A Dissertation on

CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTER.

Submitted in partial fulfillment of the requirements for

M.D. DEGREE BRANCH-I

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OF

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CHENNAI

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

MAY-2023

CERTIFICATE-I

This is to Certify that, this is the bonafide dissertation performed by ***Dr.Ezhilarasu Preetham*** *and submitted in partial fulfillment of the requirements for the Degree for* ***M.D., GENERAL MEDICINE, Branch I*** *of* ***The Tamil Nadu DR.M.G.R University Chennai.***

Date:

Prof.Dr.C.Hariharan M.D

Guide & Director

Institute of Internal Medicine,

RGGGH

CERTIFICATE-II

This is to Certify that, this is the bonafide dissertation performed by ***Dr.Ezhilarasu Preetham*** *and submitted in partial fulfillment of the requirements for the Degree for* ***M.D., GENERAL MEDICINE, Branch I*** *of* ***The Tamil Nadu DR.M.G.R University Chennai.***

Date:

DR.E.THERANIRAJAN,

MD.,DCH.,MRCPCH(UK).,FRCPCH(UK).

DEAN

Madras Medical College

Rajiv Gandhi Government General Hospital

CERTIFICATE-III

This is to certify that, that dissertation work titled **"CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE"** of candidate **Dr.Ezhilarasu Preetham** with registration number 200120100511 for the award of **DOCTOR OF MEDICINE** in the branch of **GENERAL MEDICINE.** I personally verified the urkund.com website for the purpose of plagiarism check and found the uploaded thesis contains from introduction to conclusion pages and the result shows **9%** percentage of plagiarism in the dissertation.

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I solemnly declare that the dissertation titled **"CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE"** was done by me from July 2022 to December 2022 under the guidance and supervision of **Prof.Dr.C.Hariharan M.D.** This dissertation is submitted towards the partial fulfillment of the requirement for the award of MD Degree in General Medicine (Branch I).

.

Date:

Place:

Dr.Ezhilarasu Preetham
POST GRADUATE STUDENT
INSTITUTE ON INTERNAL MEDICINE
MADRAS MEDICAL COLLEGE

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I thank all my **PATIENTS**, who formed the backbone of this study without whom this study would not have been possible.

Lastly, I am ever grateful to the **ALMIGHTY GOD** for always showering his blessings on me and my family

Dr. EZHILARASU PREETHAM

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ABSTRACT

Aims and Objectives -

1. To study the relationship between fasting lipid profile and chronic liver disease

2. To assess the variation of fasting lipid profile among patients of chronic liver disease according to severity as per child pugh scoring system.

Study Centre -

Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai

Duration of the study -

6 months

Study Design-

Prospective Cross-sectional study

Sample size-

100

Inclusion Criteria -

1. Patients above 18 years of age.
2. Patients giving consent to the study.
3. Patients with chronic liver disease proven by clinical,biochemical and sonological evidence of any etiology

Exclusion Criteria -

1. Patients under 18 years of age
2. Patient not willing to participate in the study
3. Patients suffering from co-morbidities that could affect lipid profile such as diabetes,thyroid disease,nephrotic syndrome,cancer,renal failure, history of hyperlipidemia.
4. Patients on drugs that could alter lipid profile like statins and oral contraceptive pills.

Methodology -

After obtaining clearance and approval from the institutional ethics committee, and securing informed consent as per the inclusion and exclusion criteria already mentioned, 100 CLD patients getting admitted under institute of internal medicine were studied. Detailed history was recorded - demographics, diet history, intake of drugs, duration of liver disease and alcohol consumption history general clinical examination were done to check for height,weight,blood pressure,pulse rate.Systemic examination was performed focused on abdominal examination. Biochemical tests were performed to assess liver function and coagulation profile in addition random blood sugars and thyroid profile will be performed after 12 hour period of fasting blood sample will be taken to measure the lipid profile in the patients.

Patients were subsequently categorised based on child pugh socring system according to the data obtained from proforma.

Lipid values of the patients were then compared based on severity of the liver disease as per child pugh scoring system to study the trends of values.

INTRODUCTION

Chronic liver Disease (CLD) refers to a slow deterioration of the functions of the liver for more than a period of 6 months which includes detoxification of toxic byproducts produced in the body, maintaining normal coagulation system by production of clotting factors and production of proteins.

Cirrhosis comes from the Greek word meaning “tawny” and it was used to refer to a grossly and microarchitecture distorted liver parenchyma which is also dysfunctional . Cirrhosis comes as the fourth leading cause of mortality in Asian males [2]. Chronic Liver Disease is a very commonly seen condition by practitioners through all levels of the healthcare system and Adequate knowledge on its management is key for every doctor.

Chronic Liver Disease can be caused by a plethora of causes including but not limited to infectious conditions, alcohol consumption, fatty liver , metabolic diseases . Chronic Liver Disease provides a high burden of both morbidity and mortality to countries in both developed and developing stage.Liver disease contributes to approximately 2 million deaths in a year worldwide out of which 1 million is due to cirrhosis and its complications. Cirrhosis, though referring to a single disease, can have a wide 1- year mortality ranging from 1% to 57%

based on the stage [1]. Child-Pugh score was initially created by child and turcot to estimate the operative risk for patients who undergo portosystemic shunt procedures for variceal bleed . The initial system included Total bilirubin, Hepatic Encephalopathy, ascites, albumin and nutritional status. This was then modified by Pugh removing the component of Nutrition and substituting it with albumin. But there are some drawbacks which have been expressed with regards to this score First being that both encephalopathy and Ascites are interpreted based on the subjective opinion of the physician and another drawback being that INR value that is reported tends to have a high amount of inter-laboratory variation. Chronic Liver Disease is a continuous process which leads to inflammation, destruction followed by regeneration of the parenchyma which ultimately leads onto fibrosis of the liver. Cirrhosis refers to the end stage of chronic liver disease which comprises disrupted liver architecture , nodule formation, and vascular disorganization . The mechanism of fibrosis at cellular level is due to recruitment of fibroblasts and Stellate the cells and subsequently regeneration is triggered by existing stem cells . The 2 major causes of mortality in a patient with Chronic Liver Disease is as a result of complications such as Hepatic Encephalopathy , UGI Bleed, Spontaneous bacterial peritonitis , The 2nd major cause being Hepato Cellular Carcinoma.

Management of patients with Chronic Liver Disease is mainly centered on treating and preventing complications of disease.It is also Essential to treat and abstain from the cause that had led to the chronic liver disease.Maintaining nutrition in Patients with chronic liver disease Especially those In advanced disease stages is of utmost importance. In patients with advanced disease with refractory complications of chronic liver disease will ultimately need Liver transplantation.

Lipids are an essential component of the human body needed for maintaining cell architecture , functioning of enzymes and important energy stores . The Liver plays a central role in maintaining lipid levels in the body by means of synthesis of various lipoproteins , cholesterol , triglycerides and is also involved in its excretion.

This study aims to study the correlation between Fasting Lipid Profile and Severity of Chronic Liver Disease with the aim of using Fasting lipid profile as a prognostic tool in patients with Chronic Liver Disease.

II. AIMS AND OBJECTIVES

1. TO STUDY THE RELATIONSHIP BETWEEN FASTING LIPID PROFILE AND CHRONIC LIVER DISEASE

2. TO ASSESS THE VARIATION OF FASTING LIPID PROFILE AMONG PATIENTS OF CHRONIC LIVER DISEASE ACCORDING TO SEVERITY AS PER CHILD PUGH SCORING SYSTEM

III. REVIEW OF LITERATURE

LIVER STRUCTURE

Liver is the largest organ of the human body, weighing 1-1.5 kg and representing 1.5-2.5% of body mass. Shape and size of Liver tends to vary greatly from person to person .Liver is located in the right upper quadrant of the abdomen directly under the diaphragm and right lower rib cage. It is held in place by ligaments to diaphragm, great vessels, upper gastrointestinal organs, and peritoneum [3].

Liver is larger during infancy being one eighteenth of body weight. This is due to the left lobe. The blood supply to the liver is 25% of total cardiac output necessary for performing its various metabolic functions and detoxification . Liver is involved in metabolism of carbohydrates by means of Storage of glycogen, by glycogenesis, and production of glucose by means of gluconeogenesis and glycogenolysis. It is also involved in fat and protein metabolism . Liver acts as a site of metabolism of various toxic products to neutral byproducts and its subsequent excretion in bile.

Liver daily produces 500 ml of bile, and around 250 to 500 mg of bile acids which are either stored in gallbladder or directly excreted via feces. .

FIG 1. LIGAMENTS OF LIVER

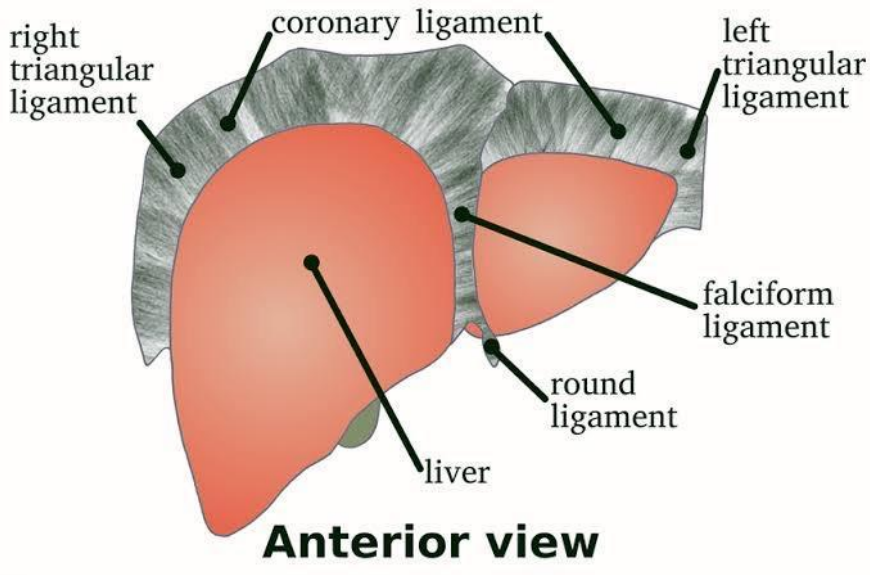
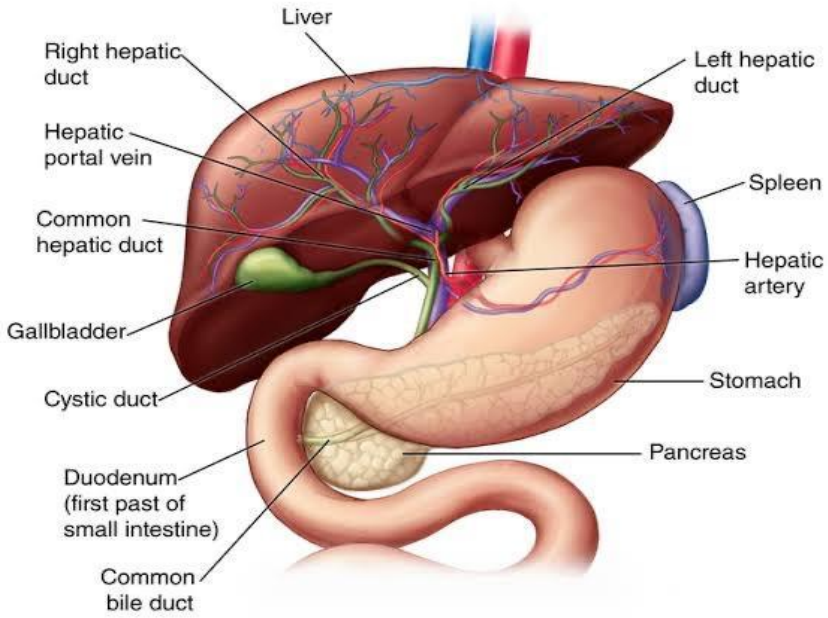


FIG 2. ANATOMY OF LIVER



LIVER BLOOD SUPPLY

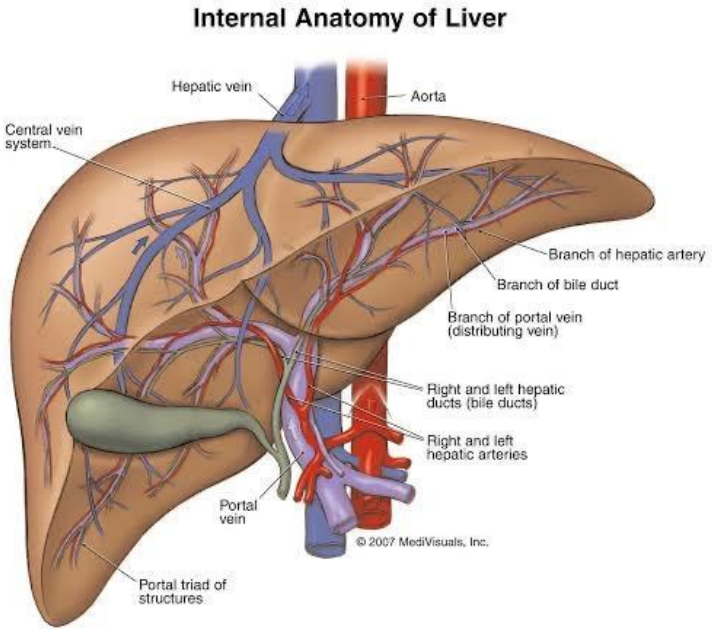
The blood supply of the liver is dual in nature comprising 2 major vessels namely The Hepatic artery and the Portal vein. Both vessels enter the liver in the region of the hilum. At this area Both the vessels divide into a right and a left branch to supply the right and left lobes of the liver respectively. The Hepatic artery is a branch Of the celiac artery and provides around 20% of the total blood supply to the liver. The blood supplied by hepatic artery is arterial in nature and richly oxygenated [4].

The Portal Vein contributes to a large portion of the liver's blood supply approximately 80%.The portal vein is formed by the joining of the superior mesenteric vein with the splenic vein behind the head of the pancreas. The portal vein is the venous drainage of the gut.The blood contains a high amount of nutrients as well toxins produced by gut bacteria but is relatively low in oxygen when compared to blood from the hepatic artery. The blood supply has a unique auto regulation mechanism wherein a reduction in blood supply from the portal vein is compensated by an increase in flow in hepatic artery.

This is based on local depletion on adenosine leading to either constriction or dilatation of hepatic artery.

The venous drainage out of the liver is by means of the hepatic veins which drain directly into the IVC.

FIG 3 . BLOOD SUPPLY OF LIVER



SEGMENTS OF THE LIVER

The liver segmental division is based on the Couinaud classification which divides the liver into eight functionally separate segments.

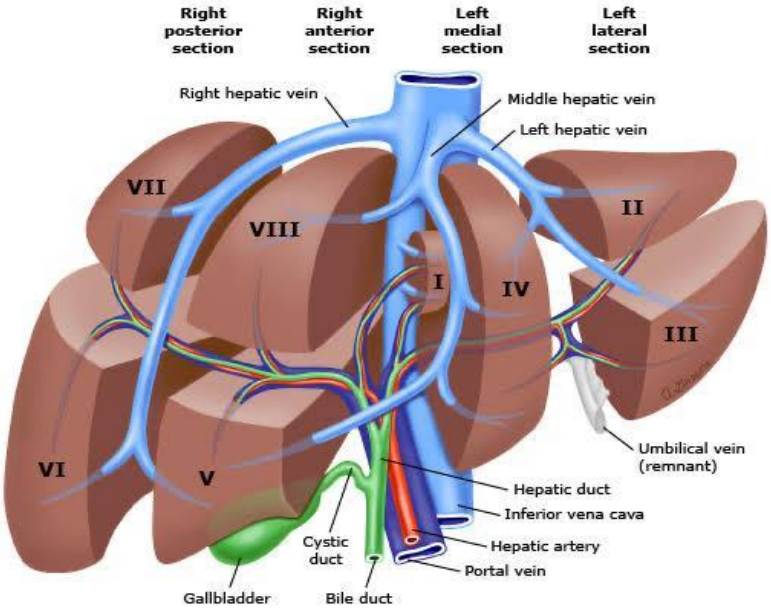
Each segment has its own separate branch of the portal vein, hepatic artery and the bile duct.

In the periphery of every segment there is outflow of blood via the hepatic veins.

Divisions are based as follows:

- The plane of right hepatic vein splits the right lobe to anterior and posterior segments.
- The plane at middle hepatic vein splits the liver into the right and left lobes of the liver. It runs along the line joining the Inferior Vena Cava to the Gall Bladder fossa.
- The umbilic plane extends from falciform ligament to the IVC which the divides the left lobe into a lateral part which forms segments two and three and a medial part which forms segment 4
- The portal vein divides the Liver into upper and lower segments [5].

FIGURE 4. SEGMENTS OF THE LIVER



ANATOMY OF THE HEPATIC ACINUS

The acinus represents the functional unit of the liver. Acinus is histologically more difficult to visualize and compared to the hepatic lobule yet represents a structure which is of more functional importance.

The acinus comprises an almost ellipsoid or diamond shaped structure constraining mass of hepatocytes aligned around the hepatic arterioles and portal venules as they are about to anastomose into sinusoids.

The acinus is divided into 3 major zones that correlate with the distance from the arterial blood supply. The hepatocytes that are closest to the arterioles are termed ZONE 1 and are best oxygenated while those farthest ZONE 3 have the poorest supply of oxygen.

FIGURE 5. FUNCTIONAL ANATOMY OF ACINUS

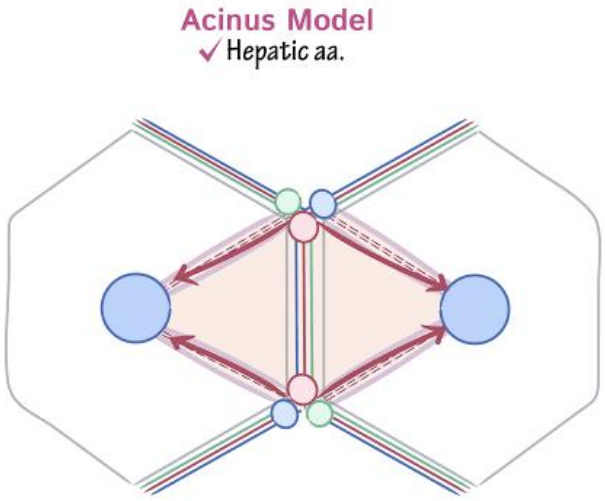
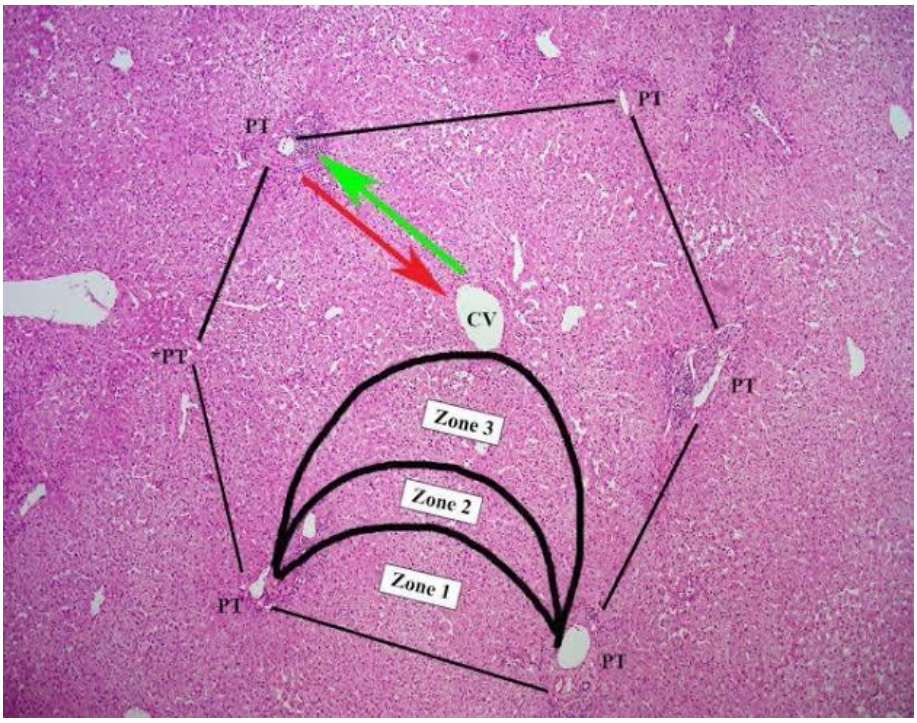


FIGURE 6. HISTOLOGIC MODEL OF LIVER



CELLS OF THE LIVER

There are mainly 4 main cell types in the liver:

1. The Hepatocytes
2. Stellate cells
3. Kupffer cells
4. Liver endothelial cells.

Hepatocytes

- Make up about 80% of parenchyma
- Large polyhedral cells grouped into interconnected plates and are arranged into lobules
- They participate in the metabolic functions of the liver.

ITO cells / Stellate cells

- These cells lie in close proximity to the hepatocytes in the perisinusoidal space.
- Store important vitamins and variety of other lipids
- When The liver is injured the cells are activated to form highly fibrogenic cells that secrete factors such as TGF beta.

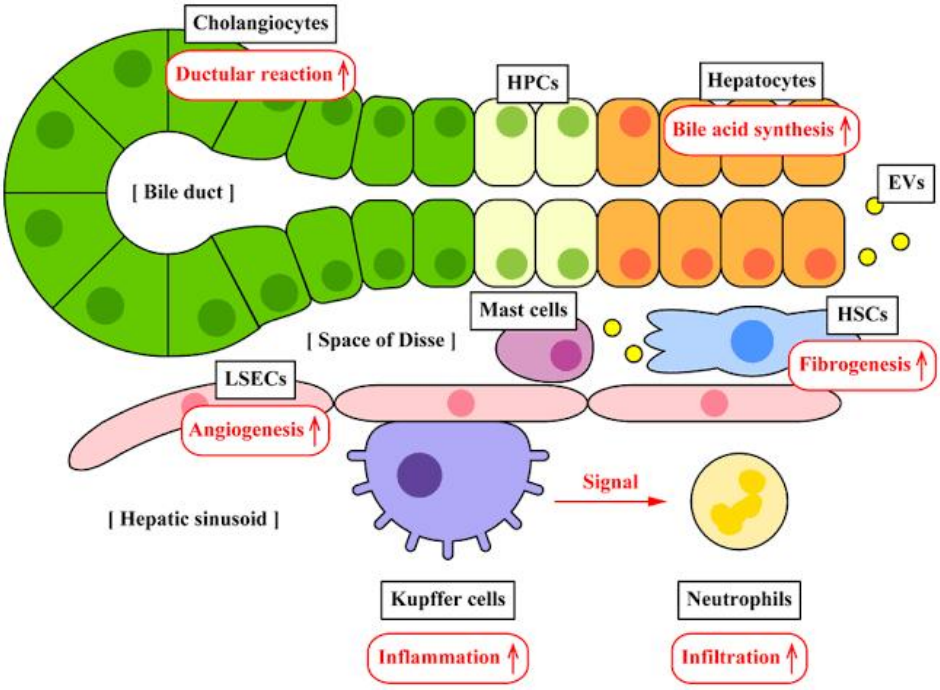
Kupffer cells

- Specialized macrophage cells adherent to sinusoidal endothelium mainly near portal areas.
- They clear blood of pathogens that enter via portal blood
- Act as antigen presenting cells for adaptive immunity.

Endothelial cells

- Form the wall of blood vessels via forming a single layer with spaces in between each cell called fenestra [6].

FIG 7. CELLS OF THE LIVER



CHRONIC LIVER DISEASE

Chronic liver disease refers to a disease process of the liver which involves destruction and regeneration of the parenchyma of liver leading to fibrosis.

The term is typically used to describe liver disease that has existed for a period of more than 6 months.

EPIDEMIOLOGY

Cirrhosis is a major reason for Mortality and morbidity in the world. It represents the 15th leading cause of morbidity and the 11th leading cause of death.

Chronic Liver disease accounted for 2.2% of deaths. And 1.5% DALY in the world during 2016 [7].

Chronic liver disease has caused around 13.2 lakh deaths in the year of 2017 out of which two thirds were men and one third were women.

In the past viral hepatitis was the main cause of CLD. But of late due to improved prevention and treatment strategies being employed have led to a decline in viral causes of chronic liver disease.

Meanwhile, causes such as alcohol and obesity which are growing in various regions of the world are on the rise and are currently the leading risk factors for CLD.In addition these factors in their current trend are expected to further rise in the future.

The trends in mortality from 1980 to 2010 have greatly varied between nations. For example, there has been a decrease in mortality in countries like the United States and China which has mainly been attributed to a reduction in transmission of HBV.

But in our country India has seen an increase in mortality due to Chronic

liver disease by 18% (17-20 per 1 lakh population) which can be attributed to the increasing trend in alcohol consumption and obesity rates along with a large number of cases of viral hepatitis.

Current absolute number of Chronic Liver disease cases in the world has been estimated at around 1.5 billion. The most common etiologies of CLD are as follow

- NAFLD (59%)
- HBV (29%)
- HCV (9%)
- Alcohol related (2%)

Other rarer causes which account for 1% include:

- Primary biliary cholangitis
- Primary Sclerosing cholangitis
- Wilson's disease
- Autoimmune hepatitis.

ETIOLOGY OF CHRONIC LIVER DISEASE

Although Chronic Liver Disease represents a single disease entity there are a wide variety of causes that can lead to this final end product.

The table given below summaries the most commonly seen causes of liver cirrhosis.

FIG 8. ETIOLOGY OF LIVER CIRRHOSIS

Alcoholism	Cardiac cirrhosis
Chronic viral hepatitis	Inherited metabolic liver disease
Hepatitis B	Hemochromatosis
Hepatitis C	Wilson's disease
Autoimmune hepatitis	α_1-Antitrypsin deficiency
Nonalcoholic steatohepatitis	Cystic fibrosis
Biliary cirrhosis	Cryptogenic cirrhosis
Primary biliary cirrhosis	
Primary sclerosing cholangitis	
Autoimmune cholangiopathy	

Cryptogenic cirrhosis refers to a term used when the cause of the underlying cirrhosis in a patient is unknown despite thorough investigation into the etiology [8].

In the past a vast majority of these cases of cryptogenic cirrhosis were attributed to NAFLD.

Among the metabolic causes of liver disease a common and prominent cause in India remains Wilson's disease.

The reason for its relatively high prevalence as compared to the Rest of the world is not entirely sure although it has been attributed in part due to the higher incidence of consanguineous marriage among the Indian population.

In India the current most common cause of Chronic Liver disease is Hepatitis B virus although there is a trend of rapid increase in cases of ethanol related liver disease which will possibly replace HBV as the leading cause of CLD in India.

PATHOGENESIS OF CIRRHOSIS

When injured tissue is substituted by a collagen scar,it is termed as fibrosis.The development of this fibrosis needs several years of ongoing injury.

The hallmark pathologically for liver cirrhosis is the development of scar tissue which tends to replace the normal liver parenchyma,which acts as a disruption to normal portal blood flow and leads to dysfunction of the liver.

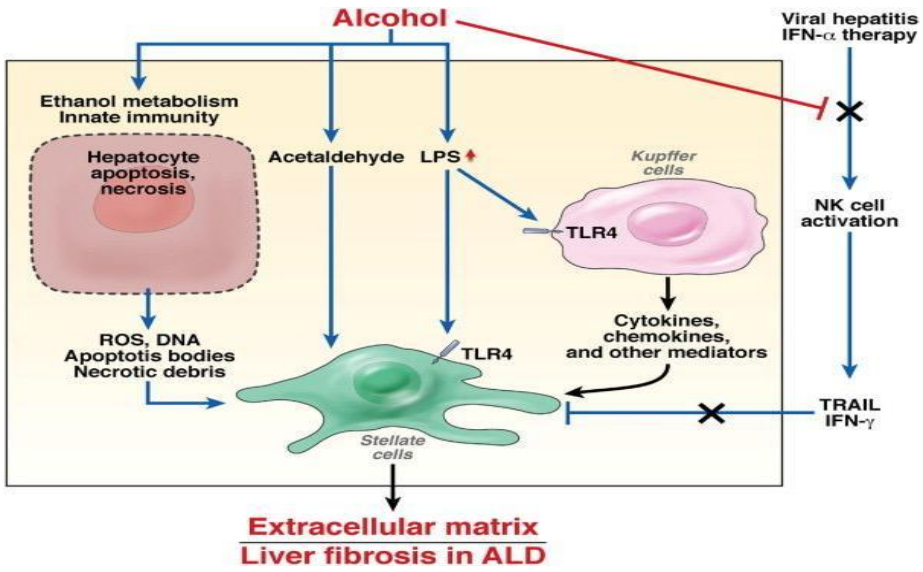
When the process of fibrosis progresses to a state where it distorts the normal hepatic vasculature the term “cirrhosis” is used.

The basic cellular mechanisms which ultimately lead to the formation of liver cirrhosis remain same despite the etiology of cirrhosis

Cirrhosis mainly involves the following major steps:

- Inflammation
- Hepatic Stellate cell activation
- Angiogenesis
- Fibrogenesis

FIG 9. PATHOGENESIS OF ALCOHOL RELATED CIRRHOSIS



Hepatic Stellate cell Activation

Kupffer cells, which are the specialized macrophages of the liver, are responsible for the activation of Stellate cells during injury.

The Stellate cell(also known as ITO cells) are usually located in the subendothelial space of Disse and become activated to a cell known as myofibroblast in areas of liver injury.Subsequent contraction of this myofibroblast leads to obstruction in blood flow in the circulation.

The Stellate cell secretes Transforming Growth factor (TGFB1) and this factor is responsible for majority of the fibrogenesis that occurs during live cirrhosis by proliferation of connective tissue.

This connective tissue produced consists mainly of:

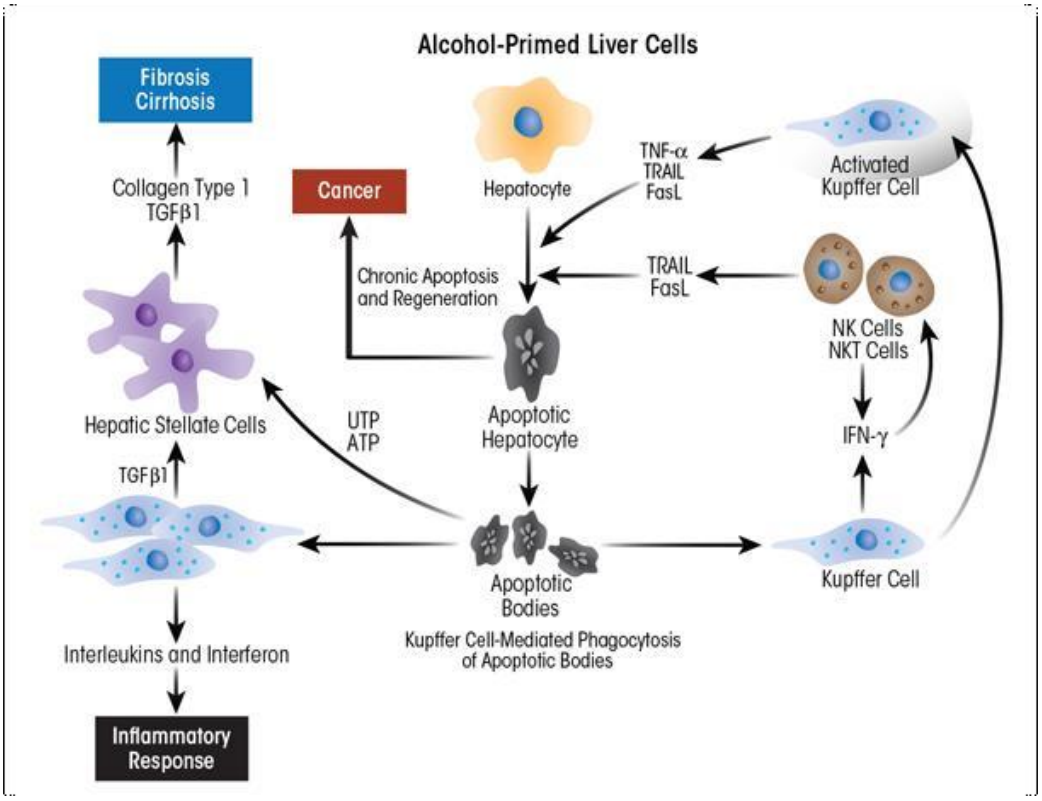
- Collagens(Type 1, 3 and 4)
- Glycoproteins
- Proteoglycans

The matrix formed by stellate cells is deposited in the sub endothelial space of Disse and this leads to loss of the normal fenestrations that normally exist between the endothelial cells.This process is known as capillarization of endothelium.

Activation of stellate cells in addition leads to a disturbance between matrix metalloproteinase and its inhibitors (TIMP1 and TIMP2) which

adds to the process of connective tissue deposition and fibrogenesis.

FIG 10. KEY CELLS IN CIRRHOSIS OF LIVER



Microvascular Changes

The brunt of the damage as a result of hepatic injury falls on the endothelium leading to a disruption in its normal functioning

Liver injury leads to changes such as formation of intra hepatic shunt as a product of angiogenesis

Endothelial cells when dysfunctional produce inadequate amounts of vasodilator substances such as NO and increase production of vasoconstrictors such as endothelins.

Angiogenesis

In response to hepatocytes injury the liver responds by forming new vessels and the key mediators involved in this process are:

- Nitric oxide
- Platelet derived growth factor
- Vascular Endothelial growth factor
- Carbon Monoxide

The vessels that are produced as a result of angiogenesis are immature and permeable and tend to further exacerbate live injury .

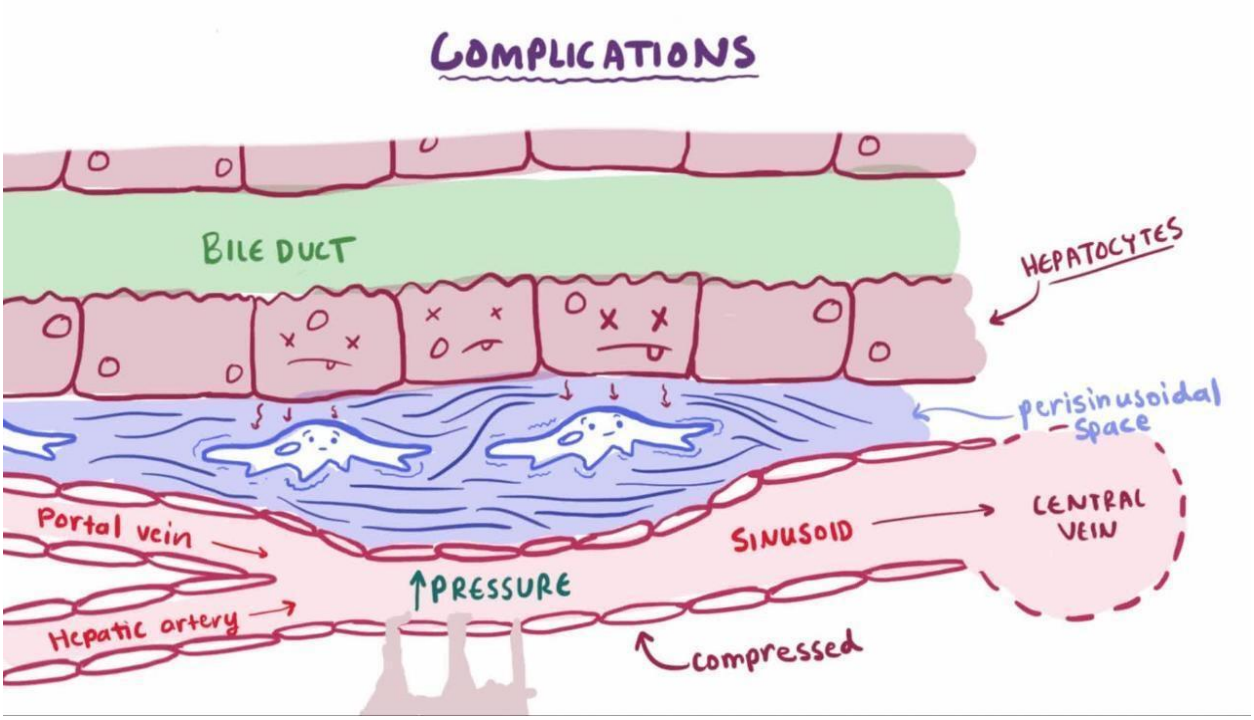
Fibrosis

Fibrosis leads to formation of structures called fibrous septa which. Greatly distort the liver architecture which includes both vasculature and parenchyma.

These fibrous septa lead to compromise in sinusoidal exchange process by shunting both the portal and arterial blood directly to the central veins (Outflow).

As the fibrotic process continues forward the liver parenchyma tends to gradually be replaced by many of these fibrous septa along with regenerating nodules. Eventually the majority of the parenchyma is replaced by fibrous septa that leads to hepatic dysfunction and increased resistance to blood flow [9].

FIG 11. FIBROSIS AND CAPILLARIZATION OF SINUSOIDS



Pathogenesis of cirrhosis according to specific causes

Alcoholic Liver disease :

Alcohol injures the liver by inhibiting normal metabolism of carbohydrates,fats and proteins. Liver may also be damaged as a result of alcoholic hepatitis repeatedly which can go on to cirrhosis.

Chronic Hepatitis C:

Infection with this organism leads to low grade inflammation over a long span of years which gradually leads to cirrhosis.

Primary Sclerosing Cholangitis:

Progressive cholestasis leads to back pressure on the biliary ductless leads to biliary hypertension and damage of hepatocytes leading to cirrhosis.

HISTOLOGY OF LIVER CIRRHOSIS

Based on Gross Morphologically the cirrhosis of liver can be classified into:

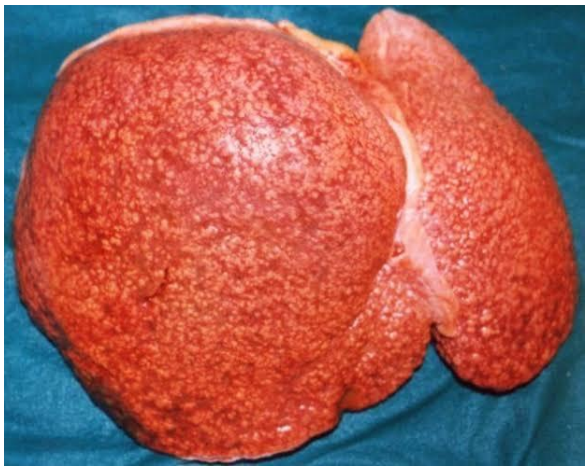
- Macronodular
- Micronodular
- Mixed

Grossly on examination with the naked eye the cirrhosis liver can be nodular on the external surface. Variation in liver color, shape and size tends to be relevant on a gross specimen as it may give a clue into the etiology of the cirrhosis.

The liver usually is shrunken and has a slight yellow-tan but this is not always the case. In alcoholic fatty cirrhosis the liver may be enlarged and yellow. In disease of biliary obstruction the liver maybe large and green.

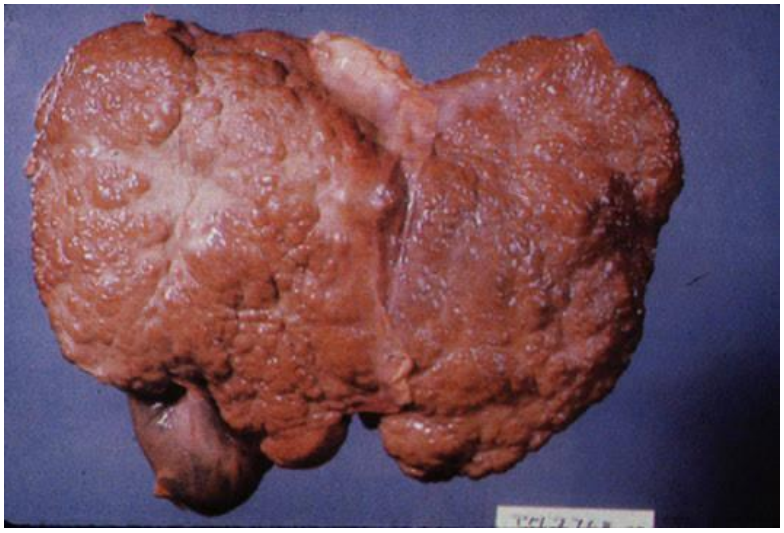
Micronodular cirrhosis on the other hand have small nodules lesser than 3mm which are separated by thin fibrous septa and are more uniformly distributed throughout the parenchyma of the liver. The most common cause of this pathology encountered is alcohol induced cirrhosis of the liver.

FIG 12. GROSS SPECIMEN OF MICRONODULAR CIRRHOSIS



Macronodular cirrhosis represents larger nodules greater than 3mm separated by wider scars which are usually irregularly distributed throughout the liver and the common causes of such a finding are viral hepatitis.

FIG 13 . GROSS SPECIMEN OF MACRONODULAR CIRRHOSIS



Microscopic changes in liver cirrhosis are mainly two hallmark findings:

- Nodules
- Fibrous Septa

Nodules of Liver cirrhosis can further be classified into two types

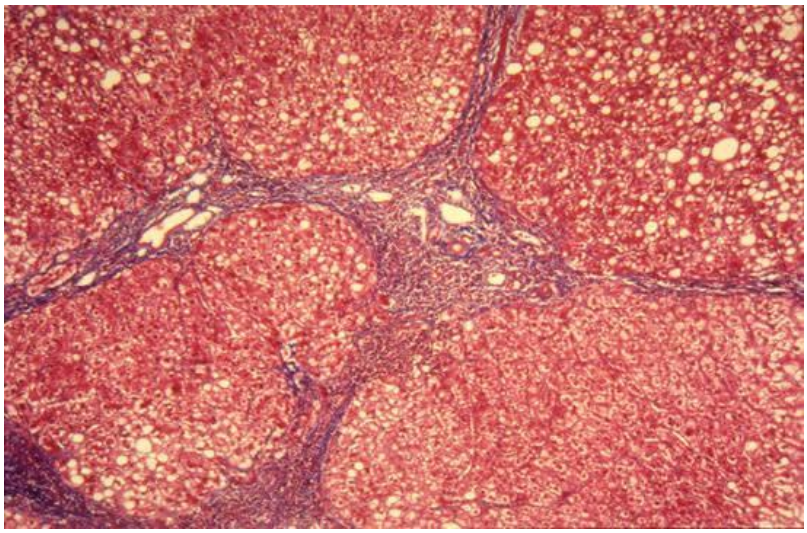
- Dissection nodules
- Hyperplastic Regenerative Nodules

Dissection Nodules

These contain remnants of central veins and portal tracts and are separated by wide scars but they in turn contain thin fibrous septa.

They contain dilated sinusoids which are most prominent in the periphery region which tend to resemble central veins.

FIG 14. DISSECTION NODULE OF CIRRHOSIS

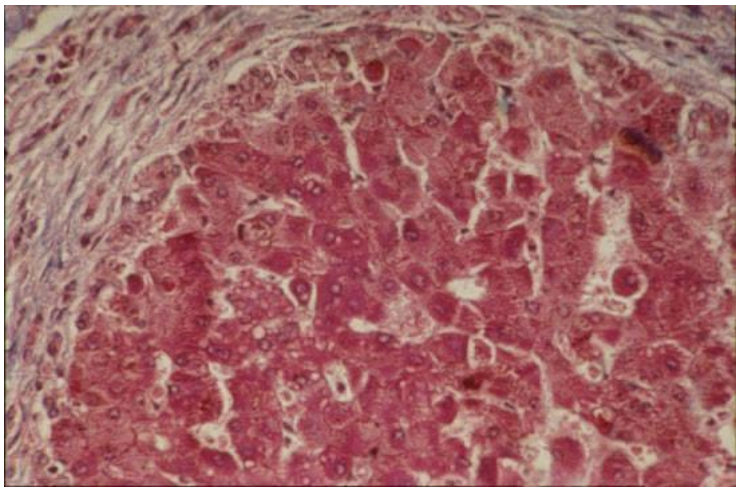


Hyperplastic Regenerative nodules

They occur in Macronodular and micronodular cirrhosis and tend to arise in the midst of scars favored by rich arterial blood of scar tissue.These nodules are round with a fibrous pseudo capsule

These may undergo dysplastic or malignant changes and the capsule tends to compress the vessels leading to perpetuation of the cirrhosis process.

FIG 15. HYPERPLASTIC REGENERATIVE NODULE



The Fibrous Septa

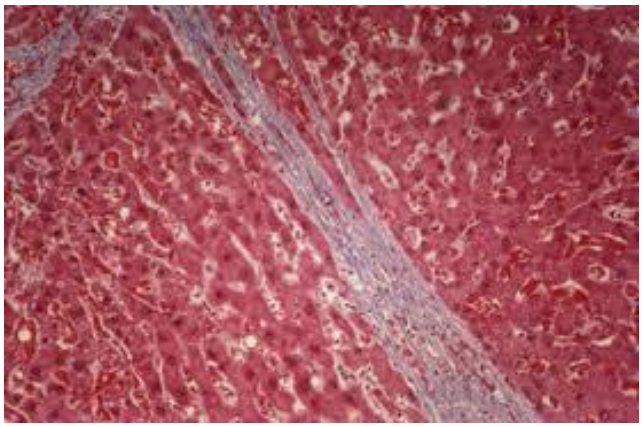
Invisible to the naked Eye they have been termed fibro-vascular membranes because they provide a diversion of flow of blood through an alternate route along these septa instead of the normal route through the hepatic sinusoids thus affecting normal function of the hepatocytes.

Based on activity these fibrous septa can further be divided into:

- Passive septa
- Active septa

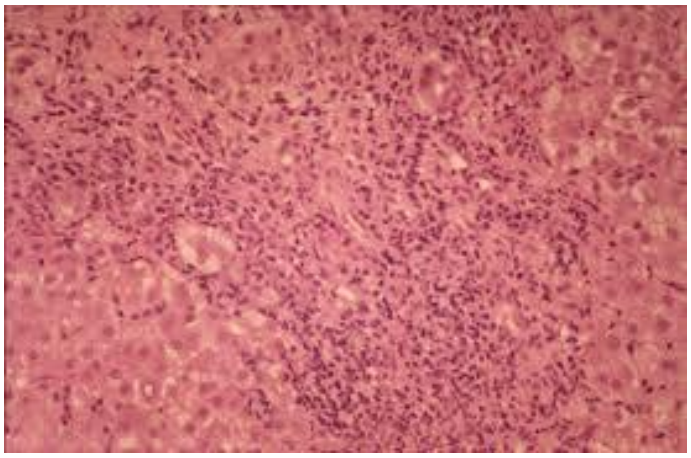
Passive septa are slender connective tissue bands which contain few inflammatory cells and have a fairly sharp demarcation with the surrounding liver parenchyma.

FIG 16 . PASSIVE SEPTA IN CIRRHOSIS



Active septa are Thicker connective tissue bands which are edematous and have many inflammatory cells and an irregular demarcation with the surrounding liver parenchyma.

FIG 17. ACTIVE SEPTA IN CIRRHOSIS



Evolution of cirrhosis

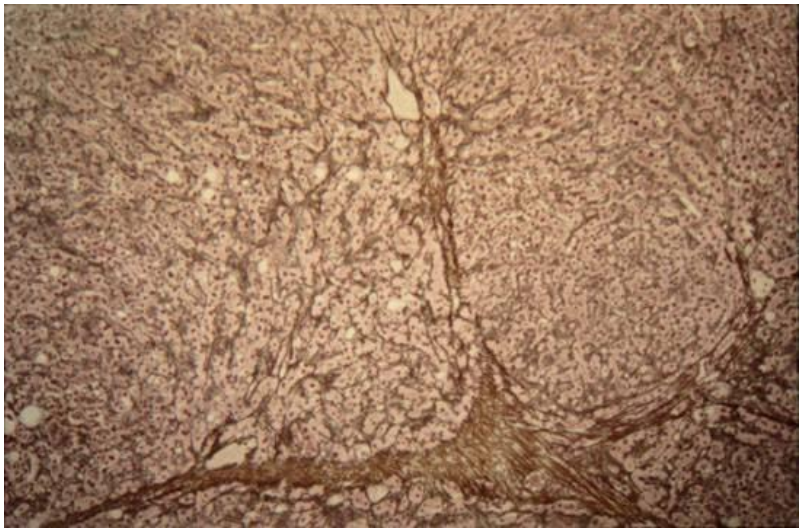
The evaluation is determined based on the extent of nodule formation and fibrosis. The following stage are capable of being identified with

some approximation on biopsy specimen:

1. Incomplete Septal cirrhosis
2. Early cirrhosis
3. Advanced Cirrhosis

Incomplete Septal cirrhosis is characterized by presence of very slender septa radiating towards the center of the lobule.These represent dilated vessels around the septum.This type of cirrhosis produces only portal hypertension with no liver failure and prognosis is good if adequate control of portal hypertension is achieved.

FIG 18 . INCOMPLETE SEPTAL CIRRHOSIS

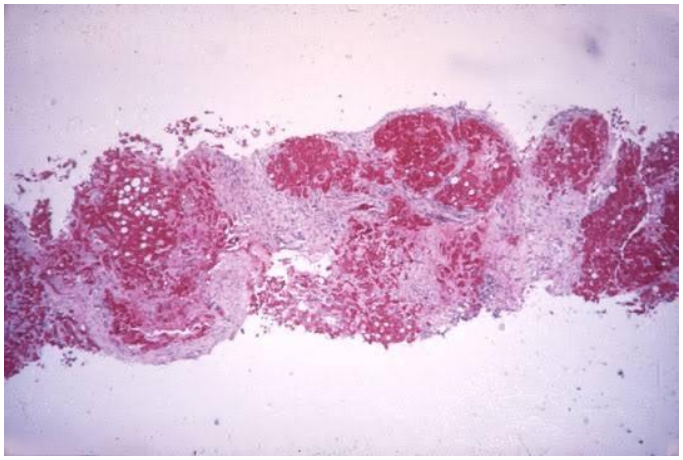


Early Cirrhosis is characterized by thin fibrous septa along With dissecting nodules and without any regenerative nodules.There is presence of multiple efferent vessels.

FIG 19. EARLY CIRRHOSIS

Advanced Cirrhosis is characterized by wide scars with clusters of regenerating nodules and large scars are present which may contain large portal fields recognizable with stain for elastic fibers [10].

FIG 20 . ADVANCED CIRRHOSIS



CLINICAL FEATURES OF CHRONIC LIVER DISEASE

The manifestation of clinical features in patients of chronic liver disease varying greatly in the spectrum of symptoms as well as clinical signs.

These variations are mainly based on :

- Severity of Liver Disease
- Whether liver disease is compensated or decompensated.
- Etiology of liver disease.

Chronic Liver disease is said to be decompensated when any one of the following events occur in a patient with CLD:

- Development of ascites
- Development of Jaundice
- Development of Hepatic Encephalopathy
- Development of Variceal Bleed

SIGNS OF LIVER DISEASE

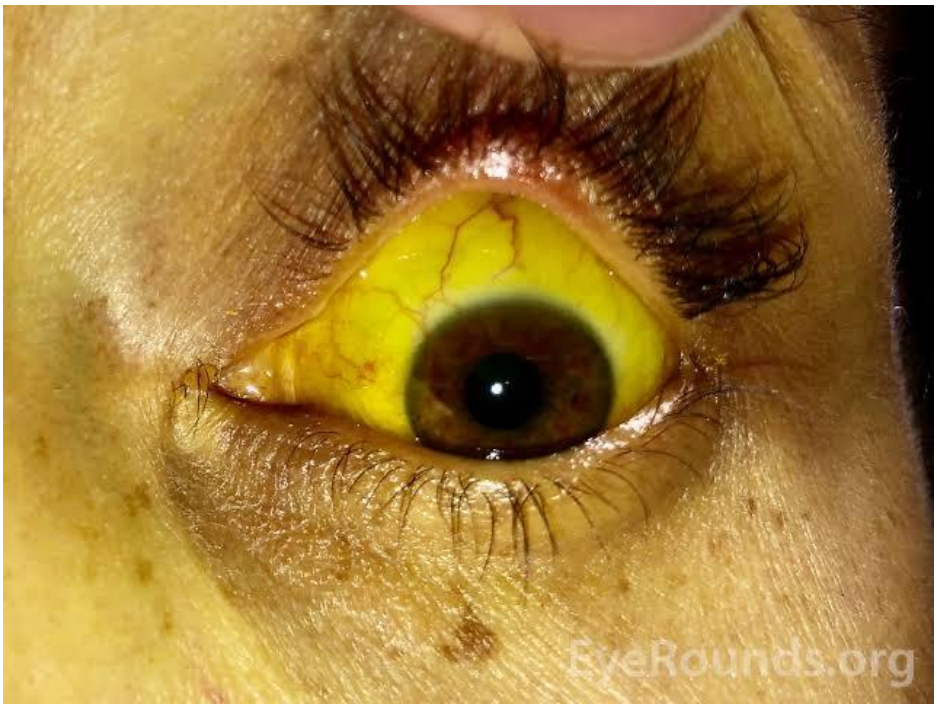
Alopecia

Liver disease is a chronic process and associated with various hormonal changes which can lead diffuse non scarring alopecia in both males and females

Jaundice

Clinically jaundice is termed as icterus and can be examined in various sites the most important being the upper sclera of the eye since this is the first site of deposition of bilirubin due to its high affinity to reticulin present in the scleral fibers. Other sites where icterus can be visualized include mucosal surfaces of the oral cavity and severe jaundice can also be visualized on palms, soles and skin.

FIG 21. ICTERUS



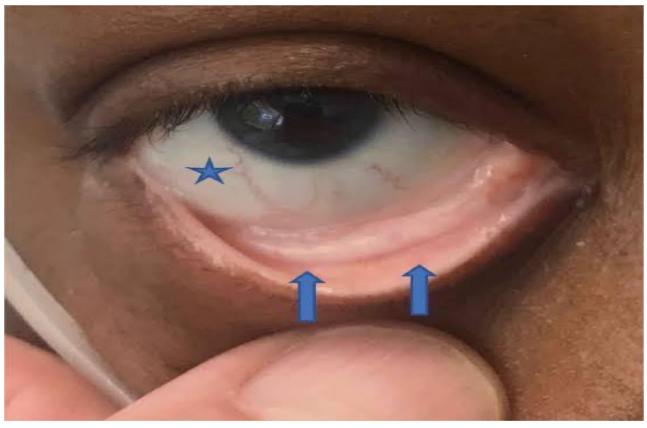
Pallor

Pallor is the clinical sign of anemia which is observed in lower palpebral conjunctiva .There maybe several reasonS for pallor in a case of CLD The commonest being variceal bleed which leads to iron deficiency anemia. Other possible causes include anemia of chronic disease due to long standing disease, In patients with alcoholic cirrhosis they may have anemia due to micronutrient deficiency such as Vitamin B12 or Iron.

Other sites where pallor can be visualized include:

- Mucosal surfaces of oral cavity
- Tongue
- By lightening of creases of palms
- On nails

FIG 22. PALLOR



Clubbing

Clubbing in general is a uncommon finding in patients with Chronic Liver disease and if present it should alert the clinician about certain important condition mentioned below:

- Primary biliary cirrhosis
- Primary Sclerosing cholangitis
- Hepatocellular carcinoma
- Hepato-pulmonary syndrome

Cyanosis

Cyanosis refers to bluish discolouration of skin and mucous membranes which can be of two types Central or Peripheral.

Cyanosis of hepatic causes is usually of central etiology and the major cause which should come to mind when a patient presents with chronic liver disease are:

- Hepatopulmonary syndrome
- Congenital heart diseases which may lead to cardiogenic cirrhosis

Pedal edema

Refers to accumulation of fluid in the subcutaneous tissue of the lower limbs.The reason for pedal edema in liver cirrhosis has been attributed to both a decrease in human albumin resulting in decreased oncotic pressure and an increase in hydrostatic pressure due to intrahepatic hypertension. The pedal edema due to cirrhosis is typically a fast edema meaning the skin once indented will recoil back within 45 seconds.

Spider naevi

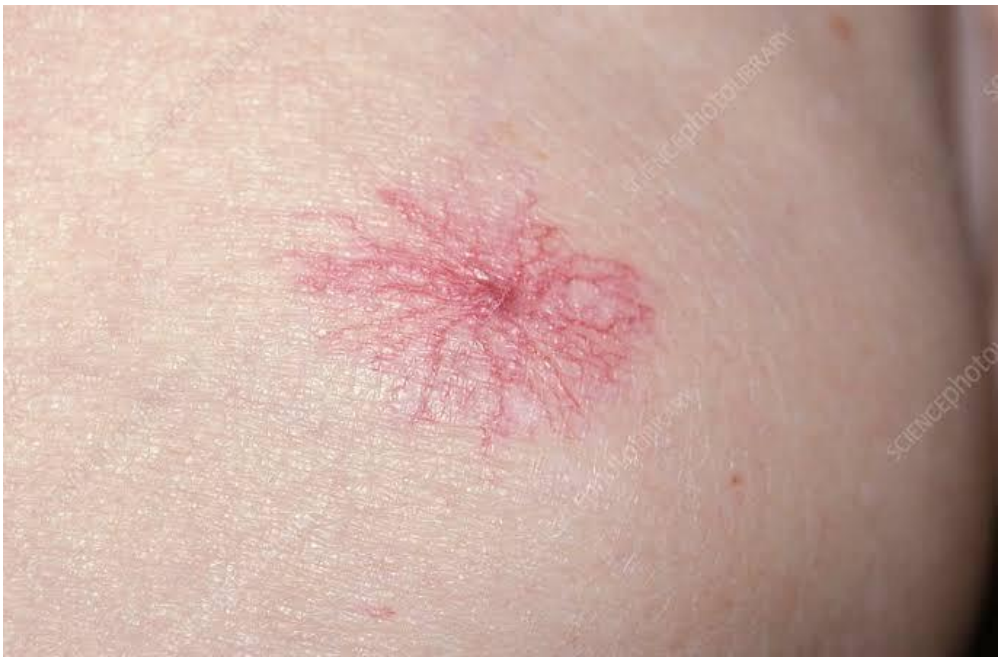
They consist of a central arteriole which is typically less than 0.5 m from which numerous small vessels radiate outward resembling spiders legs The reason has been postulated to be due to hyperestrogenism Location is typically along the distribution of the superior vena cava found on. The necklace area i.e, above the nipples, head, neck, front and back of the upper chest. The reason for its location is possibly due to the high vaso-motor gradient.

Spiders can be clinically demonstrated by 2 methods:

- Diascopy
- Pressure with a pin head

The response seen is pallor followed by refilling upon release of pressure.

FIG 23. SPIDER NAEVI

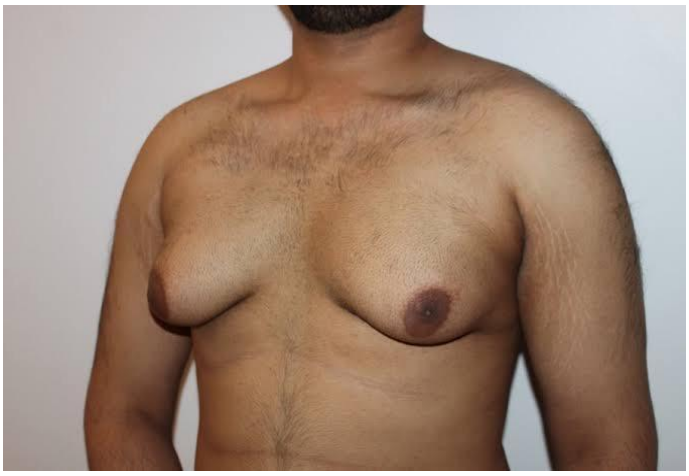


Gynaecomastia

Occurs due to increased conversion of testosterone to estrogen in peripheral adipose tissue.

Palpable as a firm nodule below the nipple areola complex of size 2cm. Or greater being significant.

FIG 24. GYNAECOMASTIA



Loss of axillary and chest hair

Seen mainly in males with loss of male hair distributions it occurs due to hyper-estrogenism

Testicular atrophy

Also due to hyperestrogenism

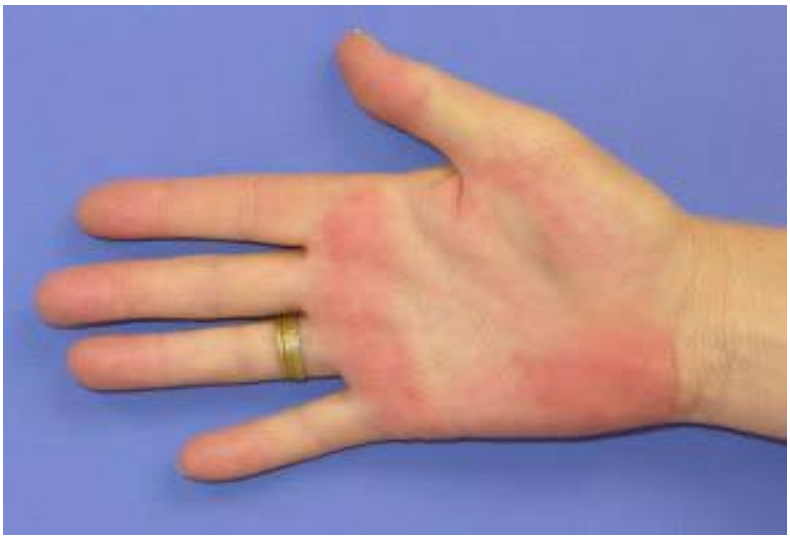
Can be clinically graded with prayers orchidometer

Palmar erythema

Can be seen early in disease but is of limited diagnostic value as it occurs in other conditions of hyper dynamic circulation such as normal pregnancy

It typically involves thenar and hypothenar eminence and spares the central portion of Palms.

FIG 25. PALMAR ERYTHEMA

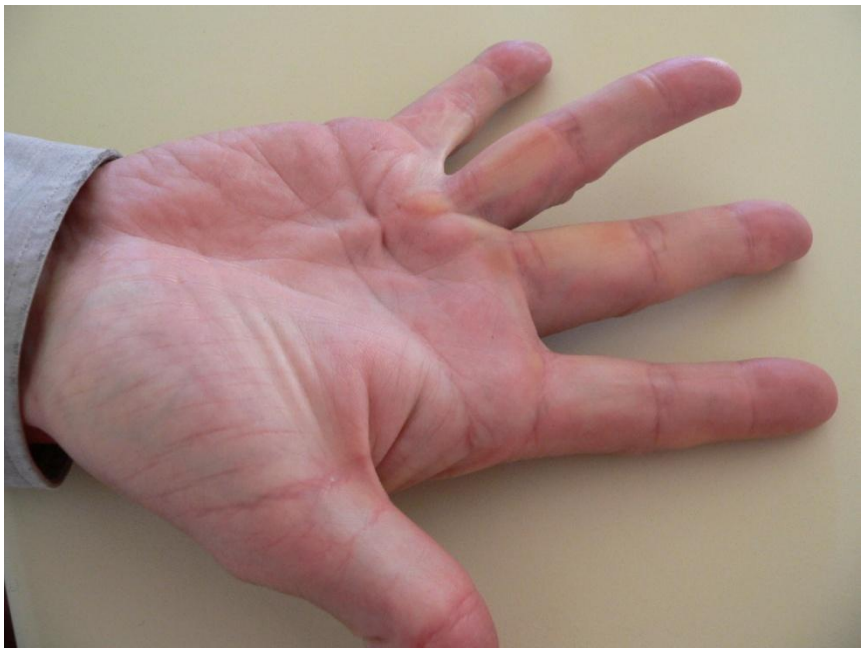


Dupuytren's Contracture

Occurs due to fibrosis of palmar aponeurosis probably caused by local microvascular ischemia

Sites involved are typically the ring and little fingers

FIG 26. DUPUYTREN'S CONTRACTURE



Nail changes

The possible nail changes seen in a patient of chronic liver disease include the following:

- Terry's nails
- Muehrcke's nails
- Leukonychia

FIG 27. TERRY'S NAILS

FIG 28. MUEHRCKE'S NAILS

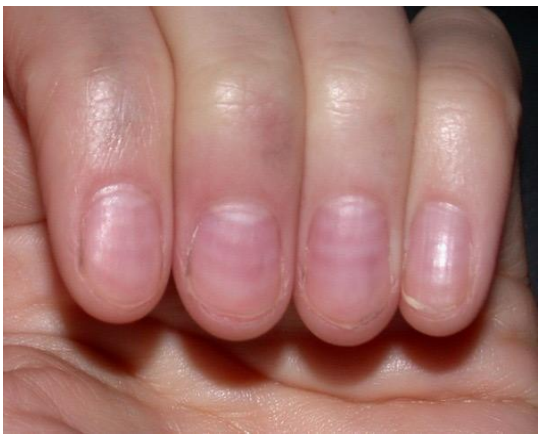


FIG 29. LEUKONYCHIA

Fetor Hepaticus

Sweet pungent smell due to volatile dimethyl sullied especially in portosystemic shunting and liver failure.

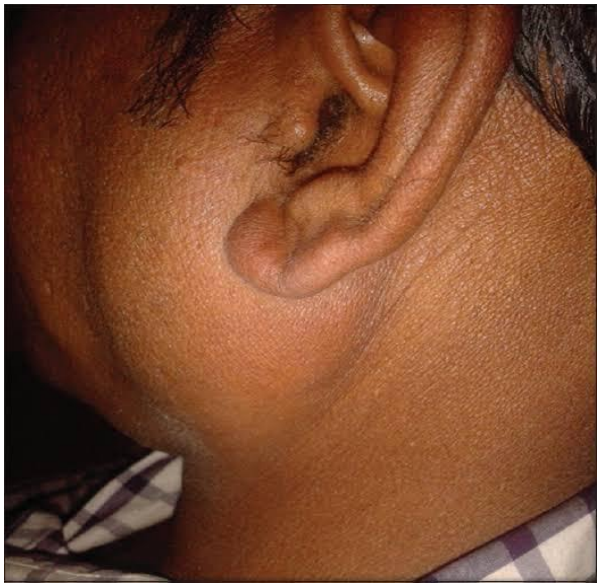
Asterixis/Flapping tremors

It is a type of negative myoclonus characterized by brief loss of tone of agonist muscles followed by a compensatory jerk of the antagonist muscles.

Parotid Enlargement

Observed commonly in alcohol induced CLD due to autonomic dysfunction.

FIG 30 . PAROTID ENLARGEMENT



HEPATIC ENCEPHALOPATHY

It is a transient, subtle reversible neurological and psychiatric manifestation of liver disease.

Decompensation features of liver disease include:Jaundice,Variceal bleed, hepatic encephalopathy and ascites

50-70% of CLD patients will have encephalopathy and precipitating events are almost always present.

1-year survival rate of encephalopathy is 40% and 3 year survival is 30%

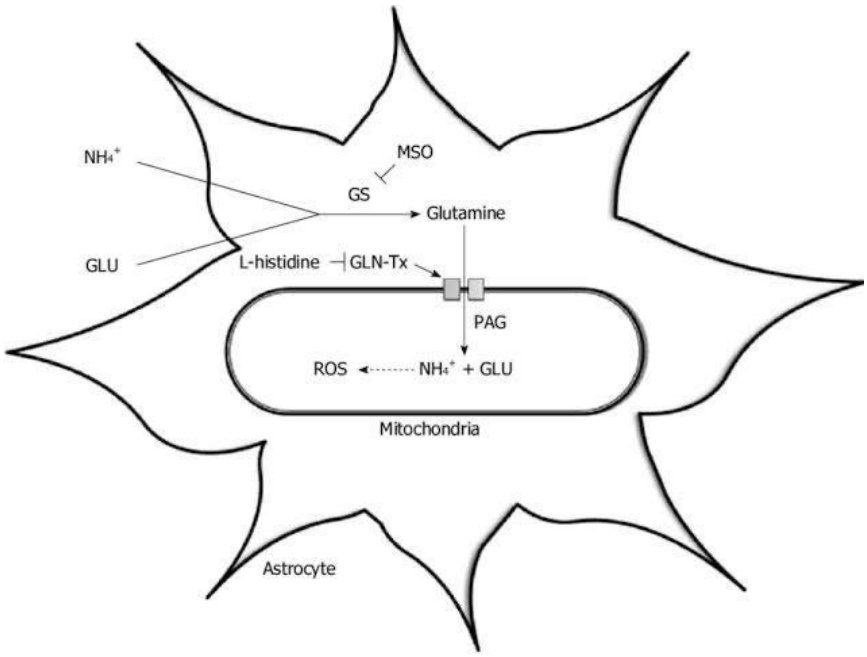
Mechanism

The major neurotoxin responsible for hepatic encephalopathy is ammonia which has 3 major sites of formation:

- Colonic bacteria by digestion of nitrogen containing food stuffs to produce ammonia.
- Enterocytes which contain glutamine synthetase and glutaminase.Glutaminase converts glutamine into glutamic acid and ammonia
- Muscle which have a large glutamine source and sarcopenia in the end stage of cirrhosis has a bad prognosis

Generally the liver detoxifies the ammonia but in case of CLD patients the ammonia bypasses the liver and reaches multiple organs like the brain.In the brain during liver disease,widespread bacterial translocation tends to occur causing endotoxemia and disruption of the blood brain barrier. The ammonia reaches the astrocytes of the brain which convert it into glutamine by means of glutamine synthase leading to cerebral edema. Along with this there is excess Gabaergic neurotransmitter activity [11].

Fig 31. Mechanism of Ammonia Metabolism in Astrocyte



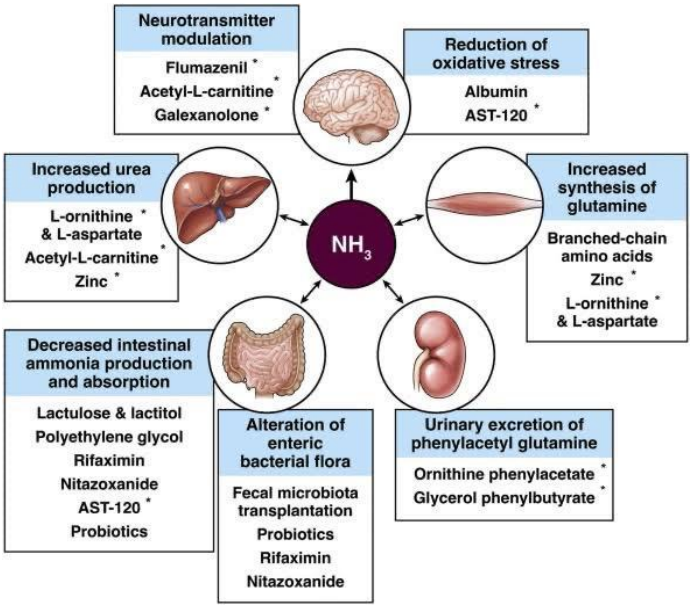
Common Precipitating factors of Hepatic Encephalopathy include:

- Hypokalemia
- Infections
- Dehydration
- UGI Bleed
- Constipation
- Sedative Drugs
- Diuretics
- Hyponatremia

FIG 32. CLASSIFICATION OF HEPATIC ENCEPHALOPATHY

<table>
<tr><th>TYPE</th><th colspan="3">DEGREE</th><th>TIME COURSE</th><th>PRECIPITATING FACTORS</th></tr>
<tr><td rowspan="2">A</td><td>MHE</td><td>Altered tests without clinical anomaly</td><td rowspan="2">Not manifested HE (COVERT)</td><td rowspan="2">Episodic</td><td rowspan="2">Spontaneous</td></tr>
<tr><td>1</td><td>Personality changes, altered sleep rhythm, attention...</td></tr>
<tr><td>B</td><td>2</td><td>Asterixis, disorientation in time, lethargy, apathy…</td><td rowspan="3">Manifested HE (OVERT)</td><td>Recurrent</td><td rowspan="3">Precipitated</td></tr>
<tr><td rowspan="2">C</td><td>3</td><td>Stupor, gross disorientation</td><td rowspan="2">Persistent</td></tr>
<tr><td>4</td><td>Coma</td></tr>
</table>

FIG 33 . TREATMENT MODALITIES FOR HEPATIC ENCEPHALOPATHY



ASCITES

Abnormal accumulation of fluid in the peritoneal cavity. The most common cause of ascites is liver cirrhosis. It is also the most common decompensating event seen in patients of cirrhosis

Mechanism of ascites:

- Splanchnic arterial vasodilation: The effective arterial blood volume decreases this decreasing the GFR further leading AKI
- Activation of RAAS and Sympathetic Nervous system which acts on the distal tubules causing salt and water retention.

Pathogenesis :

- Sodium Retention and extracellular fluid volume expansion
- Portal hypertension
- Systemic circulatory dysfunction
- Systemic inflammation

Sodium Retention:

Earliest feature in the development of ascites. There is ECF expansion secondary to splanchnic vasodilatation because of reduced renal blood flow and RAAS activation. Sodium and water retention leads to ECF expansion leading to ascites and pedal edema.

Sodium retention is the difference between sodium intake and excretion.

Patients with sodium excretion >10 Meq/d tend to have mild ascites while those with excretion less than 10 Meq/d tend to have massive ascites.

Portal hypertension :

It is a triggering factor for development of ascites.There are two components in development of intrahepatic resistance:

- Static which is Due deposition of collagen and formation of nodules which obstruct sinusoidal outflow

- Dynamic which is due to inflammation in the liver.

Systemic circulatory dysfunction:

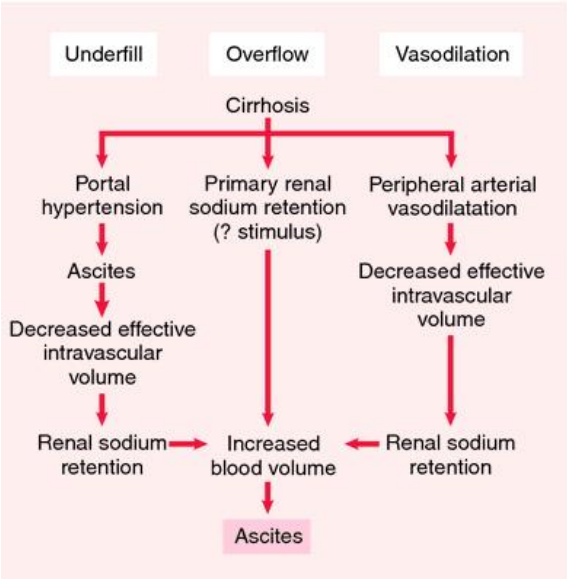
Portal hypertension leads to splanchnic vasodilatation which in turn cause reduced effective arterial blood pressure.This is balanced by cardiac output in the early stages .In advanced stages the heart in unable to compensate which causes arterial underfilling that leads to RAAS and sympathetic nervous system activation. There is also increased secretion of ADH that leads to salt free water reabsorption.

Systemic Inflammation:

Progressive systemic inflammation seen in patients with cirrhosis leads to decompensation.

In portal hypertension there is edema of the gut wall which causes leaky and defective tight junctions between endothelial cells that allow translocation of gut microbiota across the gut wall leading to systemic inflammatory response.

FIG 34. OVERFILL AND UNDERFILL THEORY



Grading of Ascites is based on amount of fluid retention:

- Grade 1 : Fluid detected only by USG
- Grade 2: Moderate ascites which is present on clinical examination
- Grade 3: Large ascites which presents with abdominal distension [12].

Recurrent ascites means ascites recurring at least thrice in a year

Refractory ascites is ascites that can't be mobilized with adequate diuretic therapy. It is of two types:

- Diuretic resistant:Ascites which does not respond to the maximum possible dose of diuretics

- Diuretic Intractable : Maximum dose of diuretics cannot be administered due to complications/Side effects.

In patients with ascites the ascetic fluid needs to be tapped and analyzed. An important parameter to assess is called Serum ascites Albumin Gradient(SAAG) and total protein.

SAAG = Serum Albumin - Ascitic fluid albumin

FIG 35. CAUSES OF HIGH AND LOW SAAG ASCITES

SAAG > 11g/L	SAAG <11g/L
Cirrhosis	Peritoneal carcinomatosis
Alcoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Mixed ascites	Bowel obstruction
Massive liver metastases	Biliary ascites
Fulminant hepatic failure	Postoperative lymphatic leak
Budd-Chiari syndrome	Serositis in connective tissue diseases
Portal vein thrombosis	
Veno-occlusive disease	
Myxoedema	
Fatty liver of pregnancy	

Management of Ascites:

The goal is to achieve negative sodium balance.Grade 1 ascites can be managed with salt restriction alone.Before development of ascites there is no role for salt restriction. Grade 2 ascites should be managed with a combination of salt restriction and diuretics. Salt is usually restricted to 2g of sodium per day (80-120 Meq/d) which equates to around 4.9-6.9 grams of salt per day.

Aldosterone antagonists like spironolactone and eplerenone are the 1st line drugs for ascites followed by loop diuretics. The half life of aldosterone antagonists is around 72 hours and so dose is slowly uptitrated.

First episode of ascites:

Treatment with anti-mineralocorticoids alone

100mg of spironolactone is started and slowly uptitrated by 100mg every 3 days till 400mg, loop diuretics are then added if there is inadequate response.

Loop diuretics are started at 40mg per day and slowly uptitrated to 160 mg/day

In patients with recurrent ascites a combination of mineralocorticoid antagonists with loop diuretics are started in a ratio of 100:40 and slowly

uptitrated based on response.

Goal is loss of 0.5kg of weight per day if there is ascites alone or 1kg per day if there is combination of ascites and pedal edema.

Treatment for grade 3 ascites is a combination of Large volume paracentesis, diuretics and salt restriction.

During paracentesis if volume removed is greater than 5L supplementary plasma expanders like 20 % albumin needs to be given at 8g of albumin for every liter of fluid removed beyond 5 liters.If albumin is not given in such large volume paracentesis it can lead To post paracentesis circulatory dysfunction on day 6 after paracentesis [13] .

SPONTANEOUS BACTERIAL PERITONITIS

Bacterial infection of ascitic fluid in the absence of any identifiable intra-abdominal source of infection.Patient with liver cirrhosis are much more likely to develop SBP and UTI. Rate of mortality in SBP is 20%.

Symptoms and signs are highly variable and fever and other signs of infection may often be absent in these patients. A diagnostic tap is mandatory in all patients admitted with CLD.

Diagnosis of SBP:

- Ascitic fluid tap : PMN more than 250 cells/mm3
- Ascitic fluid culture is positive in around 40% of patients

When Rbc's are detected in ascites on PMN is subtracted for every 250 RBC detected

Gram negative bacteria are common causes and the most common organisms seen are E.Coli and Enterobacteriaceae[14].

Antibiotic of choice of SBP is 3rd generation cephalosporin Cefotaxime.

Repeat cultures are sent after 48 hours and a decrease in PMN by 25% is expected. A failure to achieve this response indicates failure of Antibiotic therapy and then antibiotics should be changed to a higher antibiotics or based on culture reports.

Primary prophylaxis in SBP is indicated for all patients with ascites and any 1 of the following

- Ascitic fluid total protein less than 1.5 g/dl
- CTP score more than 9
- Creatinine more than 1.2 mg/dl
- Sodium less than 130 meq/L[15].

All the patient who have had an episode of SBP must receive secondary prophylaxis life long

All patients with Variceal bleed must be given IV antibiotics to prevent SBP.

HEPATORENAL SYNDROME

Functional renal disease in patients with chronic liver disease. Initial step is splanchnic vessel vasodilation leading to reduced systemic blood flow and blood pressure this leads on to reduced Renal blood flow which triggers activation of RAAS system leading to constriction of renal vessels which initially along with an increase in cardiac output helps to maintain GFR but as the disease progresses both these regulatory mechanism fail causes reduction in GFR [16].

FIG 36. PATHOGENESIS OF HEPATO-RENAL SYNDROME

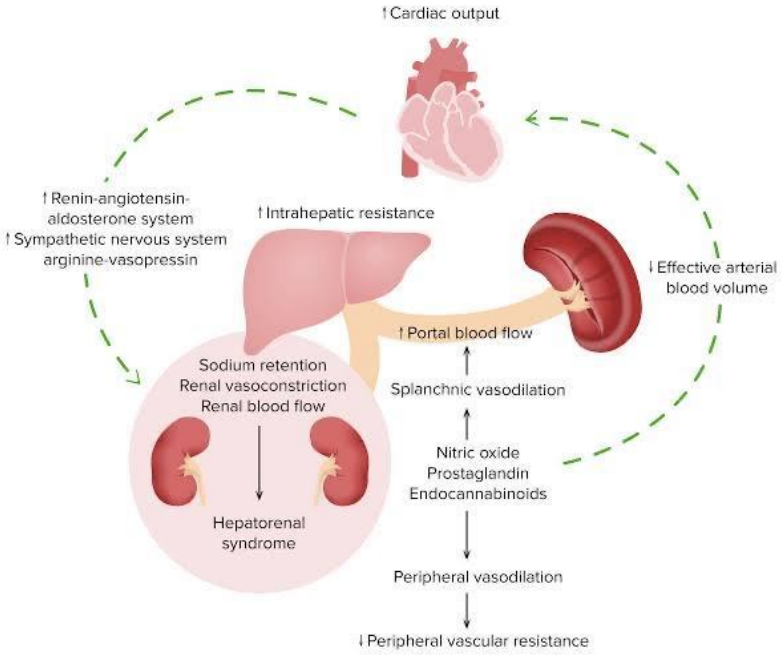
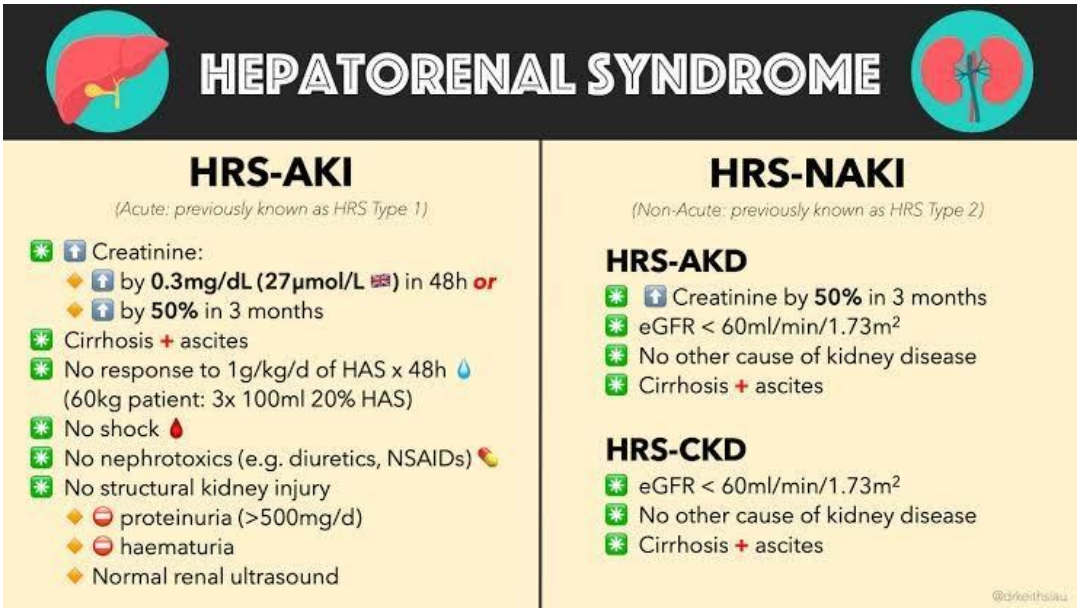


FIG 37. DEFINITION AND CLASSIFICATION OF HRS



Criteria for HRS-AKI:

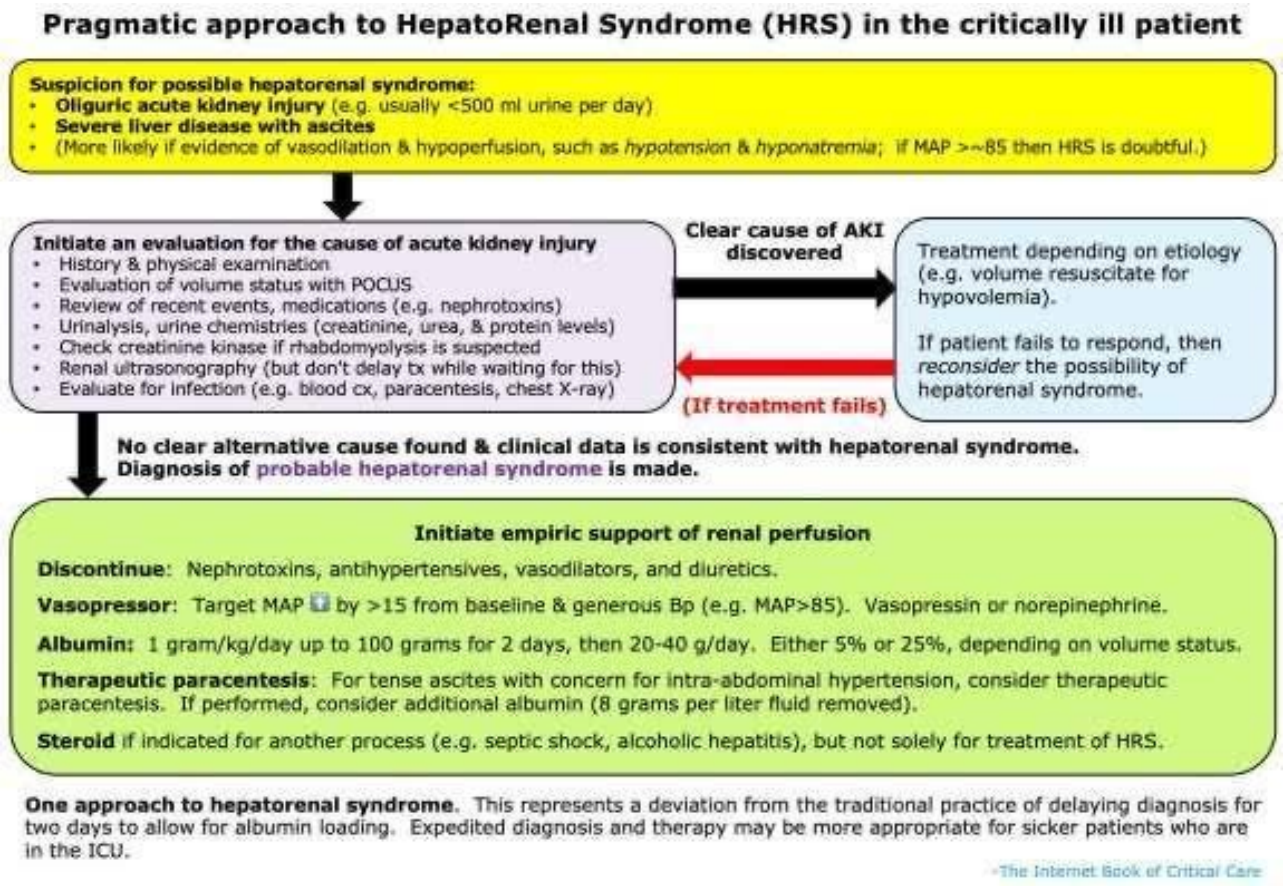
- Cirrhosis with ascites.
- Diagnosis of AKI according to International club of Ascites - AKI criteria defined as rise in creatinine more than 0.3mg/dl above baseline line or 1.5- 2 times baseline or fall of urine output to less than 0.5ml/kg/hour for at least 6 hours.
- No improvement of AKI after withdrawal of diuretics and IV albumin at dose of 1g/kg body weight for 48 hours
- No sepsis/shock
- No nephrotoxic drugs
- Normal kidneys on USG
- No proteinuria (>500mg/day)
- No microhematuria(>50 RBC/HPF) [17].

Treatment option is predominantly comprises of vasoactive agents like:

- Terlipressin
- Octreotide
- Noradrenaline with midodrine.

Given along with volume expander like human albumin.

FIG 38. MANAGEMENT OF HEPATORENAL SYNDROME



PORTAL HYPERTENSION

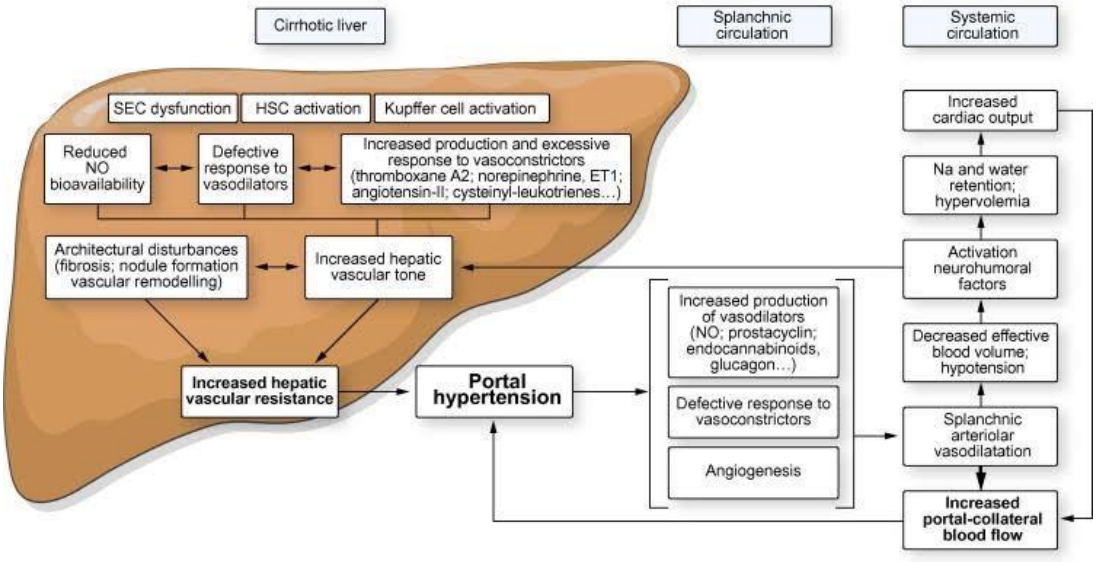
Portal Venous system is a high compliance and a low resistance system. Large amount of blood from splanchnic circulation reaches the liver and this high compliance helps in its accommodation.

Normal Portal Venous pressure = 5-10 mm Hg

Portal hypertension is defined as hepatic venous pressure gradient(HVPG) more than 5 mmhg . HVPG is the pressure difference between the hepatic and portal vein.

Clinically significant portal hypertension (CSPH) is when HVPG is more than or equal to 10 mm hg and can result in complications such as Variceal,ascites and encephalopathy [18].

FIG 39. PATHOGENESIS OF PORTAL HYPERTENSION



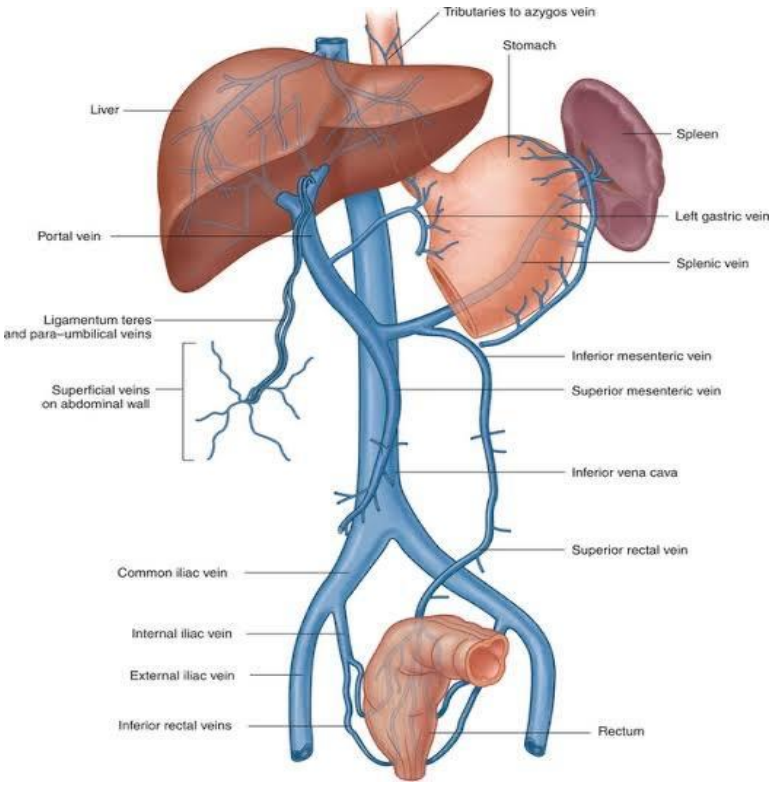
Collateral circulation develops and expands due to raised portal pressure.The is reversal in the direction of flow of blood which now flows from portal circulation to systemic circulation across the collaterals.

This occurs in the following sites:

- Distal esophagus
- Proximal Stomach
- Retroperitoneum
- Rectum
- Umbilicus

The gastric veins are formed by short gastric veins and posterior gastric veins.Whereas the Esophageal veins are formed by the coronary veins [19].

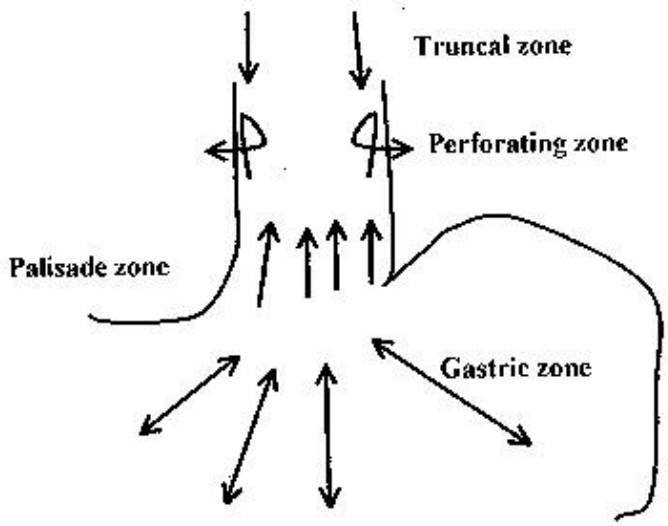
Fig 40. SITES OF PORTOSYSTEMIC SHUNTING



Esophageal Variceal occur in 4 zones:

- Gastric zone : 2-3 cm from the GEJ. It lies within the submucosa of the stomach.
- Palisade zone : The veins have perforators going to lamina propria of the esophagus. These perforators do not anastomose with the periesophageal veins hence tend to bleed.
- Perforating zone
- Truncal zone.

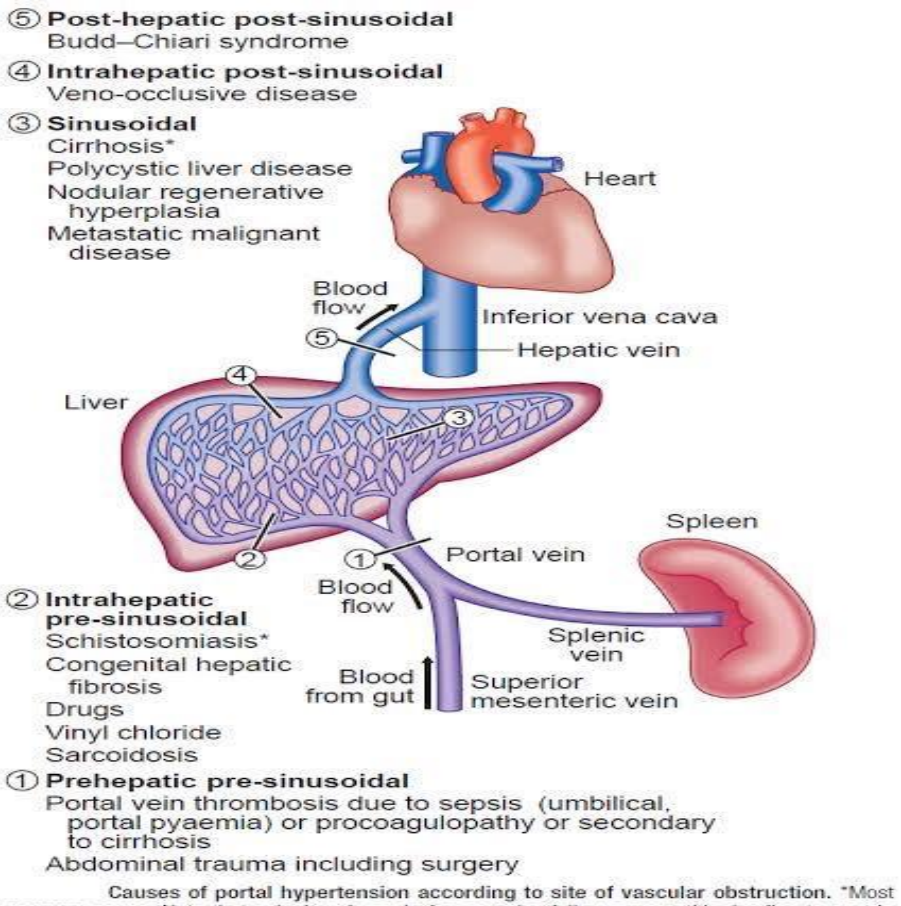
FIG 41. ZONES OF ESOPHAGEAL VARICES



Types of Portal Hypertension:

- Prehepatic
- Intrahepatic
    - Presinusoidal
    - Sinusoidal
    - Post Sinusoidal
- Post hepatic

FIG 42. TYPES AND CAUSES OF PORTAL HYPERTENSION



Causes of portal hypertension according to site of vascular obstruction. *Most common cause. Note that splenic vein occlusion can also follow pancreatitis, leading to gastric varices.

Source : Davidsons Essentials of Medicine, 2e

Detection of Esophageal Varices is done by Esophageal-gastro-duodenoscopy and once detected the varices are graded based on the classification of Japanese Research Society for portal hypertension based on :

- Location
- Size
- Red Color Signs

Red color signs include the following:

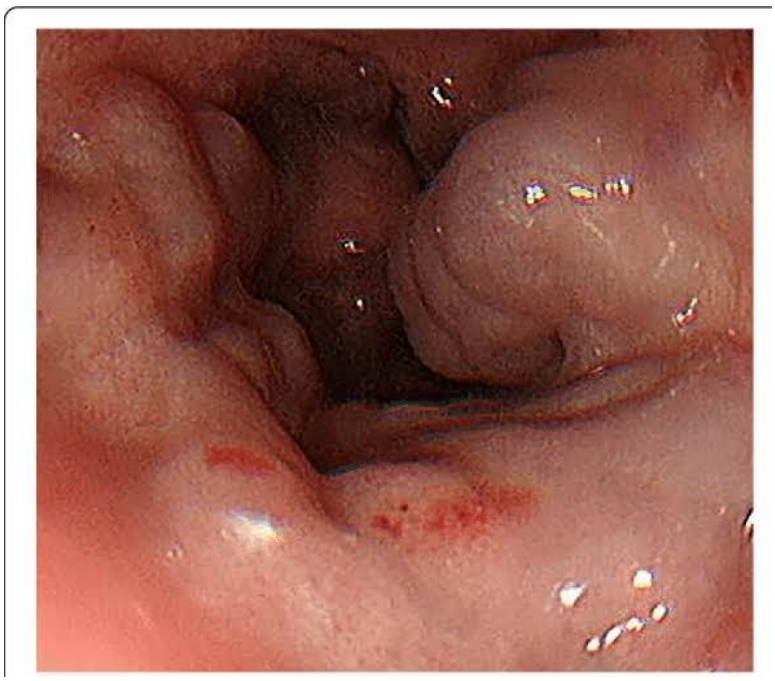
- Red wale signs
- Cherry red spots
- Hematocystic spots
- Diffuse redness

Grades of varices:

- Grade 1: straight varices
- Grade 2 : tortuous and occlusive less than 1/3rd of lumen size
- Grade 3:tortuous and occlusive more than 1/3rd of lumen size

Based on location they can be Esophageal or gastric [20].

FIG 43. OGD IMAGE SHOWING ESOPHAGEAL VARICES



INTRODUCTION OF LIPIDS

Lipids are a heterogenous group of molecules of biochemical importance. It is defined as compounds which are not soluble in water but are soluble in solvents such as ether, alcohol, benzene and acetone which are non polar organic solvents.

In our human body lipid molecules are oily and greasy substances Lipids have a major role to play in energy storage and production in our body.Lipids are one of the major forms of stored energy in adipose tissue and when broken down lipids provide energy of approximately 9 KCAL per gram of fat which is the highest calorie content among all the 3 macronutrients.

In our body lipids often combine with protein molecules forming unique molecules called lipoproteins and these lipoproteins serve important functions in cytoplasmic and cell wall functioning .

They form an important component of our daily diet due to their rich caloric content,unique function served by lipids and also because fat soluble vitamins are absorbed with the help of lipids [21].

GENERAL PROPERTIES OF LIPIDS

Lipids are a heterogeneous group of organic soluble molecules in non-polar solvents. These molecules are amides or esters of fatty acids structurally.

General Physical Properties:

- They are not soluble in water
- They are soluble in nonpolar solvents such a benzene and alcohol
- They do not possess Ionic charge
- They are greasy in texture and stored in the body's adipose tissue.
- Lipids can exist as saturated forms and unsaturated forms.

CLASSIFICATION OF LIPIDS

- **Simple lipids**

These are esters of fatty acids and glycerol or other forms of alcohol.

- **Compound lipids**

Complex or compound lipids which contain in addition to fatty acids and glycerols some other molecules which include:

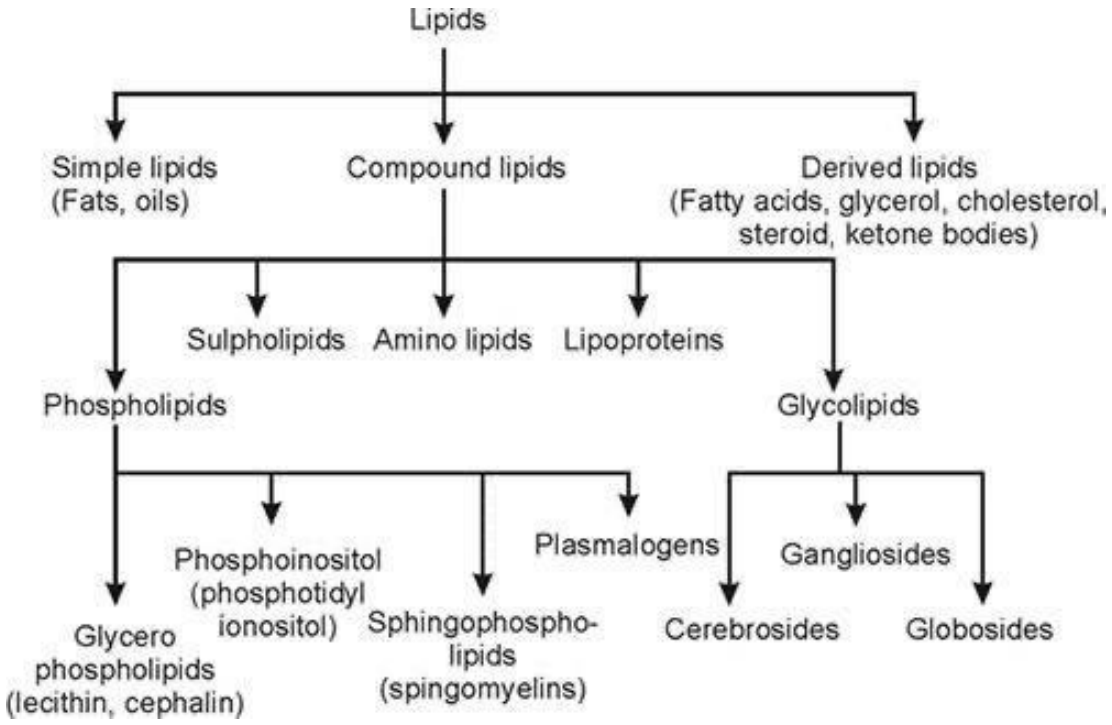
1. Phospholipids
2. Glycolipids
3. Lipoproteins

- **Derived lipids**

They are derived by hydrolysis of simple and compound lipids and precursors of lipids.

They include fatty acids and steroids [22].

FIG 44. CLASSIFICATION OF LIPIDS



FUNCTIONS OF LIPIDS

The Key metabolic roles of lipids are mentioned below:

- Chemical messenger : Lipids of various classes help in acting as messenger molecules for signaling and cellular messaging.They activate several signaling pathways such As Nuclear receptors or G-Coupled receptors.
- Energy Storage : Triglycerides and Triacylglycerols in adipose tissues are a major source of energy . The breakdown of fatty acids yields about 9 KCAL/g of fat and this breakdown process is mediated by the lipase enzyme system[23].
- Structural component of cell membrane: In cells the cell membrane is essentially made of a lipid bilayer into which various proteins are embedded. The bilayer itself is composed of a lipid called as amphipathic glycerophospholipid. While the remaining lipids such as phospholipids and glycolipids act as structural components of the membrane.
- Lipids also function as pigments(carotene), cofactors (vit K), Hormones (sex hormones and vitamin D), Detergents (bile salts)
- Prostaglandins which are involved in vasodilatation, uterine and other smooth muscle contraction and inflammation.
- The subcutaneous fat in our body serves the role of insulating us against cold.
- Thromboxanes trigger vasoconstriction and platelet aggregation

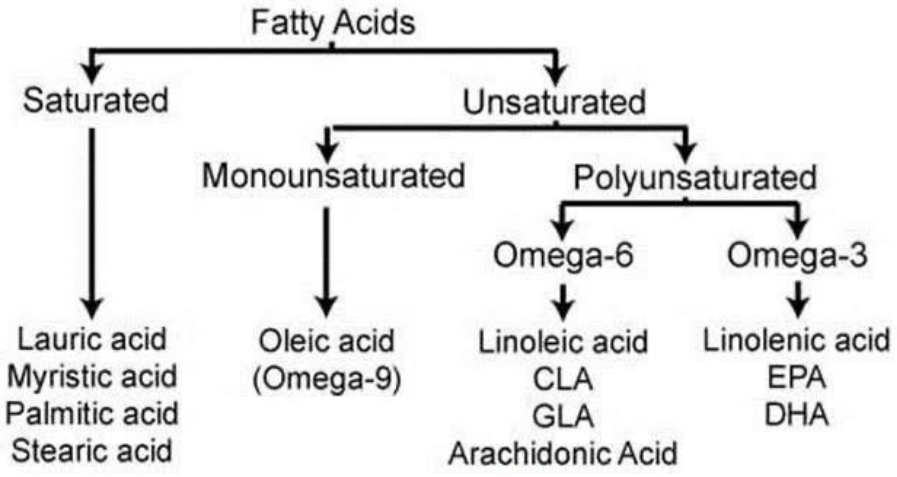
FATTY ACIDS

These are the simplest forms of lipids. They consist of a long chain which contains hydrocarbons and one carboxylate group. .

They serve as basic constituents of a variety of complex lipids.Fatty are amphipathic meaning they contain both polar and non polar terminals .

They can be either saturated or unsaturated fatty acids.

FIG 45. CLASSIFICATION OF FATTY ACIDS



CHOLESTEROL

It Consists of a four fused ring steroid molecule called the steroid nucleus. Cholesterol is a major component of the cell membranes of all the cells of the body, especially the brain. It is the precursor molecule of the steroid hormones, the bile acids and Vitamin D. Cholesterol is present in highest amounts in the following sites :

- nervous tissue (2%),
- skin (0.3%)
- liver (0.3%),
- intestine (0.2%)
- certain endocrine glands.

Cholesterol is a major factor involved in the pathological process of atherosclerosis which is essentially the deposition of excess cholesterol in the walls of vessels.

This deposition in the long run leads to the formation of atherosclerotic plaques which are responsible for the causation of cardiovascular diseases.

Hence these cholesterol molecules have come to the center of attention in recent times with regards to how To control and modulate this cholesterol so as to prevent such atherosclerotic processes.

TRIGLYCERIDES (TRIACYLGLYCEROLS)

They are Tri-esters composed of fatty acids and glycerol.These compounds are nonpolar and hydrophobic in nature. They are termed as neutral lipids due to the fact that they do not possess any charge. Their fatty acid composition can be of varying lengths and can be either saturated or unsaturated.

There are broadly two types of triglycerides namely:

- Simple : Triglycerides which contain only a single fatty acid.
- Mixed triglycerides : Contain 2 or more different fatty acids.

PHOSPHOLIPIDS

These types of lipids contain four components namely:

1. Fatty acids
2. Phosphate group
3. Glycerol or sphingosine
4. Alcohol which is attached to phosphate.

It includes 3 major groups:

- Phosphoglycerides
- Sphingophospholipids
- Ether Glycerophospholipids

Phosphoglycerides contain glycerol along with 2 fatty acid residues, phosphate and alcohol. They are the major phospholipids present in cell membranes.

Sphingophospholipids are basically sphingosine derived phospholipids. Sphingomyelin is a type of sphingophospholipid which is a major component involved in myelination of nerve fibers.

Ether Glycerophospholipids have an ether linkage at glycerol's C1 position. Platelet activating factor (PAF) is a Ether Glycerophospholipid which is involved in platelet aggregation.

LIPOPROTEINS

They are hydrophilic and spherical lipids that contain proteins on their surface which are known as apoproteins or apolipoproteins.

These apoproteins help to act as ligands and co-factors in the process for lipid transport and metabolism.

One of the major functions of these lipoproteins is to enable the solubility of lipids in blood as lipids innately are hydrophobic in nature.

Lipoproteins are classified based on their size and density into the following groups:

FIG 46. CLASSIFICATION OF LIPOPROTEINS

Classification and characteristics of lipoproteins

Lipoprotein	Density (g/mL)	Mean diameter (nm)	Electrophoretic mobility	Source	Principal function
CM	<0.95	500	remains at origin	intestine	transport of exogenous triglyceride
VLDL	0.96–1.006	43	pre-β	liver	transport of endogenous triglyceride
IDL	1.007–1.019	27	'broad β'	catabolism of VLDL	precursor of LDL
LDL	1.02–1.063	22	β	catabolism of VLDL, via IDL	cholesterol transport
HDL	1.064–1.21	8	α	liver, intestine; catabolism of CM and VLDL	reverse cholesterol transport

Each apoprotein present in the lipoprotein surface serves its own unique function and role and certain apoproteins are specific for certain types of lipoproteins [24].

Classes of apoproteins their functions and lipoproteins associated are given below.

FIG 47. APOPROTEIN CLASSES

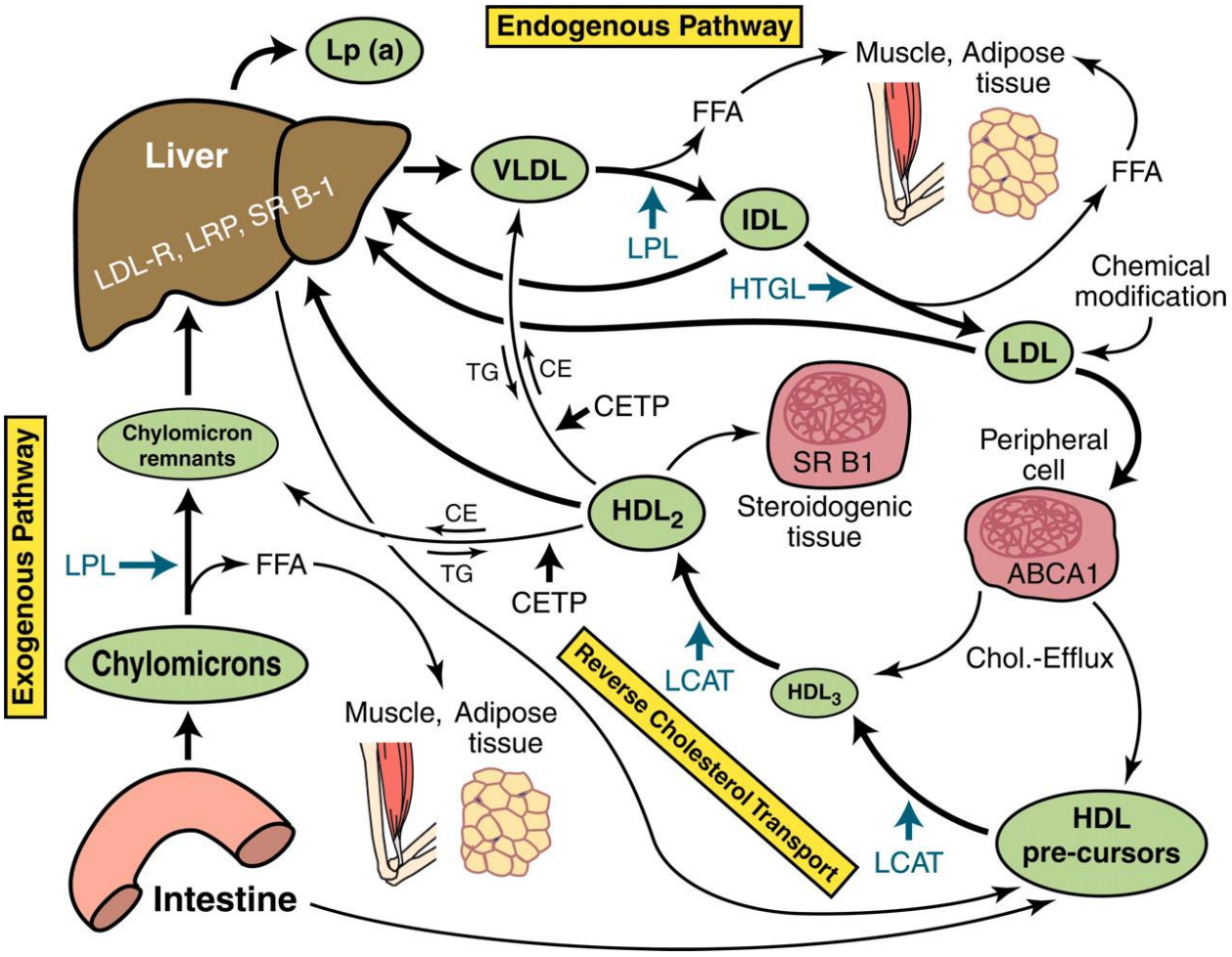
There are many types of apolipoproteins

Apoprotein	Lipoproteins	Function(s)
Apo B-100	VLDL, IDL, LDL	1) Secretion of VLDL from liver 2) Structural protein of VLDL, IDL, and HDL 3) Ligand for LDL receptor (LDLR)
Apo B-48	Chylomicrons, remnants	Secretion of chylomicrons from intestine
Apo E	Chylomicrons, VLDL, IDL, HDL	Ligand for binding of IDL & remnants to LDLR
Apo A-I	HDL, chylomicrons	1) Major structural protein of HDL 2) Activator of LCAT
Apo A-II	HDL, chylomicrons	Unknown
Apo C-I	Chylomicrons, VLDL, IDL, HDL	Activation of LCAT
Apo C-II	Chylomicrons, VLDL, IDL, HDL	Activator of LPL
Apo C-III	Chylomicrons, VLDL, IDL, HDL	Inhibitor of LPL activity

LIPOPROTEIN METABOLISM

Chylomicrons carry dietary lipids that are ingested from the intestine via the systemic circulation through the exogenous pathway. The enzyme endothelium-associated lipoprotein lipase (LPL) quickly breaks down chylomicrons into free fatty acids (FFA), which are then absorbed by the liver, muscles, and adipose tissues. Chylomicrons are reduced in size during this catabolic process to become chylomicron remnants, which are absorbed by the liver through the low-density lipoprotein (LDL) receptor and the LDL receptor-related protein (LRP).

FIG 48. LIPOPROTEIN METABOLISM



In the Endogenous pathway, Triglyceride-rich very low-density lipoprotein (VLDL) particles, which carry triglycerides from the liver to peripheral organs, are assembled and secreted by the liver . The LPL reduces the VLDL particles to intermediate-density lipoproteins (IDL), which may either be absorbed by the liver or undergo further hydrolysis to become LDL particles. The particles lose their

triglyceride content but keep a significant quantity of cholesterol throughout this conversion.

LDL distributes cholesterol to peripheral tissues in addition to hepatocytes. LDL receptors in healthy people eliminate between 60 and 80% of LDL thanks to apoB-100, which is responsible for their detection and absorption. Other specialized receptors, such LRP, or scavenger receptors remove the leftover LDL.

Scavenger receptors on macrophages and vascular smooth muscle cells are particularly capable of capturing oxidized LDL (ox-LDL). Foam cells are created when these macrophages are overwhelmed with cholesteryl esters, which is a crucial stage in the progression of atherosclerosis. Small dense LDL (sdLDL), which has a reduced affinity for the LDL receptor but is more vulnerable to oxidative alteration, is produced when LDL becomes lipid deprived. Therefore, it is thought that sdLDL particles are more atherogenic than bigger LDL particles.

Reverse cholesterol transport, which transports cholesterol from peripheral cells to the liver, is a critical step in relieving the load of cholesterol on the peripheral cells. High-density lipoprotein (HDL) plays a significant part in this process.

The ATP-binding cassette transporter 1, apoA-I, and apoA-IV are involved in the absorption of free cholesterol from cell membranes by HDL precursor particles, which are produced by the liver and gut as disc-shaped aggregates. The primary HDL apolipoprotein, ApoA-I, activates the enzyme lecithin:cholesterol acyltransferase (LCAT), which esterifies the free

cholesterol that has been taken in order to facilitate more effective packing of the cholesterol for transport. Apolipoproteins, cholesteryl esters, and triglycerides are added to HDL3 particles to make them grow into bigger HDL2 particles. There are three possible pathways for reverse cholesterol transfer. First, the liver may absorb big HDL particles with many copies of apoE by using the LDL receptor.

Second, scavenger receptor B1 allows the liver to preferentially absorb the accumulated cholesteryl esters from HDL. Most hepatic and non placental steroidogenic tissues express this receptor. Third, cholesteryl esters are transferred from HDL to triglyceride-rich lipoproteins via the cholesteryl ester transfer protein. These intricate reverse cholesterol transport pathways have an impact on plasma HDL cholesterol levels. The antiatherogenic capabilities of HDL can be significantly impacted by changes in the quantities of apoproteins, the activity of enzymes, transport proteins, receptors, other lipoproteins, and the clearance from plasma [24].

IV. MATERIALS AND METHODS

SOURCE OF THE STUDY

Data was collected by myself from patients who were admitted under the Institute of Internal Medicine in Rajiv Gandhi Hospital,Chennai.

STUDY DESIGN

Cross-Sectional Study

STUDY PERIOD

July 2022 to December 2022

METHODOLOGY

The study performed is a cross-sectional study done in patients with chronic liver disease whose fasting lipid profile levels were taken and studied and compared to the severity of chronic liver disease as per Child Pugh Scoring System.

INCLUSION CRITERIA

- Patients age more than 18 years.
- Patients giving consent to the study
- Patients with chronic liver disease proven by clinical,biochemical and sonological evidence.

EXCLUSION CRITERIA

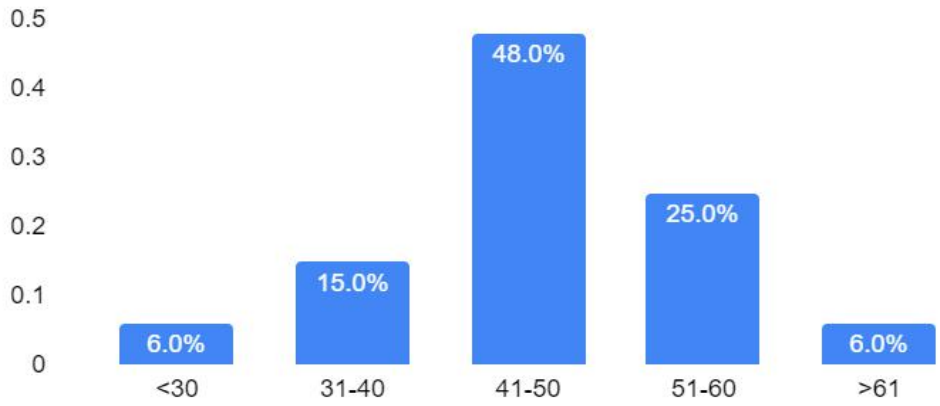
- Patients under 18 years of age.
- Patients not willing to participate in the study
- Patients suffering from co-morbidities that could alter the lipid profile such as diabetes, thyroid disease, Nephrotic Syndrome, Cancer, Renal Failure, Dyslipidemia.
- Patients on drugs that could alter the lipid profile like statins and oral contraceptive pills.

All Data analysis was done using IBM-SPSS software version 21. All continuous variables of Lipid profile values were compared using One-way ANOVA.The comparison of categorical data was done using Pearson Chi-square test and P value of <0.05 was considered statistically significant using a two-tailed test.

V. RESULTS

TABLE 1 AGE DISTRIBUTION

AGE GROUP	Frequency	Percent
<30	6	6.0%
31-40	15	15.0%
41-50	48	48.0%
51-60	25	25.0%
>61	6	6.0%
Total	100	100.0%

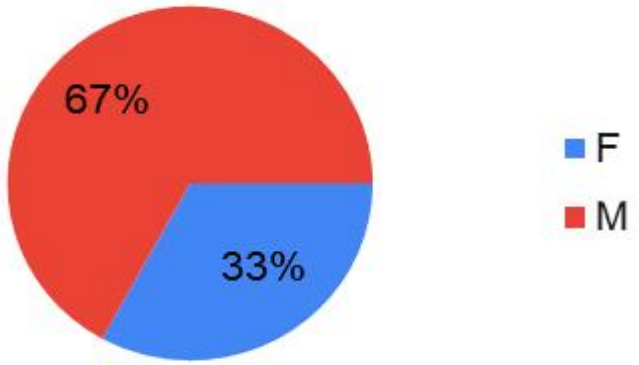


Age wise analysis shows the predominant proportion of the study population were between the ages of 41 and 50 standing at 48 in number(48%).

2nd highest age prevalence was between 51 to 60 years at 25 in number(25 %).

TABLE 2 SEX DISTRIBUTION

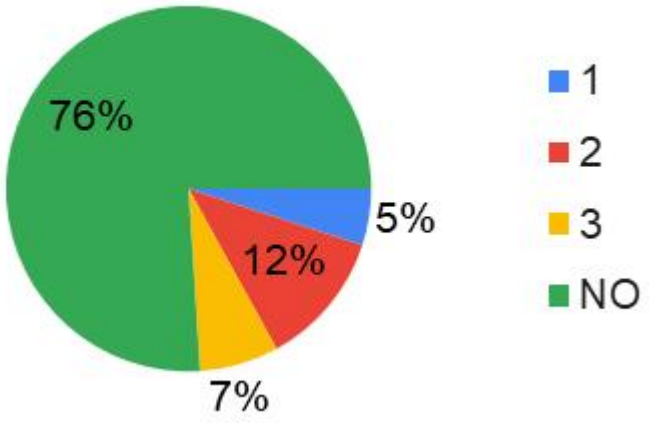
SEX	Frequency	Percent
F	33	33.0%
M	67	67.0%
Total	100	100.0%



Age analysis shows that males were in higher numbers than females in the study population. Males being 67% while females were 33%

TABLE 3 DISTRIBUTION OF PATIENTS WITH HEPATIC ENCEPHALOPATHY

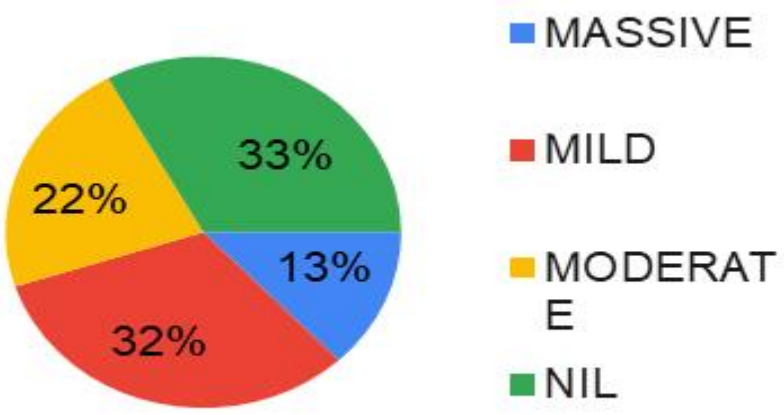
HEPATIC ENCEPHALOPATHY	Frequency	Percent
1	5	5.0%
2	12	12.0%
3	7	7.0%
NO	76	76.0%
Total	100	100.0%



Analysis of the Encephalopathy distribution shows that 73% of patients had No Hepatic Encephalopathy, 12% had grade 2 encephalopathy , 7 % had grade 3 encephalopathy while 5 % had grade 1 encephalopathy.

TABLE 4 DISTRIBUTION OF ASCITES

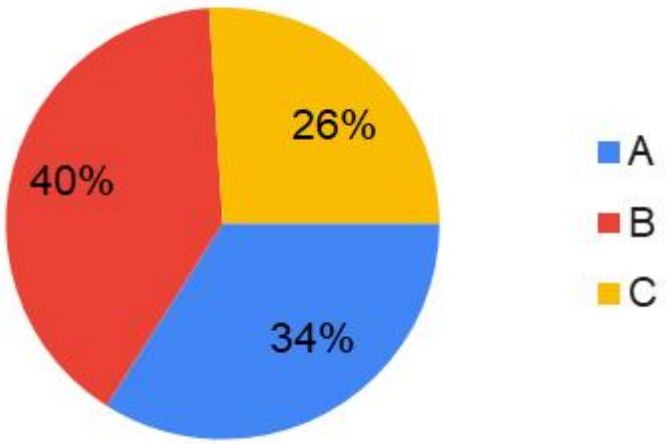
ASCITES	Frequency	Percent
MASSIVE	13	13.0%
MILD	32	32.0%
MODERATE	22	22.0%
NIL	33	33.0%
Total	100	100.0%



Analysis of ascites distribution shows that 33% of the study population had no ascites, 32% had mild ascites, 22% had moderate ascites and 13% had massive ascites.

TABLE 5 DISTRIBUTION OF CHILD PUGH SCORE

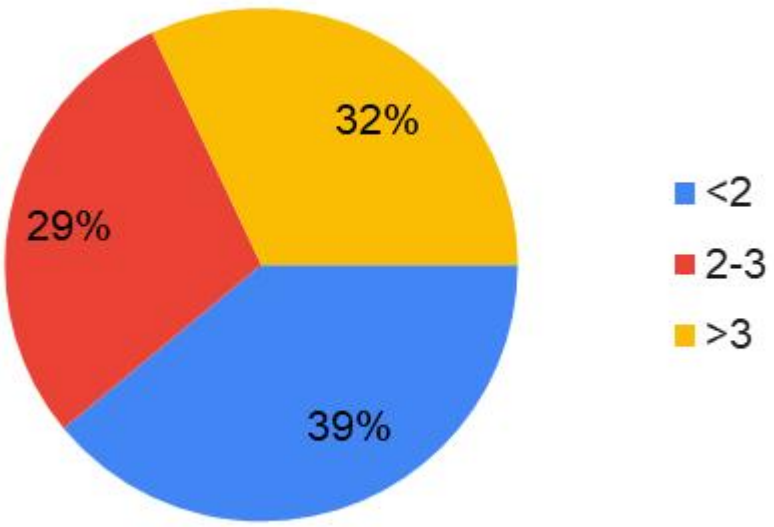
CHILD PUGH GRADE	Frequency	Percent
A	34	34.0%
B	40	40.0%
C	26	26.0%
Total	100	100.0%



Majority of patients 40% fell under Child Pugh B category while 34% came under Child Pugh A and finally 26% of the study population were in Child Pugh C category.

TABLE 6 DISTRIBUTION OF BILIRUBIN VALUES

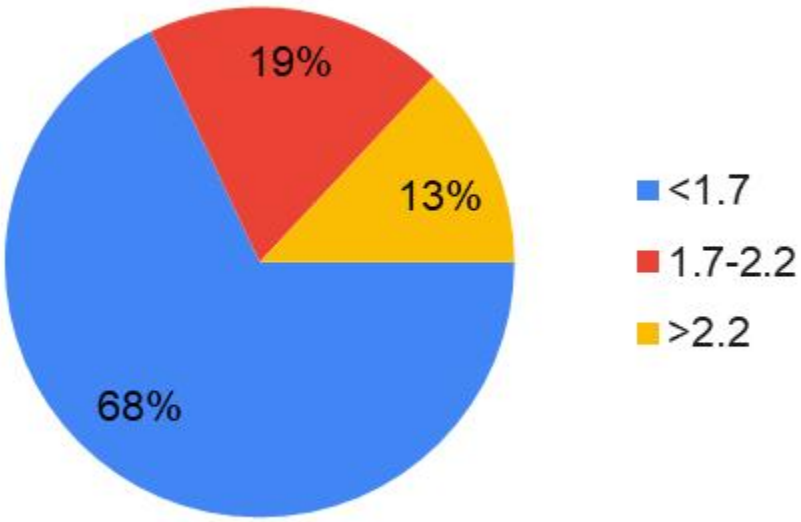
TOTAL BILIRUBIN	Frequency	Percent
<2	39	39.0%
2-3	29	29.0%
>3	32	32.0%
Total	100	100.0%



Analysis of Bilirubin Distribution shows that 39% of the population had bilirubin values less than 2 mg/dl, 32% had values more than 3 mg/dl and 29 % of the study population had bilirubin between 2-3 mg/dl.

TABLE 7 DISTRIBUTION OF INR VALUES

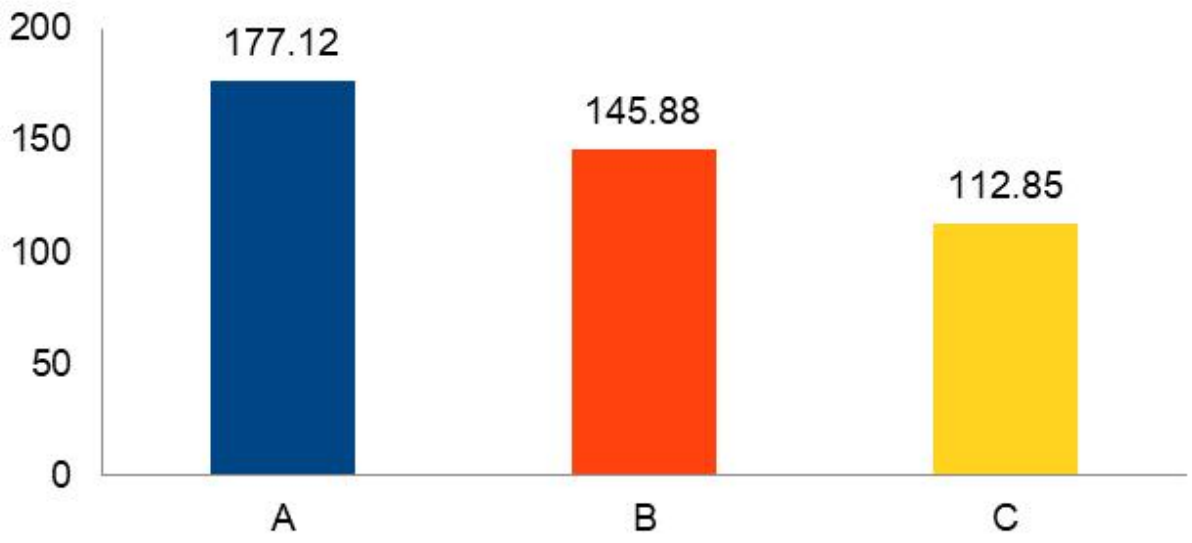
INR	Frequency	Percent
<1.7	68	68.0%
1.7-2.2	19	19.0%
>2.2	13	13.0%
Total	100	100.0%



Analysis of INR distribution shows that 68% of patients had inr less than 1.7, 19% has inr values between 1.7 and 2.2, and 13% of patients had inr value of more than 2.2.

TABLE 8 DISTRIBUTION OF TOTAL CHOLESTEROL ACCORDING TO CHILD PUGH GRADES

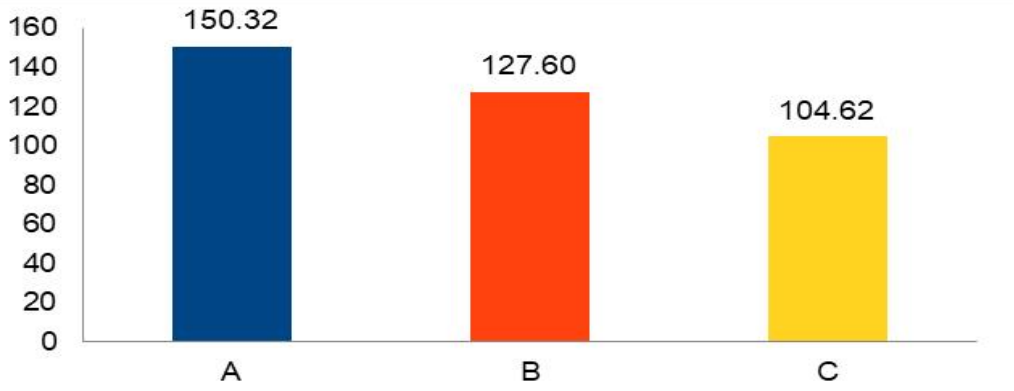
CHILD PUGH GRADE		Mean	Std. Deviation	P value
TOTAL CHOLESTEROL	A	177.12	10.39	<0.0001
	B	145.88	18.69	
	C	112.85	24.89	
	Total	147.91	30.78	



Total cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of cholesterol is group A was 177.12 ± 10.39, Group B 145.88 ± 18.69 and Group C 112.85 ± 24.89 and is statistically significant with a p value of <0.0001

TABLE 9 DISTRIBUTION OF TRIGLYCERIDES ACCORDING TO CHILD PUGH GRADES

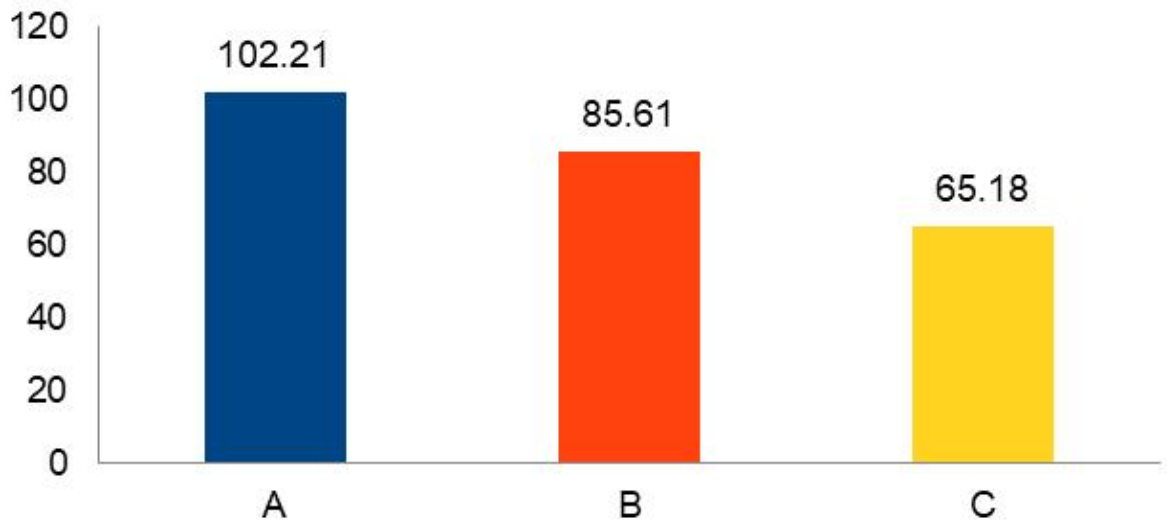
CHILD PUGH GRADE		Mean	Std. Deviation	P value
TRIGLYCERIDES	A	150.32	11.47	<0.0001
	B	127.60	12.75	
	C	104.62	19.80	
	Total	129.35	22.80	



Triglycerides level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of Triglycerides is group A was 150.32 ± 11.47, Group B 127.60 ± 12.75 and Group C 104.62 ± 19.80 and is statistically significant with a p value of <0.0001.

TABLE 10 DISTRIBUTION OF LDL CHOLESTEROL ACCORDING TO CHILD PUGH GRADES

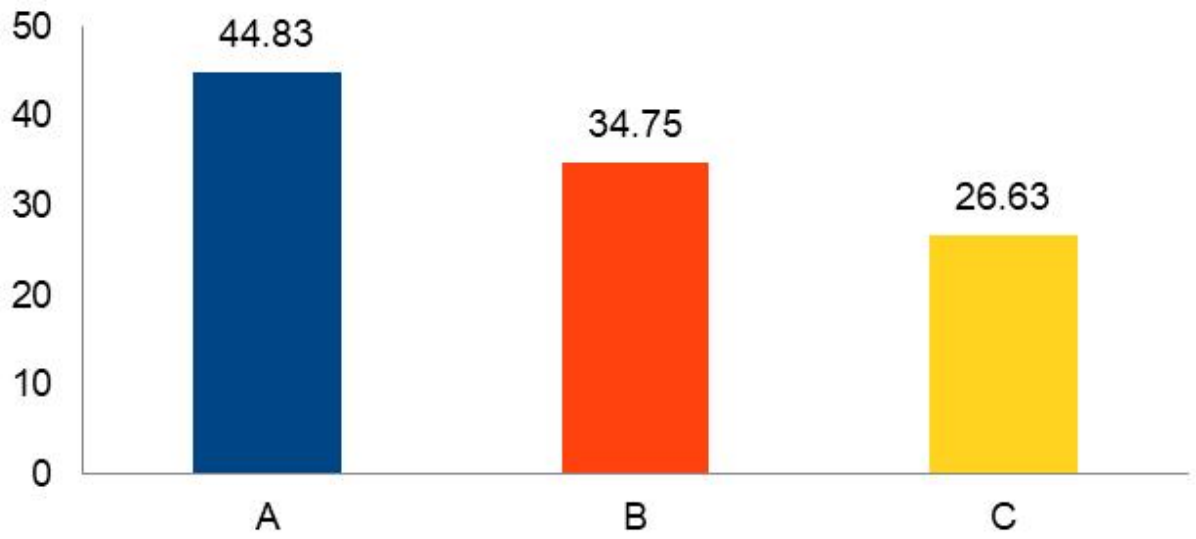
CHILD PUGH GRADE		Mean	Std. Deviation	P value
LDL	A	102.21	11.15	<0.0001
	B	85.61	14.33	
	C	65.18	25.26	
	Total	85.94	22.08	



LDL cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of LDL cholesterol is group A was 102.21 ± 11.15, Group B 85.61 ± 14.33 and Group C 65.18 ± 25.26 and is statistically significant with a p value of <0.0001.

TABLE 11 DISTRIBUTION OF HDL CHOLESTEROL ACCORDING TO CHILD PUGH GRADES

CHILD PUGH GRADE		Mean	Std. Deviation	P value
HDL	A	44.83	5.97	<0.0001
	B	34.75	6.08	
	C	26.63	5.33	
	Total	36.07	9.17	



HDL cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of HDL cholesterol is group A was 44.83 ± 5.97, Group B 34.75 ± 6.08 and Group C 26.63 ± 5.33 and is statistically significant with a p value of <0.0001.

DISCUSSION

Lipid profile is a commonly performed test in routine practice to detect dyslipidemia especially in patients with diseases such as diabetes, hypertension, patients with cardiovascular events etc.

In the era of modern medicine where communication with patients is such a vital part of practice it is important for treating physicians to know what is the prognosis of the patient with any disease so that patients can be well informed and counseled regarding what the future holds for them.

Studies have been done in the past in correlating lipid profile with Chronic liver disease but the number done in the State of Tamil Nadu have been scarce.Hence a study proposal was formed to study this lipid pattern among the patients of chronic liver disease being admitted to Rajiv Gandhi Government General Hospital.

We had selected a total of 100 patients (Male = 67 and Female = 33) of Chronic liver disease above the age of 18 years who were diagnosed based on clinical,biochemical and sonological criteria. They were subsequently examined and biochemical tests were performed such as Liver function tests, coagulation profile, thyroid status.

The Final results that were obtained in our study were consistent with previous studies. We found that the lipid profile parameters namely

Total cholesterol, Triglycerides, LDL and HDL were all significantly reduced in patients with higher grades of Child Pugh severity of chronic liver disease.

Total cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of cholesterol is group A was 177.12 ± 10.39, Group B 145.88 ± 18.69 and Group C 112.85 ± 24.89 and is statistically significant with a p value of <0.0001.

Triglycerides level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of Triglycerides is group A was 150.32 ± 11.47, Group B 127.60 ± 12.75 and Group C 104.62 ± 19.80 and is statistically significant with a p value of <0.0001.

LDL cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of LDL cholesterol is group A was 102.21 ± 11.15, Group B 85.61 ± 14.33 and Group C 65.18 ± 25.26 and is statistically significant with a p value of <0.0001.

HDL cholesterol level was found to be the lowest in child pugh category C group of patients when being compared to group A and B, The Mean value of HDL cholesterol is group A was 44.83 ± 5.97, Group B 34.75 ± 6.08 and Group C 26.63 ± 5.33 and is statistically significant with a p value of <0.0001.

A similar study that was carried out in Hyderabad by C. Suman, Ramesh kumar,Prabahar et al revealed that blood cholesterol and LDL levels had high area under curves that were statistically significant connected with the severity of cirrhosis. In that study, the outcomes were contrasted with those of healthy people [25].

Another study conducted in Pakistan by Umar Farooque et al. found that Child Pugh grade C had considerably lower mean values of serum total cholesterol, HDL, LDL and triglycerides than did the other grades [26].

The lower levels of LDL and HDL could be linked to a lower amount of apolipoproteins A and B production. The lower level of triglycerides in cirrhosis is explained by the fact that the apo B is involved in the creation of VLDL. This might be a result of the insulin resistance that liver cirrhosis causes.

Our Study has confirmed in the population of Chennai,Tamil Nadu the findings of previous studies which suggested a negative correlation between Lipid profile and Chronic Liver disease. Using these studies as a back bone further studies need to be performed to correlate complications such as Hepatorenal syndrome and UGI bleed with Lipid profile.In the future Lipid profile can definitely serve as a useful prognostic tool alongside the existing systems such as Child Pugh score and MELD score.

CONCLUSION

- Significant Negative correlation is seen between values of Total cholesterol and severity of Chronic Liver disease.
- Significant Negative correlation is seen between values of LDL cholesterol and severity of Chronic Liver disease
- Significant Negative correlation is seen between values of HDL cholesterol and severity of Chronic Liver disease
- Significant Negative correlation is seen between values of Triglycerides and severity of Chronic Liver disease
- In the future analysis of lipid profile could become an integral part in analysis of any patient with chronic liver disease as is checking their Child pugh score in order to better prognosticate the stage of the disease.

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INFORMATION SHEET

INFORMATION TO PARTICIPANTS

INVESTIGATORS: Dr. EZHILARASU PREETHAM
Dr. C. HARIHARAN
Dr. P. MALARVIZHI

NAME OF THE PARTICIPANT:

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

We are conducting a study titled "CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE" among patients admitted in Rajiv Gandhi Government General Hospital, Chennai. Your cooperation to undergo examination is valuable to us.The purpose of this study is to analyze the epidemiology, clinical profile and clinical outcome.

We are selecting certain cases and if you are found eligible, you will be subjected to examination by the principal investigator.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator
Date:
Place:

Signature/left thumb
impression of Participant

: “CROSS SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE” ,

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PATIENT CONSENT FORM

Study Detail : CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

- I confirm that I have understood the purpose of the procedure for the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.
- I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.
- I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.
- I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.
- I hereby consent to participate in this study.
- I hereby give permission to undergo detailed clinical examination and blood investigations as required.

Signature of investigator Signature/Thumb impression of Participant

: ‘’ CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE’

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MASTER CHART

NAME	AGE	SEX	TOTAL CHOLESTROL	TRI-GLYCERIDES	LDL	HDL	TOTAL BILIRUBIN	S.ALBUMIN	INR	ASCITES	HEPATIC ENCEPHALOPATHY	CHILD PUGH GRADE	CHILD PUGH SCORE
SELVARASU	55	M	181	117	126	31.2	1.9	4	1.2	NIL	NO	A	5
MURALI	54	M	91	110	44	25	0.9	2.3	1.4	MODERATE	NO	B	9
RAJAN	42	M	120	137	72	20	1.1	2	1.4	MASSIVE	2	C	10
GEETANJALI	45	F	116	105	74	21	1	3.5	1.4	MASSIVE	NO	B	8
KUMAR	40	M	75	119	29	22	13.1	2	2.7	MODERATE	2	C	14
MOSES	38	M	90	85	60	13	5	3.3	2.1	NIL	NO	B	9
SEETU	48	M	155	93	111.9	24.5	1.9	2.1	2.1	MODERATE	1	C	11
ANBU	52	M	172	152	94.6	47	1.2	3.7	1.5	MILD	NO	A	6
KALAVATHY	45	F	144	123	86.4	33	2.5	3.2	1.4	MODERATE	NO	B	9
RAMESH	48	M	178	154	110.2	37	1.3	3.5	1.3	MILD	NO	B	7
SHENBAGUM	55	F	139	132	81.6	31	3.7	3.6	1.9	MILD	NO	B	9
PUGAZHENDI	38	M	152	138	83.4	41	2.2	3.7	1.5	MILD	NO	B	7
PARVATHY	59	F	125	84	71.2	37	4.3	3.1	2.5	MODERATE	3	C	14
GIRIBABU	48	M	171	143	96.4	46	1.5	3.8	1.4	MILD	NO	A	6
MARY	45	F	151	110	94	35	2.4	2.9	1.6	MILD	NO	B	8
PALANIAPPAN	26	M	129	90	85	26	7.6	2.3	2.1	MODERATE	2	C	13
SUBASHINI	27	F	176	145	104	43	1.5	3.8	1.3	MILD	NO	A	6
MOHAMMED	45	M	122	94	74.2	29	12.3	2.4	2.7	MILD	3	C	14
SELVI	53	F	156	134	86.2	43	2.7	3	1.5	MILD	NO	B	8
MICHEAL	35	M	133	102	79.6	33	9.7	2.5	2.1	MASSIVE	1	C	13
RAJESH	48	M	187	132	115.6	45	2.1	3.6	1.6	NIL	NO	A	6
VEERAPPAN	32	M	167	142	84.6	54	1	3.9	1.2	NIL	NO	A	5
KABIR	39	M	89	129	43	20	23.6	2.4	1.9	MODERATE	2	C	13
KRISHNAPPA	44	M	188	154	107.2	50	1.7	4.2	1.5	NIL	NO	A	5

KADHER	60	M	156	122	93.6	38	2.7	3.2	1.6	MODERATE	NO	B	9
MUNUSAMY	44	M	123	126	68.8	29	13	3.3	2	MODERATE	2	C	12
MUNNUSAMY	63	M	165	126	104.8	35	1.9	2.4	1.4	MASSIVE	NO	B	9
PERIYARASU	59	M	188	158	114.4	42	1.7	3.7	1.3	MILD	NO	A	6
KANNAMMAL	35	F	178	145	116	33	2.5	2.8	1.6	MODERATE	NO	B	9
LALITHA	62	F	81	113	35	23	4.4	3.7	3	MODERATE	NO	C	11
RAGAVENDRA	50	M	192	163	115.4	44	2.3	3.6	1.5	NIL	NO	A	6
PONNIAMMA	44	F	163	129	109.2	28	7.6	3	1.6	MILD	NO	B	9
CHELLAMMAL	45	F	132	78	94.4	22	21.7	2	3.6	MASSIVE	3	C	15
SYED	55	M	186	145	123	34	1.3	4	1.2	NIL	NO	A	5
JANAKI	48	F	165	136	107.8	30	1.7	2.5	1.5	MODERATE	NO	B	9
AKBAR	53	M	145	126	83.8	36	2.4	2.9	1.6	MASSIVE	NO	B	9
SELVAM	49	M	94	107	45	27	9.4	3.3	1.8	MILD	1	C	11
RANGI	55	F	202	174	112.2	55	1.2	3.8	1.4	NIL	NO	A	5
RATHINAMMAL	43	F	179	167	91.6	54	1.3	3.7	1.6	NIL	NO	A	5
SATHYAMMAL	46	F	134	137	72.6	34	2.2	2.9	1.9	MILD	NO	B	9
RAJA	47	M	122	112	75.6	24	9.4	2.3	2.4	MODERATE	2	C	14
NANDHAKRISHNA	50	M	154	143	83.4	42	2.3	3.7	1.9	NIL	NO	B	7
ELANGOVAN	62	M	176	156	104.8	40	2.7	3.6	1.5	NIL	NO	A	6
BALU	64	M	166	158	98.4	36	1.6	3.8	1.4	MILD	NO	A	6
GURU	36	M	142	132	80.6	35	5.6	3.7	1.6	MODERATE	NO	B	9
SRINIVASAN	56	M	157	162	110	14	4.3	2.4	1.5	MASSIVE	2	C	12
PACHAIAMAL	47	F	166	155	97	38	2.4	3.8	1.5	NIL	NO	A	6
PRABHU	50	M	137	123	84.4	28	5.3	3.7	2.1	MILD	NO	B	9
KHUSBHU	52	F	188	145	113	46	1.4	3.8	1.2	NIL	NO	A	5

BHARATHI	50	M	132	102	75.6	36	5.9	2.4	2.3	MASSIVE	NO	C	13
RAJAKUMARI	48	F	155	134	83.2	45	2.6	3	1.5	NIL	NO	B	7
VELU	42	M	114	93	63.4	32	4.6	2.7	2.7	MASSIVE	NO	C	13
SHEELA	45	F	137	122	75.6	37	2.1	3.2	2	MILD	NO	B	9
MURUGAN	59	M	135	132	69.6	39	1.8	3.4	1.4	MILD	NO	B	7
SELVAM	50	M	183	152	108.6	44	1.4	3.3	1.3	NIL	NO	A	6
LINGORIYA	29	M	66	109	18.2	26	21	3.1	2.9	MODERATE	3	C	14
KUPPUSAMY	53	M	142	121	85.8	32	2.9	3	1.5	MODERATE	NO	B	9
BABU	46	M	187	154	114.2	42	1.3	4.1	1.2	NIL	NO	A	5
MUTHUVEL	49	M	166	149	100.2	36	1.7	3.3	1.5	NIL	NO	A	6
MANIYAN	51	M	143	115	82	38	2.5	3.3	1.3	MILD	NO	B	8
JAYAVEL	49	M	102	74	65.2	22	16.4	2.6	2.8	MODERATE	2	C	14
RAMCHANDRAN	52	M	160	136	89.8	43	1.4	3.8	1.4	NIL	NO	A	5
PRABHU	40	M	130	112	75.6	32	5.4	2.9	1.6	MILD	NO	B	9
GOPAL	42	M	178	143	101.4	48	1.3	3.6	1.3	MILD	NO	A	6
MEERA	46	F	119	94	72.2	28	18.8	2.2	2.1	MASSIVE	3	C	15
GEORGE	28	M	177	148	108.4	39	1.6	3.9	1.3	NIL	NO	A	5
ABHI	51	F	154	121	94.8	35	2.7	3.2	2	NIL	NO	B	8
KALAIPPAN	51	M	142	118	81.4	37	2.1	3.4	1.4	MILD	NO	B	8
BHAGYAM	49	F	123	96	73.8	30	4.2	2.7	1.6	MODERATE	NO	C	11
SELVI	44	F	144	132	77.6	40	1.4	2.8	1.5	MASSIVE	NO	B	8
RANI	45	F	178	157	94.6	52	1.8	3.9	1.2	MILD	NO	A	6
SARAVANAN	41	M	68	124	19	24	37.1	2.8	2.3	MODERATE	3	C	14
VALLIAMMAL	47	F	143	136	78.8	37	2.7	3.1	1.5	NIL	NO	B	7
RAMAPPAN	38	M	178	156	100.8	46	1.1	4	1.1	NIL	NO	A	5

SUBBATHAI	48	F	167	145	104	34	1.8	2.5	1.7	NIL	NO	B	8
MARIAMMA	33	F	188	158	107.4	49	1.4	3.8	1.2	MILD	NO	A	6
SELVAKRISHNA	49	M	134	89	92.2	24	7.9	2.9	2.1	MODERATE	2	C	12
SANDHIYA	44	F	176	125	98	53	1.2	3.7	1.5	NIL	NO	A	5
GOPINATHAN	47	M	133	132	75.6	31	2.3	3.2	1.9	NIL	NO	B	8
PERARASI	54	F	167	137	94.6	45	1.5	3.6	1.4	MILD	NO	A	6
SURIYAPRAKASH	58	M	143	133	80.4	36	5.8	3.6	1.5	MILD	1	B	9
KANGAVALLI	50	F	163	152	86.6	46	1.9	3.7	1.6	MILD	NO	A	6
TAMILPRIYAN	61	M	114	98	64.4	30	9.2	2.9	2.7	MASSIVE	3	C	14
LOGAIYAN	60	M	139	124	74.2	40	2.3	3.4	1.4	MILD	NO	B	8
RAZAKL	57	M	109	83	60.4	32	2.5	2.4	2.8	MILD	2	C	12
DHANUSH	48	M	177	142	105.6	43	3.8	3.3	1.5	NIL	2	B	9
MANIKAVEL	48	M	187	154	102.2	54	1.1	4	1.3	NIL	NO	A	5
CHARLESTON	35	M	164	132	96.6	41	2.9	3.2	1.6	MILD	NO	B	8
SUNDARAJAN	44	M	136	121	73.8	38	2.5	2.9	1.4	MODERATE	NO	B	9
LALITHA	51	F	184	154	110.2	43	1.7	3.7	1.3	NIL	NO	A	5
VIJAYA	51	F	122	101	69.8	32	3.6	2.9	1.5	MILD	2	C	10
SARAVANAN	38	M	143	123	85.4	33	2.3	3.4	1.9	NIL	NO	B	8
BASKAR	44	M	153	122	96.6	32	2.4	3	1.6	MODERATE	NO	B	9
PRABESH	33	M	168	160	88	48	1.6	3.8	1.3	NIL	NO	A	5
MUTHUVEL	38	M	176	156	105.8	39	2.6	3.7	1.4	NIL	NO	A	6
NAGAVALLI	62	F	143	134	78.2	38	2.2	3.4	1.6	MILD	NO	B	8
PRAKASH	42	M	74	111	25.8	26	16.5	2.4	2	MASSIVE	1	C	13
SARAVANNAN	23	M	159	154	83.2	45	1.5	3.4	1.3	MILD	NO	A	6
KABEER	24	M	156	143	93.4	34	4.4	2.9	1.8	NIL	NO	B	9
RAJAKRISHNAN	45	M	162	160	83	47	1.1	3.9	1.6	NIL	NO	A	5

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

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EC Reg. No(DHR).EC/NEW/INST/2021/1618
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.EZHILARASU PREETHAM,
MD Internal Medicine Post Graduate student,
Institute of Internal Medicine,
Madras Medical College,
Chennai – 600 003.

Dear Dr. EZHILARASU PREETHAM,

The Institutional Ethics Committee has considered your request and approved your study titled **"CROSS – SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE IN A TERTIARY CARE CENTRE"- NO.26052022**in the meeting held on **04.05.2022** conducted at Madras Medical College, Chennai 3.

1. Prof.P.V.Jayashankar,MS Orth ,D.Orth.,M.Ch Orth (Liverpool) :Chairperson
2. Prof.N.Gopalakrishnan,MD.,DM., FRCP, Director, Inst.of Nephrology,MMC,Ch. : Member Secretary
3. Prof. K.M.Sudha, Prof. Inst. of Pharmacology,MMC,Ch-3 : Member
4. Prof. Alagarsamy Jamila ,MD, Vice Principal, Stanley Medical College, Chennai : Member
5. Prof.Meena Suresh, MD.,DGO.,Prof.of Obst & Gynaec, IOG,Chennai : Member
6. Prof.S.Lakshmi, Prof. of Paediatrics ICH Chennai :Member
7. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
8. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
9. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003.

Document Information

Analyzed document	CROSS-SECTIONAL STUDY ON CORRELATION BETWEEN FASTING LIPID PROFILE AND SEVERITY OF CHRONIC LIVER DISEASE.docx (D152610283)
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Analysis address	preetham1996.tnmg@analysis.urkund.com

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