2	14	0.66	12	C
31	3.3	10.7	91.8	32.4	35.3	6490	78.8	14.9	1.5	4.3	0.5	1.3	20.9	7.6	13.6	2	217	109	186	3.14	141	3.5	1.8	105	ALCOHOL	MODERATE ASCITES	16CMS	GRADE 1 ESOPHA GEAL VARICES	1	2	240	2	13	0.61	14	C
32	1.46	3.4	65.8	15.8	24.2	1870	62.3	29.9	1.8	6	0	0.43	1.2	1	0.2	2.1	21	14	111	1.92	139	3.5	0.8	64	ALCOHOL	MODERATE ASCITES	12CMS	GRADE 2 ESOPHA GEAL VARRICE S	3	4	45	0	1	0.04	10	C
33	3.05	9.6	90.2	31.5	34.9	7980	67.9	21.9	1.6	8.3	0.3	0.87	4.1	2.6	1.5	2.5	92	44	89	2.17	133	3.6	0.6	48	ALCOHOL	GROSS ASCITES	16CMS	GRADE 1 ESOPHA GEAL VARICES	2	3	50	1	4	0.19	13	C
34	4.07	12.6	91.4	31	33.9	6520	93.2	4.6	0	2	0.2	0.37	5.1	3.3	1.8	2.8	102	46	153	2.26	132	4.1	0.6	83	ALCOHOL	MODERATE ASCITES.	13.5 CMS	GASTRIC EROSINS	1	2	140	2	12	0.57	13	C
35	3.87	11.9	86.3	30.7	35.6	16360	86.7	6.2	1.4	5.4	0.3	4.09	13.9	5.4	8.5	2.5	96	19	219	1.4	132	3.5	1.7	90	ALCOHOL	MODERATE ASCITES	11.5 CMS	GRADE 1 ESOPHA GEAL VARICES	1	2	150	2	14	0.66	12	C
36	2.72	9.4	96.7	34.4	35.6	17430	80	11.2	1.7	6.9	0.2	2.4	18.1	8	10.1	2.2	207	30	119	4.36	138	3.8	0.7	100	ALCOHOL	GROSS ASCITES	11 CMS	GRADE 2 ESOPHA GEAL VARICES	0	2	INCOM PLETE	3	16	0.76	15	C
37	3	10.2	98	33	34	5500	70	25	2	3	0	1.5	16	6	10	2	115	130	65	4.42	138	5.1	2.4	117	ALCOHOL	GROSS ASCITES	13.9 CMS	NORMAL	0	1	INCOM PLETE	3	17	0.8	15	C
38	3.89	11.7	91.3	30	32.9	4700	50.4	32.6	12.1	4.2	0.7	1.5	2.28	1.35	0.93	2.1	88	63	137	1.4	140	4.5	0.9	82	HCV	MODERATE ASCITES	15.8 CMS	EARLY ESOPHA GEAL VARICES	2	3	120	1	8	0.38	11	C
39	2.46	7.3	79.7	29.7	37.2	5110	58.1	33.1	3.7	4.9	0.2	0.74	3.6	1	2.6	1.6	66	33	97	2.4	132	4.9	3.6	82	ALCOHOL	MODERATE ASCITES	13 CMS	GRADE1 ESOPHA GITIS	1	2	188	2	13	0.61	14	C
40	4.2	11.2	79.4	35	38	13420	54.7	37	2.6	5.2	0.6	1.21	1.2	0.8	0.4	3.9	28	31	58	1.3	136	3.5	0.6	101	ALCOHOL	MILD ASCITES	14.9 CMS	GRADE 3 ESOPHA GEAL VARICES	2	3	98	1	7	0.33	7	B
41	2.28	4.6	63.6	20.2	31.7	7890	68.4	25.5	0.8	5.3	0	0.84	4.7	1	3.7	1.9	131	37	96	1.63	134	3.5	1.7	101	ALCOHOL	GROSS ASCITES	10 CMS	GRADE 2 ESOPHA GEAL VARICES	2	3	90	1	9	0.42	12	C
42	1.45	4.7	92	32.5	35.4	8250	77.9	14.8	2.3	4.5	0.3	1.12	5.3	1.2	4.1	2.5	32	137	209	2.43	135	5	2.5	70	ALCOHOL	GROSS ASCITES	12.5 CMS	NORMAL	2	3	45	0	1	0.04	13	C
43	3.46	12.6	97.3	33.2	35.3	25790	80	4	2	4	0	0.16	4.6	0.8	3.8	2.5	31	71	157	1.53	135	5	6	74	ALCOHOL	MODERATE ASCITES	13.7 CMS	NORMAL	3	4	114	1	7	0.33	12	C
44	1.9	4.6	103	25	31	19300	64	20	5	3	0	1.26	4.2	3.4	0.8	4	124	37	222	1.8	144	4.5	0.5	91	ALCOHOL	MODERATE ASCITES	11 CMS	GRADE 1 ESOPHA GEAL VARICES	2	3	68	1	8	0.38	12	C
45	4.3	12.7	76.7	29.5	38.5	9030	85.1	10.1	0.1	4.7	0	1.92	14	6	8	1.8	1000	908	285	3.21	139	3.5	0.7	137	HBV	MODERATE ASCITES	9.5 CMS	GRADE1 ESOPHA GEAL VARICES	0	1	INCOM PLETE	3	19	0.9	15	C
46	4	11.3	100.6	33.2	33	7620	51	33	7.2	6.9	0	0.82	3.1	1.1	2	2.9	133	35	202	1.58	136	4.1	0.9	82	ALCOHOL	MODERATE ASCITES	15.5 CMS	GATRITI S	2	3	70	1	6	0.28	11	C
47	2.8	7.5	82	27	32	18310	90	6.3	0	3	0.1	1.29	1.3	0.5	0.8	1.7	45	26	79	1.81	134	4.4	2.3	94	ALCOHOL	MODERATE ASCITES	12 CMS	ND	2	3	84	1	9	0.42	11	C
48	5.29	15.6	84.7	29.5	34.8	13090	68.7	20.6	0.7	9.6	0	1.62	27	7.8	19.2	2.4	306	187	212	1.67	138	4.6	1.6	110	ALCOHOL	GROSS ASCITES	13 CMS	ND	0	1	INCOM PLETE	3	19	0.9	13	C
49	3.3	10.6	92.8	34	34	7640	90	5	1	5	0	1.8	2.8	2	0.8	3.7	98	86	68	1.93	138	4	0.9	39	ALCOHOL	MILD ASCITES	10.5 CMS	NORMAL	2	3	45	0	1	0.04	8	B
50	3.09	10.4	85.8	33.6	39.2	5060	67	9	2	3	0	0.46	15.9	5.3	10.6	2.3	76	33	101	3.5	148	3.8	0.9	163	ALCOHOL	GROSS ASCITES	15 CMS	GRADE 2 ESOPHA GEAL VARICES	0	1	INCOM PLETE	3	20	0.95	15	C