"THE STUDY OF SERUM THYROID PROFILE IN LIVER CIRRHOSIS"

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TABLE

FIGURES

LIST OF ABBREVATIONS USED

SERUM FT3	FREE TRIIODO THYONIN
SERUM FT4	FREE THYROXINE
SERUM TSH	THYROID STIMULATING HARMONE
CTP	CHILD TORCOTTE-PUGH
NAFLD	NON-ALCOHOLIC FATTY LIVER DISEASE
INR	INTERNATIONAL NORMALIZED RATIO
TRH	THYROID REGULATING HARMONE
SRIF	SOMATOTROPIN RELEASE INHIBITTING FACTOR
TBG	THYROXINE BINDING GLOBULIN
TPO	THYROID PEROXIDASE OXIDATION
DIT	DIIODOTYROSINE
MIT	MONOIODO TYROSINE
TTR	TRANSTHYRETIN
SHBG	SEX HARMONE BINDING GLOBULIN
PBC	PRIMARY BILARY CHOLANGITIS
SGPT	SERUM GLUTAMIC PYROVIC TRANSAMINASE
SGOT	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
CLD	CHRONIC LIVER DISEASE
CPH	CHRONIC PERSISTANT HEPATITIS
LC	LIVER CIRRHOSIS
MELD	MODEL FOR END STAGE LIVER DISEASE

ABSTRACT

INTRODUCTION

Cirrhosis of liver is a leading cause of mortality and morbidity worldwide[1]. Liver plays a vital role in thyroid hormone metabolism and circulation of thyroid hormone by producing thyroid binding globulin The liver is the most important organ in the peripheral conversion of tetraiodothyronine (T4) to triiodothyronine (T3) by type 1 deiodinase, playing an important role in thyroid hormone metabolism.

OBJECTIVE OF THE STUDY:

Thyroid profile in liver cirrhosis patients and its association with liver cirrhosis severity.

METHODOLOGY:

From November 2019 to September 2021, information for the study will be collected from patients admitted to BLDE(DU) Shri B.M Patil Medical College Hospital and Research Centre, Vijayapura 586103.This cross sectional- study included 65 decompensated liver cirrhosis patients (59 males and 6 females). Serum FT3, FT4, and thyroid stimulating hormone (TSH) levels were measured using electrochemiluminescence immunoassay. Results were also analyzed for severity of liver disease according to Child Pugh score and Child–Turcotte–Pugh (CTP).

RESULTS

Serum levels of FT3 and FT4 fall into low-normal or below normalvalue as the severity of cirrhosis increases, as indicated by the Child PughScore. There is a significant inverse correlation between FT3 and FT4 serum levels and cirrhosis severity. There was a significant correlation between Serum Bilirubin, INR, and Child Pugh Score in this study.

Conclusion:

Levels of FT3, FT4, and TSH also determine the severity of liver disease, so levels of FT3 and FT4 can be used as prognostic markers for liver cirrhosis patients.

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INTRODUCTION

Liver disease is any disturbance of liver function that causes illness. The liver is responsible for many critical functions within the body and should it become diseased or injured, the loss of those functions can cause significant damage to the body. Liver disease is also referred to as a hepatic disease.

Liver illnesses are frequent all over the world (prevalence ranges from 4-17.5 percent) and are expected to become more prevalent in India in the future. The liver has many roles, one of which is the creation of carrier proteins and hormone metabolism.[1]

Hepatocytes perform numerous and vital roles in maintaining homeostasis and health. As a result, liver illnesses are linked to a variety of endocrine problems. Due to toxic effects and indirectly due to changes in carrier protein synthesis, liver failure causes endocrine gland dysfunction. As a result, chronic liver disease may be linked to hormonal imbalances.[2,3]

The cirrhosis term is derived from the Greek word *kirrhosis*(tawny) referring to the tan color of the liver. Pathological features consist of the development of fibrosis which results in a decrease in hepatocellular mass, function, and alteration of blood flow.

Fibrosis occurs with the activation of hepatic stellate cells, resulting in the formation of the increased amount of collagen and other components of the extracellular matrix. Cirrhosis is considered the twelfth leading cause in the United States. Men are more affected than women.

Human beings require thyroxine and tri-iodothyronine for normal development, function, and growth. These hormones control hepatic function by regulating the basal metabolic rate of all cells, including hepatocytes. The liver is a vital organ. The liver in the metabolism of thyroid hormone in conjugation and the formation of thyroid-binding globulin, it plays a significant role., and peripheral de-iodination[4-6].

"A healthy thyroid and liver axis are required for proper thyroid function."

The thyroid gland produces 110nmol of thyroxine and 10nmol of tri-iodothyronine per day in a healthy person. Despite the fact that thyroxine is released at a higher rate than tri-iodothyronine in terms of quantity, it is classified as a pro-hormone because it must be de-iodinated and converted to tri-iodothyronine in order to be physiologically active.

The thyroid and extrathyroidal systems are both affected by this response. The liver, kidneys, and pituitary are all extrathyroidal organs. The liver is responsible for 30-40% of extrathyroidal conversion.

In the inactivation of thyroid hormones by D3, the liver also plays a significant role. The liver conducts particular processes related to thyroid hormone transport in addition to its central involvement in de-iodination to active and deactivate thyroid hormones. Thyroid hormones have a 99 percent affinity for thyroxine-binding globulin, thyroid-binding prealbumin, and albumin in plasma. The free hormone component is in balance with the protein-bound component, making it available for metabolic function.

Various investigations have shown that the serum T4 content varies according to the stage of liver disease and is connected to disease progression. T3 can be used as one of 12 useful laboratory markers for assessing the severity of liver disease. The serum T3 content, as well as liver variables like bilirubin, can now be used as a useful marker for tracking thyroid-liver patho-physiology trends.

To avoid misdiagnosis of a hypothyroid patient with liver illness, it is critical to measure free and T4 thyroid stimulating hormones (TSH) as well as any other laboratory test that may be of assistance. After liver transplantation, only a few endocrine abnormalities associated with CLD have been found to improve[5,6].

Low total and FT3 levels may be considered an adaptive hypothyroid state that lowers basal BMR within hepatocytes to help maintain liver function and total body protein stores.

This adaptation may give a survival benefit by adapting an organism to chronic disease by lowering the basal metabolic rate within cells and therefore lowering caloric requirements.

As a result, the goal of this study is to determine if there is a link between hypothyroidism (as measured by FT3, FT4, and TSH) and chronic liver disease, with FT3 serving as a severity factor by correlating with Child-Pugh score and Child-Turcotte-Pugh (CTP) score using clinical and biochemical parameters available at our hospital.

AIMS AND OBJECTIVE

To examine thyroid profile of liver cirrhosis patients and its association with severity of liver cirrhosis

REVIEW OF LITERATURE

Chronic liver disease is a disorder that lasts longer than six months and involves the breakdown and regeneration of the liver parenchyma, eventually leading to fibrosis and cirrhosis. Cirrhosis is a liver disease that causes gastroesophageal varices, ascites, or hepatic encephalopathy in those who have had chronic liver disease before.[1]

Physical findings of an enlarged left hepatic lobe with splenomegaly, as well as cutaneous stigmata of liver disease suggestive of cirrhosis, especially in the setting of thrombocytopenia and impaired hepatic synthetic function, are suggestive of cirrhosis in patients with a diagnosis of chronic liver disease without these complications (e.g., hypoalbuminemia, prolongation of the prothrombin 15 times). Imaging tests can aid in the diagnosis of cirrhosis if physical and laboratory data are not suggestive of cirrhosis.[5, 6]

Cirrhosis is identified by a small nodular liver with splenomegaly and intraabdominal collaterals, as well as the presence of ascites on abdominal ultrasonography (or other cross-sectional imaging examinations). The natural architecture of the liver, as well as the blood flow through it and the activities of the liver, have been altered.

Physiological anatomy of the Liver

The liver is the largest organ in the human body, accounting for around 2% of total body weight, or around 1500 grammes in the average human body. The primary functional unit of the liver is the lobule, which is a cylindrical structure with a diameter of 0.8-2 millimeters and a length of several millimeters. Individual lobules in the human liver range from Fifty thousand to One Lakh.[1 3]

The liver lobule is circulated around a central vein that drains into the hepatic veins and then into the vena cava. The lobule is made up of several liver cellular plates that radiate outwards from the central vein like spokes in a wheel.

Each hepatic plate is normally two cells thick, with small bile canaliculated running between them and draining into bile ducts in the fibrous septa that separate the adjacent liver lobules.

Septas contain small portal venules that receive blood mostly through the portal system's venous drainage of the gastrointestinal tract.
Blood flows from these venules into the central vein via the flat, branching hepatic sinusoids that reside between the hepatic plates. As a result, the hepatic cells are continuously exposed to portal venous blood.

The interlobular septa also contain hepatic arterioles. These arterioles supply arterial blood to the septal tissues that connect the adjacent lobules, and many of the small arterioles drain directly into the hepatic sinusoids, with the majority of them emptying into those around one-third the distance from the interlobular septa.

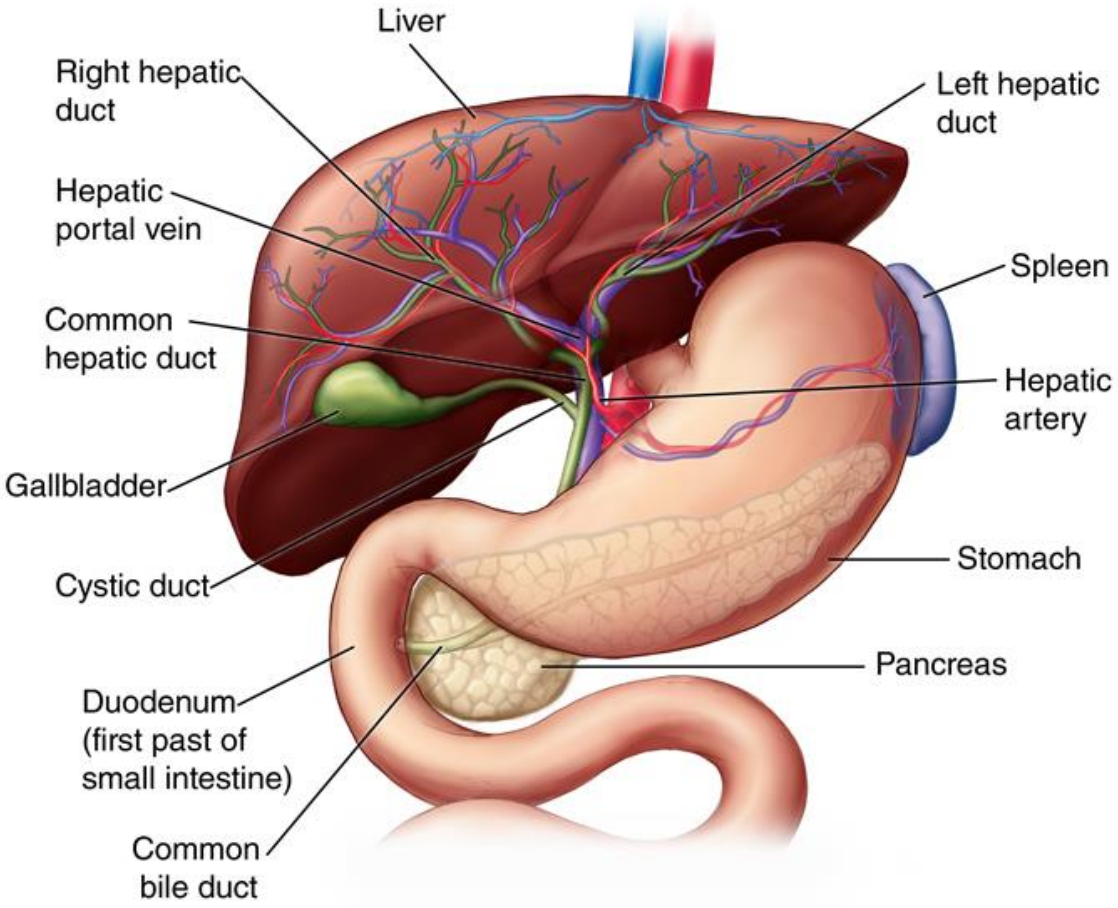
In addition to the hepatic cells, the venous sinusoids are lined by two other cell types:
(1) Large Kupffer cells (reticuloendothelial cells)
(2) Typical Endothelial cells

Which are macrophages that live in the sinusoids and can phagocytize germs and other foreign things in the hepatic sinus flow.

The sinusoids' endothelium lining has exceptionally wide holes, some of which are nearly 1 millimeter in diameter. The gaps of Disse, also known as the perisinusoidal spaces, are thin tissue spaces that lie beneath this lining, between the endothelial cells and the hepatic cells.

In the interlobular septa, Disse's millions of gaps interact with lymphatic veins. Thus, excess fluid in these spaces is removed through the lymphatics.[3]

Because of the wide holes in the endothelium, plasma substances can freely travel into the Disse gaps. Similarly, substantial amounts of plasma proteins freely diffuse into these gaps.



Blood Supplies to the Liver

1. Hepatic Artery

2. Portal Vein

The liver receives a lot of blood and has a low level of vascular resistance. Each minute, around 1.05 litres of blood flow from the portal vein into the liver sinusoids, with an additional 0.30 litre flowing into the sinusoids via the hepatic artery, for a total of 1.35 litres each minute.[3]

The pressure in the portal vein entering into the liver is around 9 mm Hg, while the pressure in the hepatic vein leading from the liver to the vena cava is generally exactly 0 mm Hg.

This little variation in pressure, about 9 mm Hg, indicates that blood flow resistance through the hepatic sinusoids is generally quite low, especially when considering that about 1.35 liters of blood pass through this pathway per minute.[13]

Liver failure causes a considerable increase in blood flow resistance. When liver parenchymal cells are destroyed, fibrous tissue replaces them, eventually contracting around the blood arteries and obstructing the flow of portal blood through the liver. Cirrhosis of the liver is the medical term for this condition. Chronic alcoholism or excess fat accumulation in the liver with subsequent liver inflammation, a condition known as non-alcoholic steatohepatitis, or NASH, are the most common causes.

Non-alcoholic fatty liver disease (NAFLD), a rare form of fat accumulation and inflammation of the liver, is the most frequent cause of liver disease in many industrialized countries, including the United States, and is generally associated with obesity and type-II diabetes.

Cirrhosis can also be caused by toxins like CCl4, viral infections such Infectious hepatitis, bile duct obstruction, and infectious processes in the bile ducts.[18]

A big clot that advances through the portal system and its branches might also obstruct the portal vein. The arrival of blood from the intestines and spleen through the liver portal system to the systemic circulation is greatly obstructed when the portal system is suddenly obstructed, resulting in portal

hypertension and an increase in capillary pressure in the intestinal wall of up to 20 mm Hg above average.

Because of the massive loss of fluid from the capillaries into the lumens and walls of the intestines, the patient typically dies within a few hours.[18]

Metabolic Functions of the Liver: -

Carbohydrate Metabolism: -

1. Galactose and fructose to glucose conversion.

2. Storing of Glycogen

3. Synthesis of many chemical compounds through intermediate products of carbohydrate metabolism
4. Gluconeogenesis

Fat Metabolism: -

1. Oxidation of fatty acids to supply energy for other body utilities.
2. Formation of large amount of cholesterol, phospholipids, and most lipoproteins.
3. Formation of fat through protein and carbohydrates.

Protein Metabolism: -

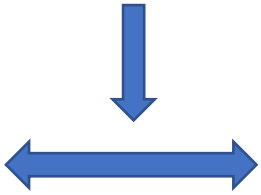
1. Synthesis of urea for removal of ammonia as of the body fluids.
2. De-Amination of amino acids
3. In-between conversion of various amino acids and formation of other products from Amino acids.

4. Synthesis of plasma proteins.

Other Metabolic Functions

1. Storage of Vitamins.
2. Storage of Iron as Ferritin.
3. Blood substances and coagulants are formed from the Liver.
4. Detoxification of drugs, hormones, and other substances.

Classification of Cirrhosis:



MORPHOLOGICAL **ETIOLOGICAL**

MICRONODULAR HEPATITIS AND OTHER VIRUSES MACRONODULAR

AUTOIMMUNE HEPATITIS

MIXED TOXIC AND DRUG-INDUCED

METABOLIC

1. **MORPHOLOGICAL**:

Micronodular, macronodular, and mixed cirrhosis of the liver were previously categorised morphologically. Alcohol, hemochromatosis, cholestatic causes of cirrhosis, and hepatic venous flow restriction all induce micronodular liver cirrhosis, which is defined by nodules less than 3mm in diameter.

Chronic viral hepatitis caused macronodular liver cirrhosis, which was characterised by differently sized nodules larger than 3mm in diameter. Although historically significant, the morphological classification system has major flaws and has consequently been largely abandoned.

1. In terms of aetiology, it is very amorphous.

2. As the disease advances, the appearance of the liver may change; micronodular cirrhosis frequently evolves to macronodular cirrhosis.

3. Today's serological indicators are more specific than the physical appearance of the liver responsible for cirrhosis aetiology.

2**. ETIOLOGICAL: -**

Cirrhosis should be categorised by aetiology in order to determine preventative and therapeutic strategies, as well as prognosis. If all diagnostic options have been exhausted and the patient has cooperated to the best of his or her abilities. In almost all cases, cirrhosis may now be diagnosed at the etiological level.

The group of so-called cryptogenic cirrhosis has been consistently reduced because to increased thorough diagnostic possibilities.

HEPATITIS AND OTHER VIRUSES:(post hepatitis)

Cirrhosis is caused primarily by Hepatitis B;however, hepatitis C is the most common cause in Egypt and the United States. The three viruses that induce post-hepatic cirrhosis are HBV, HCV, and HDV. When co-infection with HBV is present, the latter is a dysfunctional organism that can multiply.

Infection with these viruses causes the majority of cases of chronic active hepatitis that develops to post-hepatic cirrhosis.

AUTOIMMUNE HEPATITIS:

The immune system attacks the liver in autoimmune hepatitis, producing cell destruction that leads to cirrhosis[42].

TOXIC AND DRUG-INDUCED

Fatty liver, alcoholic hepatitis, chronic hepatitis with hepatic fibrosis, and cirrhosis are among hepatic symptoms associated with excessive alcohol consumption.

Although steatosis (fatty liver) will occur in anyone who consumes a substantial number of alcoholic beverages over a lengthy period of time, it is a temporary and reversible condition. Only 15- 20% of chronic heavy drinkers develop cirrhosis or hepatitis, which can occur simultaneously or in succession.

Pro-inflammatory cytokines (TNF-alpha, Interleukin 6, and Interleukin 8) are secreted in response to chronic alcohol consumption, as well as oxidative damage. Inflammation, apoptosis, and eventually fibrosis of liver cells is caused by these causes.

. •Cirrhosis can be caused by drugs such amiodarone, methotrexate, and nitrofurantoin [44].

METABOLIC

• Non-alcoholic fatty liver disease –

NAFLD is a condition in which the liver accumulates too much fat in the form of triglycerides (steatosis). In addition to increased fat, a portion of NAFLD patients exhibits liver cell damage and

inflammation (steatohepatitis). The latter disorder, known as NASH, is histologically almost identical to alcoholic steatohepatitis.

- Hemochromatosis.
- Wilson's disease.

COMPLICATIONS

1. Variceal bleeding-

Portal hypertension, or a rise in pressure within the portal vein, causes variceal haemorrhage (the large vessel that carries blood from the digestive organs to the liver). Cirrhosis produces a blockage in blood flow through the liver, which raises blood pressure. In reaction to increasing pressure in the portal vein, other veins in the body, such as those in the oesophagus and stomach, widen (varices) and bypass the obstruction. These varices become unstable and bleed quickly, resulting in significant haemorrhage and abdominal effusion.

2. Hepatic encephalopathy:

   Cirrhosis has been present for at least 21 days when hepatic encephalopathy develops. The liver ordinarily detoxifies toxins produced in our intestines, but if cirrhosis sets up, the liver is unable to do so. Toxins enter the bloodstream, causing bewilderment, behavioural abnormalities, and even coma.

3. Ascites:

   Increased intrahepatic resistance increased portal pressure, splanchnic arterial system vasodilation, and hypoalbuminemia cause fluid to accumulate in the peritoneal cavity.

4. Synthetic disorders:

    1. Hypoalbuminemia

2. Coagulopathy

5. Hepatopulmonary syndrome:

Cirrhosis of the liver can cause a hepato-pulmonary syndrome marked by platypnea and orthodeoxia.

6. Hepatorenal Syndrome-

Because of an increase in renal vascular resistance coupled by a decrease in systemic vascular resistance, functional renal failure occurs in around 10% of individuals with severe cirrhosis.

7. Hepatocellular carcinoma.

Child-pugh scoring

It was originally developed to predict mortality during surgery, but it is now also used to assess prognosis, therapeutic efficacy, and the need for liver transplantation. The score is calculated using five clinical markers of liver disease. Each measure is graded on a scale of one to three, with three indicating the most severe aberration.

Child Turcotte pugh score

1)	Encephalopathy	score
	None 0 grade	+1
	Mild to moderate 1 to 2 grade	+2
	Severe 3 to 4 grade	+3
2)	Ascites	
	None	+1
	Mild to moderate	+2
	Severe	+3
3)	Bilirubin	
	<2 mg/dl	+1
	2-3 mg/dl	+2
	>3mg/dl	+3
4)	Albumin	
	>3.5 gm/dl	+1
	2.8 to 3.5 gm/dl	+2
	<2.8 gm/dl	+3
5)	INR	

<1.7	+1
1.7 to 2.8	+2
>2.8	+3
Total	=_____

CTP score is obtained by adding the score for each parameter CTP class:

A Mild = 5-6 points

B Moderate = 7-9 points

C Severe = 10-15 points

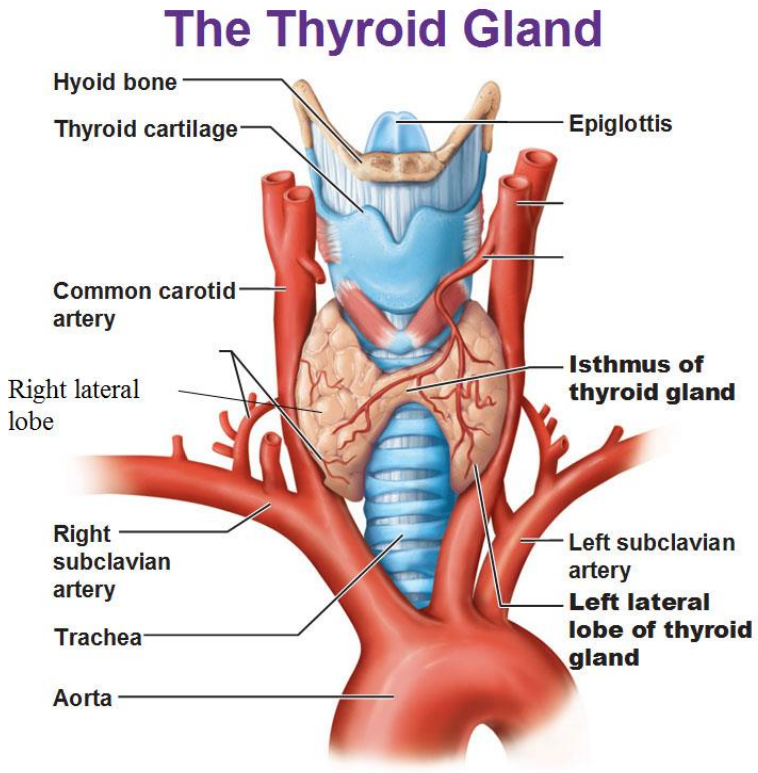
One- and two-year survival according to **CTP** score

Class	One year	Two years
A	100%	85%
B	80%	60%
C	45%	35%

Physiologic Anatomy of Thyroid

The Thyroid Gland is composed of large numbers of closed follicles 100-300 micrometres in Diameter filled with secretory substances called colloid and lined with cuboidal epithelium cells that secrets into the Interior of the Follicle.

The major constituents of colloid are large glycoproteins called ‘Thyroglobulin’ which contain Thyroid Hormone.



Gross anatomy of the thyroid gland, anterior view

Blood & Nerve Supply

1. Arterial supply: - Superior thyroid artery, Inferior Thyroid Artery, and Thyroid-ima artery.

2. Venous Supply: - Superior, Middle, and Inferior Thyroid Gland
3. Nerve Supply: - Sympathetic from Superior, Middle, and inferior ganglion of the sympathetic trunk, Parasympathetic from Superior & Recurrent Laryngeal nerves.

Physiology of the Hypothalamic-Pituitary-thyroid axis:

In a nutshell, the thyroid gland works in a traditional feedback regulation loop involving the brain and pituitary. The hypothalamus, anterior pituitary, thyroid gland, and higher brain centres have a strong interaction, with the availability of thyroid hormones modifying the operation of the entire complex in a classic negative-feedback manner.

The TRH that regulates TSH secretion is produced in the parvocellular area of the paraventricular nuclei of the hypothalamus. TRH is released at the hypothalamic-pituitary portal plexus after passing via the median eminence in the axons of peptidergic neurons.[13]

Thyrotropin (TSH) is a key regulator of the thyroid's morphologic and functional states. The two most important factors on TSH synthesis are TRH and thyroid hormone. TRH raises and thyroid hormone suppresses. TSH is present in normal serum at concentrations of 0.5 to 5.0 mU/L.Primary hypothyroidism raises the level, while thyrotoxicosis lowers it. TSH has a half-life of about 3 minutes in plasma, and human production rates range from 40 to 150 mU per day.[35]

TSH in the blood has pulsatile and circadian fluctuations. The former is distinguished by 1- to 2-hour intervals of actuation. Fasting, sickness, and surgery all reduce the magnitude of TSH pulsations. The circadian variation is marked by a nocturnal spike that occurs just before sleep begins, and it appears to be unaffected by cortisol cycles or fluctuations in serum T4 and T3 concentrations.The serum TSH concentration is an exceedingly sensitive indicator of thyroid status in patients with an intact hypothalamic-pituitary axis because the serum-free T4 concentration and the log of the TSH have a linear inverse relationship.[35]

The primary screening test for thyroid function is the measurement of serum TSH. TSH levels might change by up to 50% of their mean values during the day. TSH secretion is particularly sensitive to both modest increases and decreases in serum FT4, and aberrant TSH levels begin before FT4 abnormalities are detected during the development of hypothyroidism and hyperthyroidism.

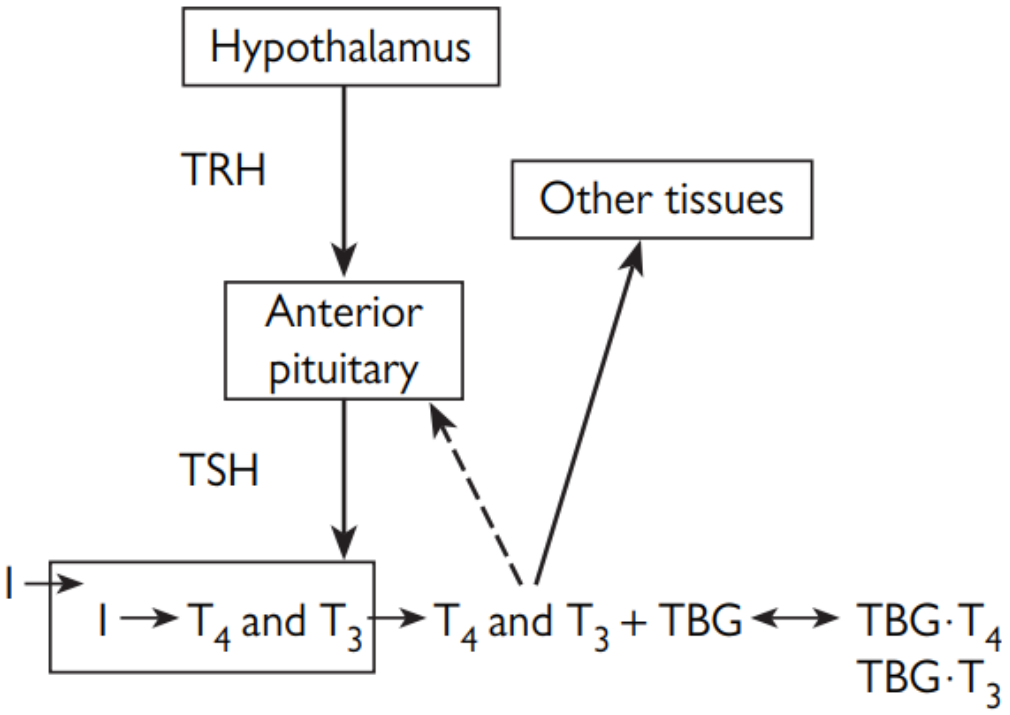
Somatostatin (somatotropin release-inhibiting factor [SRIF]) reduces TSH production in vitro and in vivo via the inhibitory G protein (Gi), although extended somatostatin analogue therapy does not produce hypothyroidism.

Both dopamine infusion and the injection of bromocriptine, a dopamine agonist, have similar acute effects because they both inhibit adenylate cyclase. Metoclopramide, on the other hand, elevates the baseline serum TSH concentration in both euthyroid and hypothyroid patients by blocking the dopamine receptor.[31]

These findings suggest that dopamine regulates TSH secretion, although chronic dopamine agonist administration (e.g., for the treatment of prolactinoma) does not result in central hypothyroidism, implying that compensatory mechanisms counteract these acute effects.

Direct and indirect modulators of TSH production and secretion rely on neurotransmitters. Thanks to a complex network of neurotransmitter neurons terminating on the cell bodies of hypophysiotropic neurons, certain neurotransmitters (e.g., dopamine) are directly released into hypophyseal portal blood, exerting direct effects on anterior pituitary cells.

Many dopaminergic, serotoninergic, histaminergic, catecholaminergic, opioidergic, and GABAergic systems also project from the hypothalamus or other brain regions to the hypophysiotropic neurons that regulate TSH.



IODINE AND THE SYNTHESIS AND SECRETION OF THYROID HORMONES

The thyroid glands job is to produce enough thyroid hormone to keep up with the needs of the body's peripheral tissues. This necessitates iodide uptake by the thyroidal sodium-iodide symporter (NIS), colloid transfer, and thyroid peroxidase oxidation (TPO).TPO also catalyses the creation of T4 and T3, respectively, by linking two DIT molecules or one DIT and one MIT molecule. These compounds are subsequently kept as part of the thyroglobulin molecule within the colloid. When stored colloid is pinocytosed, it creates phagolysosomes, which are colloid droplets in which species proteases breakdown Thyroglobulin, releasing T4, T3, DIT, and MIT when the droplet is translocated toward the cell's basal portion. T4 and T3 are liberated from phagolysosomes and transported through the cell's basolateral membrane, exiting the cell and into circulation. The iodotyrosine dehalogenase deiodinatesDIT and MIT, allowing the iodide to be recycled.[35]

THYROID HORMONES IN PERIPHERAL TISSUES

Plasma contains a wide range of iodothyronines and their metabolic products. T4 has the highest concentration and is the only one produced exclusively by the thyroid gland by direct secretion. In healthy people, T3 is made by removing a single 5' iodine atom from T4 (outer ring or 5' Mono-deiodination). T3, on the other hand, is produced by peripheral tissues to the tune of 80%. The plasma proteins with which T4 is most usually associated are TBG, transthyretin (TTR, formerly known as T4-binding prealbumin [TBPA]), and albumin. TBG binds about 75 to 80 percent of T3, with the rest bound by TTR and albumin.[13]

Because TBG is the primary T4- and T3-binding protein, changes in total plasma T4 and T3 are mirrored by changes in TBG or its binding, despite the fact that T4 and T3 production are essentially unchanged. The TBG binding site has a 20-fold lower affinity for T3 than it does for T4. Although albumin has a lesser affinity for T4 and T3 binding than TBG or TTR, due to its high quantity, this protein binds 10% of the thyroid hormones in the blood. Lipoproteins bind between 3% and 6% of plasma T4 and T3 respectively. Free T4 makes up around 0.02 percent of total T4 in normal serum (about 20pmol/L, or 1.5ng/dL). Because TBG has a 20-fold weaker affinity for T3, there is a greater fraction of unbound T3 (0.30 percent).

The free T4 and T3 concentrations can only be maintained at normal levels if the bound hormone changes in the same direction as TBG. For example, if oestrogen increases TBG 31 concentrations, the reduction in free T4 reduces T4 clearance, allowing for an increase in plasma total T4 concentration. This is an iterative mechanism that eventually normalises free T4 at a new equilibrium while keeping the T4 secretion rate constant. The outer ring (5') mono deiodination of T4 to the active thyroid hormone, T3, is the most critical mechanism for T4 metabolism.

D1 and D2 catalyse this process, which accounts for more than 80% of the circulating T3 in humans. D3 catalyses inner ring deiodination, an inactivating phase that inactivates T3 and prevents activation of T4 by converting it to rT3.

Tissues producing D3 have lower T3 levels than would be expected based on plasma contribution and a gene expression profile similar to hypothyroid cells. The inactivation of T3 and T4 hormones that occurs immediately after they enter the cell explains this. T3 levels are likely to be reduced by D3 in a variety of physiologic and pathologic circumstances (e.g., development, regeneration) where D3 is elevated (e.g., cancer cells, inflammation, myocardial infarction).Reduced production of thyroid hormone is the central feature of the clinical state termed hypothyroidism. A high blood TSH level with a normal serum fT4 concentration is described as subclinical hypothyroidism. Overt hypothyroidism, which is defined as elevated TSH with decreased FT4, can develop from subclinical hypothyroidism.[35]

TSH shortage produced by acquired, congenital hypothalamus or pituitary gland diseases causes central hypothyroidism. Secondary hypothyroidism is caused by pituitary dysfunction, while tertiary hypothyroidism is caused by hypothalamic dysfunction; nevertheless, this distinction is not necessary for the first differentiation of primary from central hypothyroidism. TSH release can be temporarily suppressed by dopamine, dobutamine, high-dose glucocorticoids, and acute sickness, resulting in a pattern of thyroid hormone abnormalities that suggests central hypothyroidism.

THYROID HORMONE AND LIVER RELATIONSHIP:

Conjugation, excretion, peripheral deiodination, and the synthesis of thyroid-binding globulin (TBG) and sex hormone-binding globulin are all functions of the liver in thyroid and gonadal hormone metabolism (SHBG). The liver, and to a lesser extent, the kidneys, play a key role in thyroid hormone metabolism, which is often overlooked.

The bulk of 3, 5,3'triiodothyronine(T3), the thyroid hormone with the highest metabolic activity, is generated in peripheral tissue. Outside of the thyroid gland, the majority of its competitive inhibitor, 3, 3', 5'-triiodothyronine (rT3; reverse T3), is produced.

T2 and T1 isomer transitions are nearly exclusively found in peripheral tissue. The outer phenolic hydroxyl group of the outer phenolic ring of thyroid hormone is conjugated with sulphate or glucuronic acid in the second pathway of thyroid hormone metabolism. T4 and T3 are bio

transformed as a result of these conjugation events, which take place largely in the liver and, to a lesser extent, in the kidney. The metabolites that result is ready to be eliminated and are deemed inactive.[39]

The metabolites that arise are poised for removal and are deemed inactive.

T4, T3, and rT3 are all produced by the thyroid gland, but T4 is the most abundant secretory product. Unless exogenously supplied, all T4 detected in circulation is produced in the thyroid.

The thyroid produces very little amounts of T3 and rT3, and it is not regarded significant in comparison to peripheral output.

In peripheral tissues, T4 is either converted to T3 or rT3, or it is eliminated through conjugation, deamination, or decarboxylation activities. Over 70% of T4 generated in the thyroid is thought to be de-iodinated in peripheral tissues, either at the outer phenolic ring to form T3 or at the inner tyrosyl ring to form rT3.

T3 is considered to be the most metabolically active thyroid hormone. Although the thyroid produces some T3, the majority of T3 is created outside of the thyroid, mostly through T4 conversion in the liver and kidneys. The bulk of circulating T3 is bound, similar to T4, although the binding molecules with the highest affinity for T3 are TBPA and albumin (not TBG).The free form of T3 (fT3) found in circulation is more than an order of magnitude greater than fT4, with estimates suggesting fT3 is approximately 8-10 percent of circulating T3.

Because the liver and, to a lesser extent, the kidney have such a strong influence on the circulating levels of thyroid hormone metabolites, their health and function are crucial but underappreciated in thyroid hormone function. T4 is deiodinated to form T3 or rT3, and then rT3 is disposed of in the liver and kidneys.[39]

In certain conditions, evidence suggests that the activity of hepatic antioxidant enzyme systems and lipid peroxidation may modify thyroid hormone peripheral metabolism.

The synthesis and removal of certain thyroid hormone metabolites can be influenced by hepatic decarboxylation and deamination enzyme activities.

Isoforms type I, II, and III are the three deiodinase families now recognised. These three groups differ in terms of tissue distribution, reaction kinetics, substrate consumption efficiency, and inhibitor sensitivity. Type I de-iodinase is a key enzyme found in the liver, kidneys, and skeletal muscle that may deiodinate T4 in two ways, producing T3 or rT3. With selenocysteine in the active site, type I 5'-deiodinase is a selenium-dependent enzyme; however, type I 5'-deiodinase does not require selenium for activity.

In the brain, pituitary, and brown adipose tissue, type II enzyme is the predominant deiodinase.Because tissue equipped with type II isoforms is largely independent of circulating T3 for metabolic demands, type II 5'-deiodinase is especially important for supplying the T3 required to stimulate the pituitary to synthesise and generate TSH.

Two Types III deiodinase isoforms are present in the central nervous system, and they catalyse the 5-deiodination of T4 to produce rT3. Alterations in hepatic deiodination, resulting in higher rT3 and a parallel drop in T3 levels, have been seen in chronic liver illness such as hepatic cirrhosis[39].

In animal models, ethanol consumption was linked to a reduction in hepatic 5'deiodination. Low T3 and T4, increased rT3, and normal TSH readings have been found in patients with alcohol-induced liver cirrhosis. While severe alcohol-induced liver impairment is harmful to thyroid hormone peripheral regulation, it is uncertain if moderate alcohol consumption has an effect.

Chronic liver disease can manifest itself in a variety of ways.

There is a higher prevalence of autoimmune thyroid disease in patients with chronic hepatitis associated with primary biliary cirrhosis (PBC) or chronic autoimmune e hepatitis. As a result, problems may emerge as a result of thyroid gland dysfunction or liver disease. Autoimmune hypothyroidism is a common symptom of PBC, affecting 10–25% of individuals. There is often an increase in total T4 in PBC due to a rise in thyroid binding globulin levels, which might mask hypothyroidism, highlighting the significance of a free T4 and TSH assay. Antithyroid microsomal

antibodies, as well as antithyroglobulin antibodies, are common in PBC (34 percent) (20 percent). Thyroid dysfunction can occur before or after a diagnosis of PBC.[44]

Grave's disease (6 percent) and autoimmune hypothyroidism (12 percent) are both frequent in autoimmune hepatitis. People with primary sclerosing cholangitis are more likely to develop Hashimoto's thyroiditis, Graves' disease, and Riedel's thyroiditis.

Although TSH and free T4 values are generally normal, and patients are clinically euthyroid, total T4, total T3, and thyroxine binding globulin levels are frequently high in patients with chronic hepatitis who do not have concurrent autoimmune liver and thyroid disease. The use of alpha-interferon in the treatment of viral hepatitis has given thyroid function abnormalities seen in chronic liver diseases a whole new meaning[46,47].

Thyroid dysfunction was seen in 2.5–10% of patients treated with alpha-interferon for hepatitis C in several studies, with both thyrotoxicosis (owing to acute thyroiditis) and hypothyroidism being detected[49,50].

The stimulation of an autoimmune reaction, which results in the formation of antithyroid and ant thyrotrophin receptor antibodies, has been proposed as a possible explanation. However, a distinct effect on iodine organification in the intrathyroidal cavity has been reported. It should be highlighted that interferon therapy causes weakness and muscle aches, and the myopathy of hypothyroidism may be overlooked in this environment. Thyroid function tests (including thyroid antibodies) should be performed before to starting interferon therapy and evaluated at 3–6-month intervals during treatment.

In chronic hepatitis B, which is largely a male illness, the incidence of pre-treatment thyroid antibodies, as well as the development of thyroid antibodies and thyroid dysfunction after interferon therapy, are all lower. A normal high-sensitivity TSH test and a normal thyroid function test show that the majority of people with liver disease are clinically euthyroid.

The latter test is performed on a regular basis and avoids the need to account for changes in thyroid-binding globulin levels reported in liver disease patients.

Punekar, Ashvanee Kumar Sharma, A. Jain in 2019 concluded that the mean FT3 and FT4levels were significantly decrease and mean TSH levels were significantly increase in liver cirrhosis patients compared to healthy controls. Level of FT3, FT4, and TSH also correlate with the severity of liver disease, level of FT3 can be used as prognostic marker for liver cirrhosis patients.[77]

Nilesh Kumar Patira1, et al in 2019 concluded that study in all cirrhotic patients should undergo thyroid function evaluation as these patients are definitely associated with development of hypothyroidism.[78]

Sudhir kumar Verma1, et al in 2017 concluded that derangement in thyroid profile is common in patients with cirrhosis of liver. Low free T3 and T4 levels are associated with more severe liver injury and may be used for prognostication in patients with cirrhosis of liver.[79]

Fariborz Mansour-Ghanaei et al in 2012 confirmed that a more severe liver status was inversely associated with serum total T3 levels.[80]

MATERIAL AND METHOD

INCLUSION CRITERIA: -

Patients with age >18years, either sex with evidence of chronic liver disease

Known and established cases of cirrhosis liver by clinical (Child Turcotte pugh score), radiological (ultrasound abdomen), and biochemical study.

EXCLUSION CRITERIA: -

Known case of thyroid disorder

Patient using drugs that interfere with thyroid metabolism such as levothyroxine, propylthiouracil, carbimazole, iodine, amiodarone

STUDY DESIGN: Cross sectional study.

STUDY PERIOD: November 2019 to November 2021.

Department of Medicine, Shri B M Patil Medical College, Hospital, Research Centre BLDE Deemed to be University Vijayapura, Karnataka 583103

SAMPLE SIZE: - 65

METHODOLGY: -

Patients with chronic liver disease are chosen for our study based on the following criteria:

A disease that has prolonged more than six months

* Chronic liver disease is defined as a condition that has been present for more than six months. The presence of a thin hyper echoic line, paucity of peripheral hepatic vessels, accentuated echogenic walls of the portal vein, nodular liver cirrhosis, contracted, signs of portal hypertension, and imaging features (absence of thin hyper echoic line, paucity of peripheral hepatic vessels, accentuated echogenic walls of the portal vein, nodular liver cirrhosis, contracted, signs of portal hypertension) can help confirm the diagnosis of cirrhosis

* **Child Pugh Score**

It is used to estimate prognosis, treatment strength, and the need for liver transplantation. Five clinical markers of liver disease are used to calculate the score. Each measure is scored 1-3, with 3 indicates the most severe derangement.

Child Turcotte pugh score (CTP)

1)	Encephalopathy	score
	None 0 grade	+1
	Mild to moderate 1 to 2 grade	+2
	Severe 3 to 4 grade	+3
2)	Ascites	
	None	+1
	Mild to moderate	+2
	Severe	+3
3)	Bilirubin	
	<2 mg/dl	+1
	2-3 mg/dl	+2
	>3mg/dl	+3
4)	Albumin	
	>3.5 gm/dl	+1
	2.8 to 3.5 gm/dl	+2
	<2.8 gm/dl	+3
5)	INR	
	<1.7	+1
	1.7 to 2.8	+2
	>2.8	+3

Total =_____

CTP score is obtained by adding the score for each parameter CTP class:

A Mild = 5-6 points

B Moderate = 7-9 points

C Severe = 10-15 points

* **USG findings diagnostic of chronic liver disease**-

- Nodular irregular surface of liver
- Distorted vascular pattern
- Ascites
- Signs of portal hypertension (splenomegaly or dilated portal venous system on ultrasonography)

* Hormone: -

Thyroid diseases are currently diagnosed most accurately by blood tests.

The best approach to evaluate thyroid hormone levels FT3 and FT4 - is to take a fasting venous sample in the vacutainer in the early morning.

The Access 2 free T3 and free T4 reagent pack, as well as the Access 2 free T3 and free T4 calibrators, will be used to perform free T3 and free T4 tests on the **Access 2 Immunodiagnostic system.**

TSH

The **Access 2 TSH** test is used to determine TSH levels. The Access 2 TSH test is performed with the Access 2 TSH Reagent and an Intellicheck-based system. The method utilised is an instantaneous immunoassay, which involves a simultaneous reaction of TSH contained in the sample. According to the biochemistry laboratory, the normal readings of the thyroid function test were as follows. Shri B M Patil Medical College, Hospital, Research Centre BLDE Deemed to be University Vijayapura, karanataka 583106.where the evaluation was carried out.

TSH- 0.25-5.0 MIU/ml

FT3- 2.5-3.9 pg/dl

FT4- 0.8-1.8 ng/d

STATISTICAL ANALYSIS: -

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean±standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value. C= (number of rows-1) *(number of columns-1) and Pearson Correlation were used to see the association between two numerical variable and Analysis of variance (ANOVA) were used for than 2 numerical variable to see the statistically significant difference.

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.20 (IBM Statistics) and Microsoft office 2007.

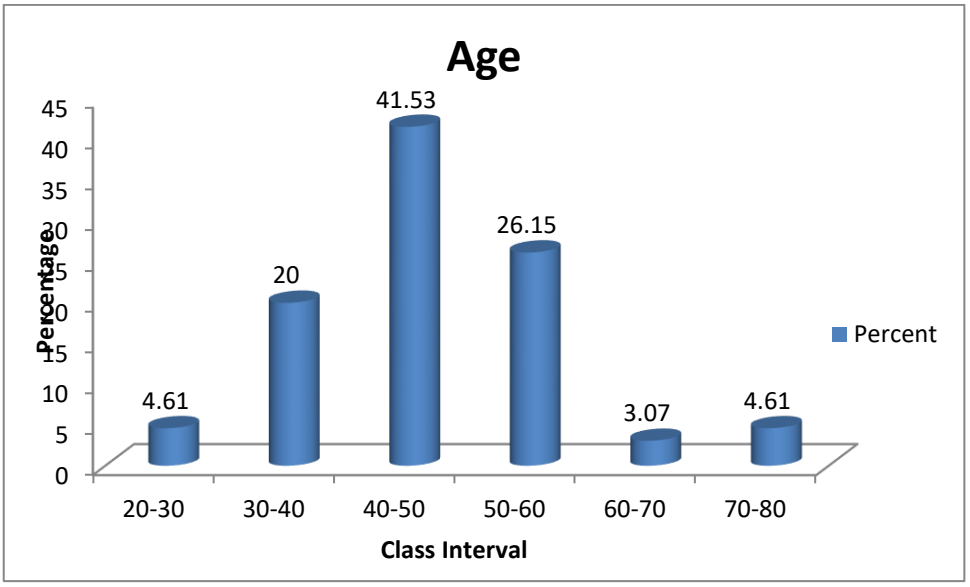
OBSERVATION AND RESULTS: -

AGE: -

Table No. 1 AGE

	Frequency	Percent
20-30	3	4.61
30-40	13	20
40-50	27	41.53
50-60	17	26.15
60-70	2	3.07
70-80	3	4.61
Total	65	100.0

Figure No. 1



Above table and figure showing variation in the ages between 20-80 years and mean age of study is 46.11.

SEX: -

Figure No. 2

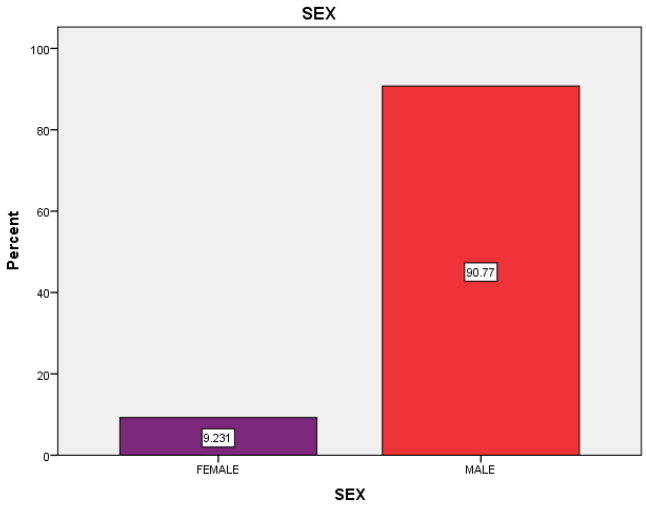


Table No 2

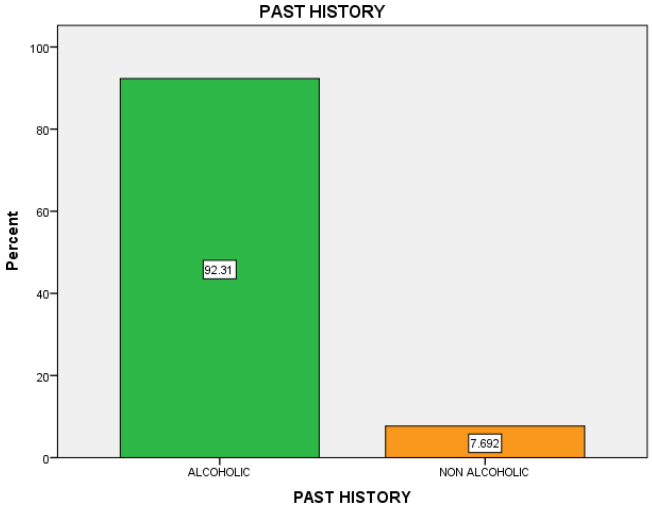
	Frequency	Percent
FEMALE	6	9.2
MALE	59	90.8
Total	65	100.0

Above table and figure showing distribution of male comprised 90.8 percent (59 patients), while females comprised 9.2 percent (6 patients).

PAST HISTORY: -

Table No 3 and figure No 3

		Frequency	Percent
Valid	ALCOHOLIC	60	92.3
	NON-ALCOHOLIC	5	7.7
	Total	65	100.0

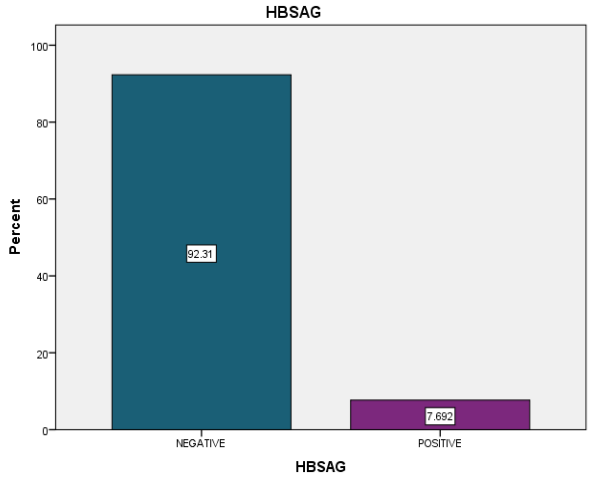


Above table and figure showing distribution of cases according to past history around 92.3 percent patients in my study were alcoholic and 7.692 percent patients were non-alcoholic.

HBsAg Table No 4:

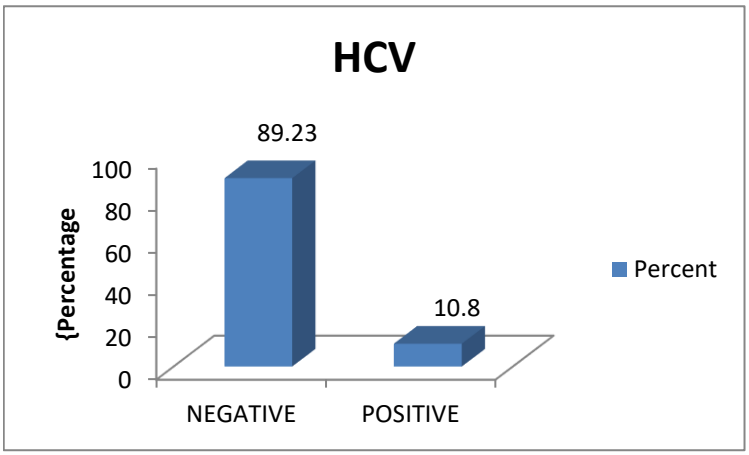
		Frequency	Percent
Valid	NEGATIVE	60	92.3
	POSITIVE	5	7.7
	Total	65	100.0

Figure No. 4:



Above table and figure showing distribution of cases according to HBsAg, positive (7.7%) and negative (92.3%).

HCV : Table No. 5 and Figure No. 5



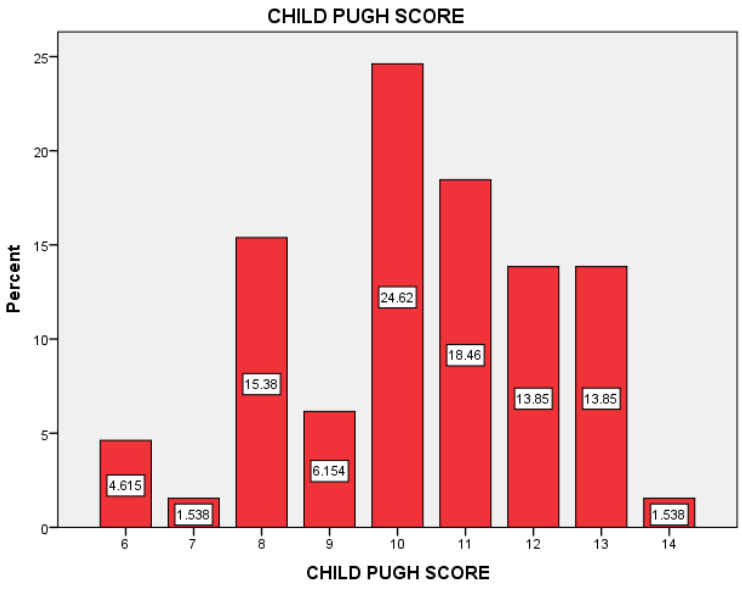
	Frequency	Percent
NEGATIVE	58	89.23
POSITIVE	7	10.8
Total	65	100.0

Above table and figure showing distribution of cases according to HCV positive (10.8%) and negative (89.23%).

CHILD PUGH SCORE: - Table No 6 and figure No 6

CHILD PUGH SCORE

		Frequency	Percent
Valid	6	3	4.6
	7	1	1.5
	8	10	15.4
	9	4	6.2
	10	16	24.6
	11	12	18.5
	12	9	13.8
	13	9	13.8
	14	1	1.5
	Total	65	100.0



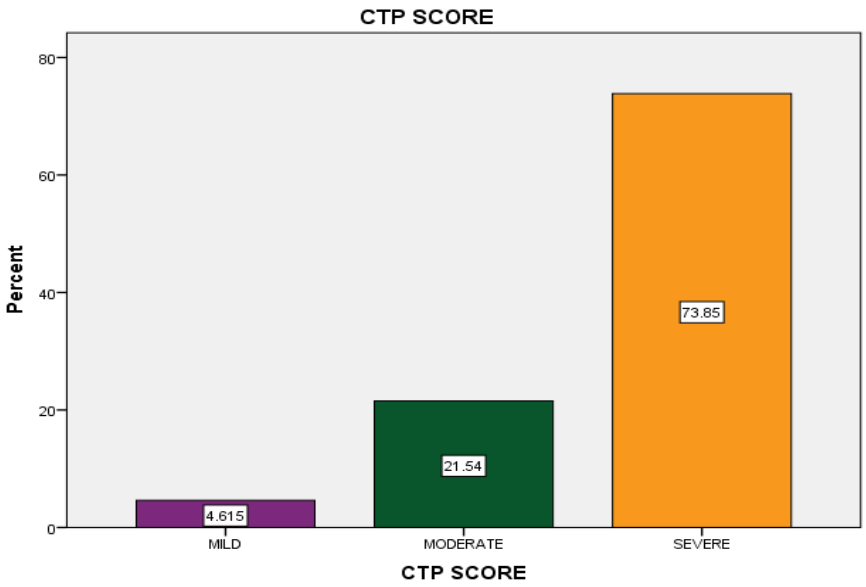
Above table and figure showing frequency of cases according to child pugh score

Child Turcotte Pugh Score: -

CTP SCORE Table No 7

	Frequency	Percent
MILD	3	4.6
MODERATE	14	21.5
SEVERE	48	73.8
Total	65	100.0

Figure No. 7



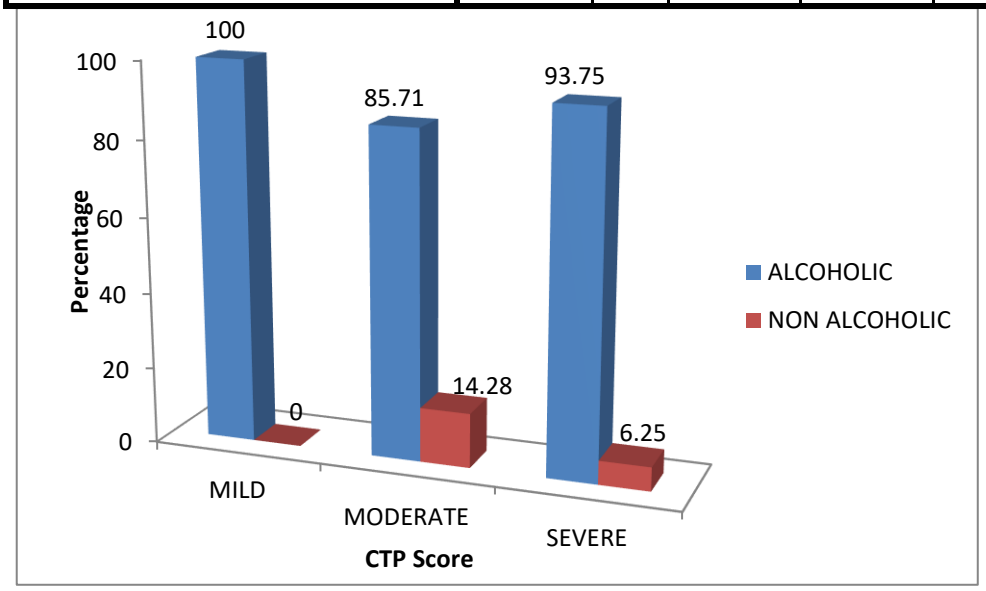
Above table and figure showing frequency of cases according to Child Turcotte Pugh Score (mild, moderate, severe).

Correlation between Past history and CTP score: -

Table No. 8

Figure No 8

		CTP SCORE						Chi-Square Value	P-Value
		MILD	%	MODERATE	%	SEVERE	%		
PAST HISTORY	ALCOHOLIC	3	100	12	85.71	45	93.75	1.248	**0.536**
	NON-ALCOHOLIC	0	0	2	14.28	3	6.25		
Total		3	100	14	100	48	100		



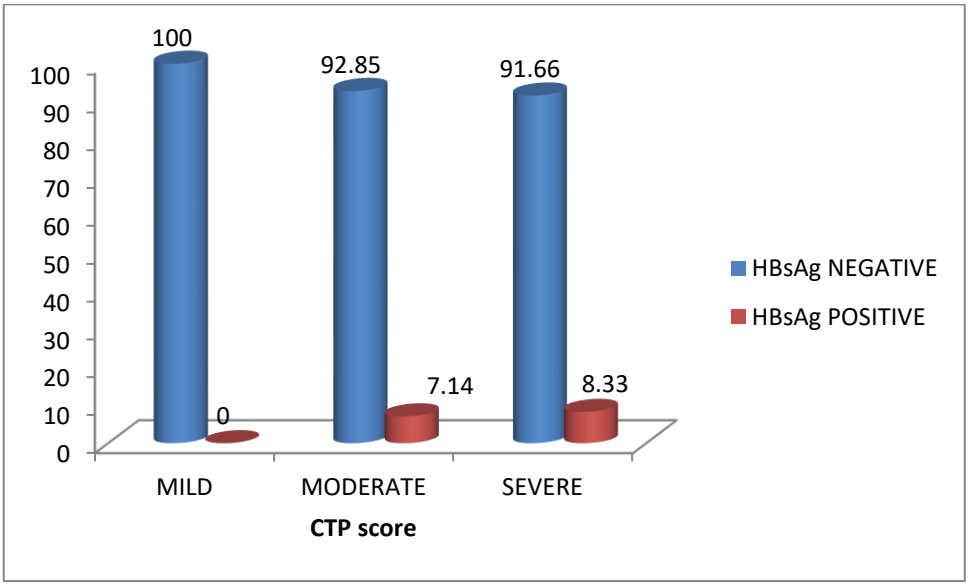
Above table and figure showing correlation of past history with CTP score, p value 0.536 that is non-significant (p value <.005 significant)

According the above table, maximum cases were alcoholic which were severe (CTP score)

Correlation between HBsAg and CTP score: -Table No 9

		CTP SCORE						Chi-square value	P-value
		MILD	%	MODERATE	%	SEVERE	%		
HBSAG	NEGATIVE	3	100	13	92.85	44	91.66	0.284	**0.868**
	POSITIVE	0	0	1	7.14	4	8.33		
Total		3	100	14	100	48	100		

Figure No. 9



Above table and figure showing correlation of HBsAg with CTP score

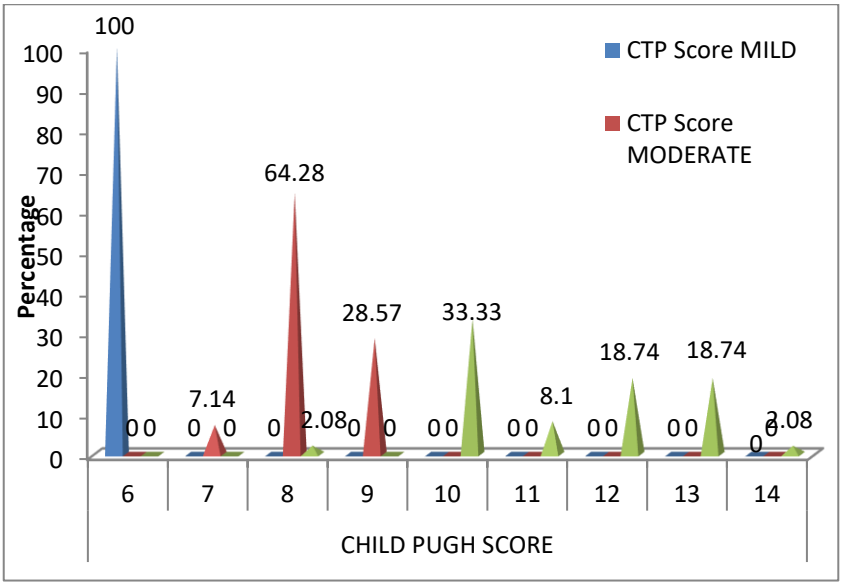
p value 0.868 that was not significant (p value <.005 significant).

Maximum HBsAg cases were positive that were severe (CTP score).

Correlation between CHILD PUGH SCORE AND CTP SCORE: - Table No 10

		CTP SCORE						Chi-square value	P-value
		MILD	%	MODERATE	%	SEVERE	%		
CHILD PUGH SCORE	6	3	100	0	0	0	0	124.603	**0.000**
	7	0	0	1	7.14	0	0		
	8	0	0	9	64.28	1	2.08		
	9	0	0	4	28.57	0	0		
	10	0	0	0	0	16	33.33		
	11	0	0	0	0	12	8.10		
	12	0	0	0	0	9	18.74		
	13	0	0	0	0	9	18.74		
	14	0	0	0	0	1	2.08		
Total		3	100	14	100	48	100		

Figure No. 10

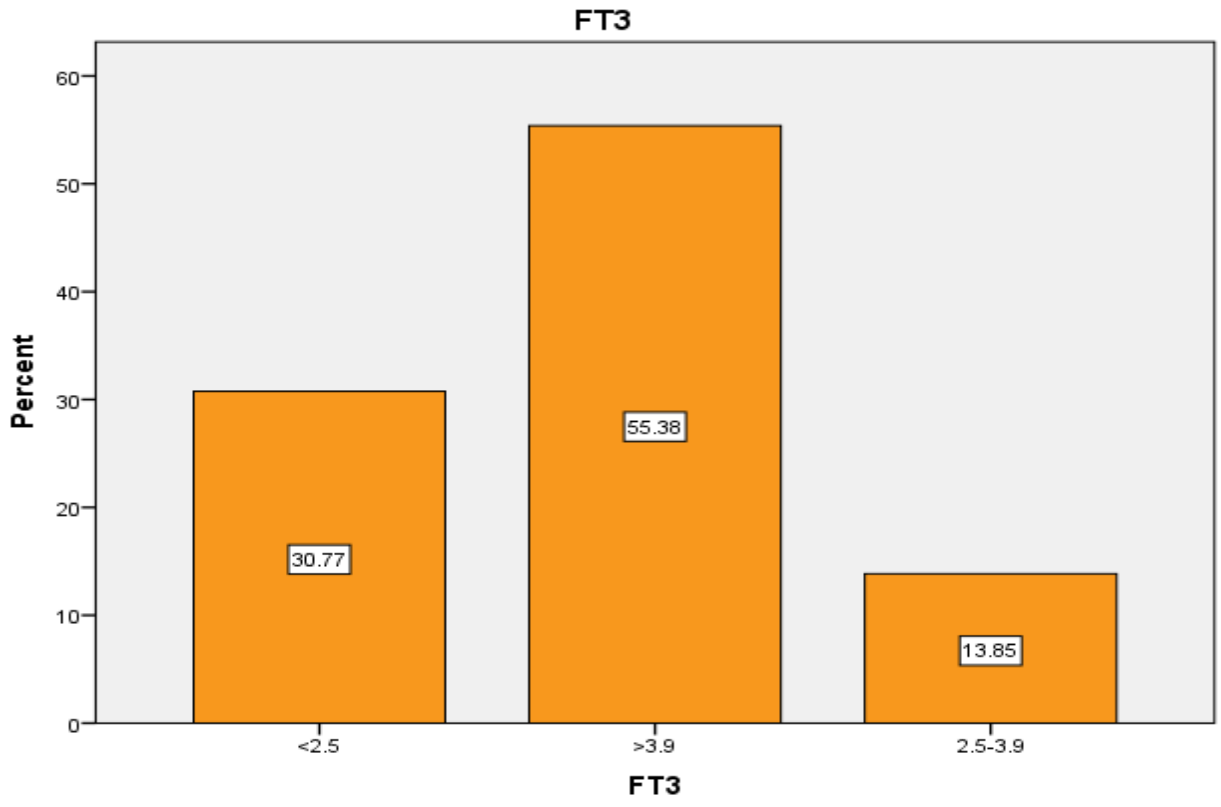


Above table and figure showing Correlation between CHILD PUGH SCORE AND CTP SCORE that was significant that is 0.000 (p value <.005 significant).

FT3: TABLE NO 11

	Frequency	Percent
<2.5	20	30.8
>3.9	36	55.4
2.5-3.9	9	13.8
Total	65	100.0

FIGURE NO 11

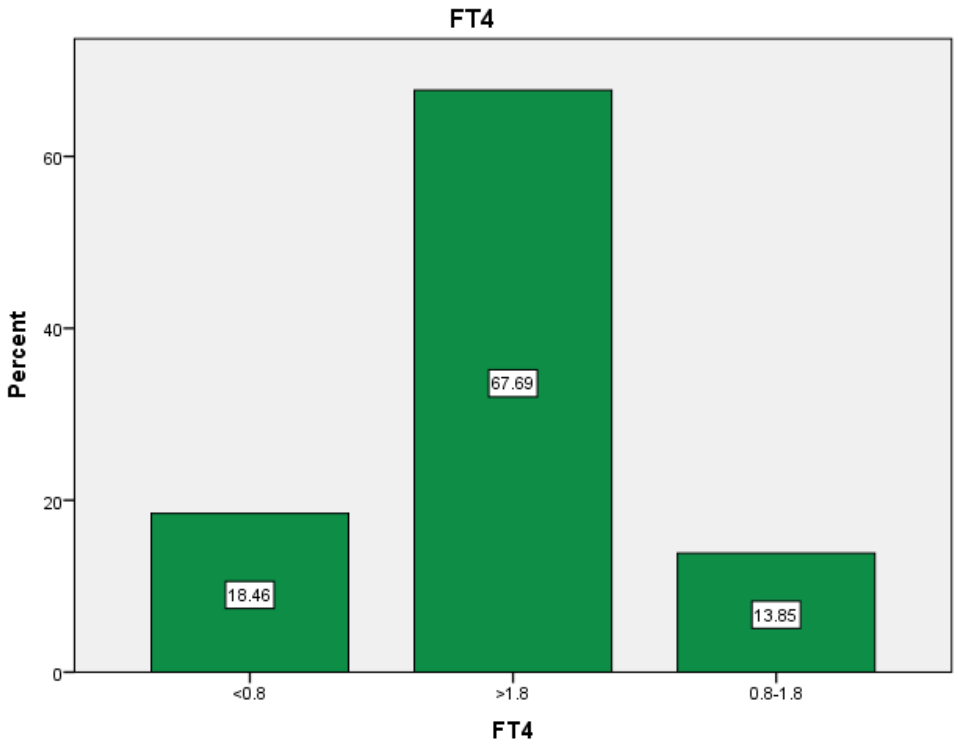


In our study 30.77 percentage of patients were found to have FT 3 value less than 2.5, 13.85 percentage were within the normal range (2.5-3.9) and 55.38 percentage were above the normal range.

FT4: TABLE NO 12

	Frequency	Percent
<0.8	12	18.5
>1.8	44	67.7
0.8-1.8	9	13.8
Total	65	100.0

FIGURE NO 12

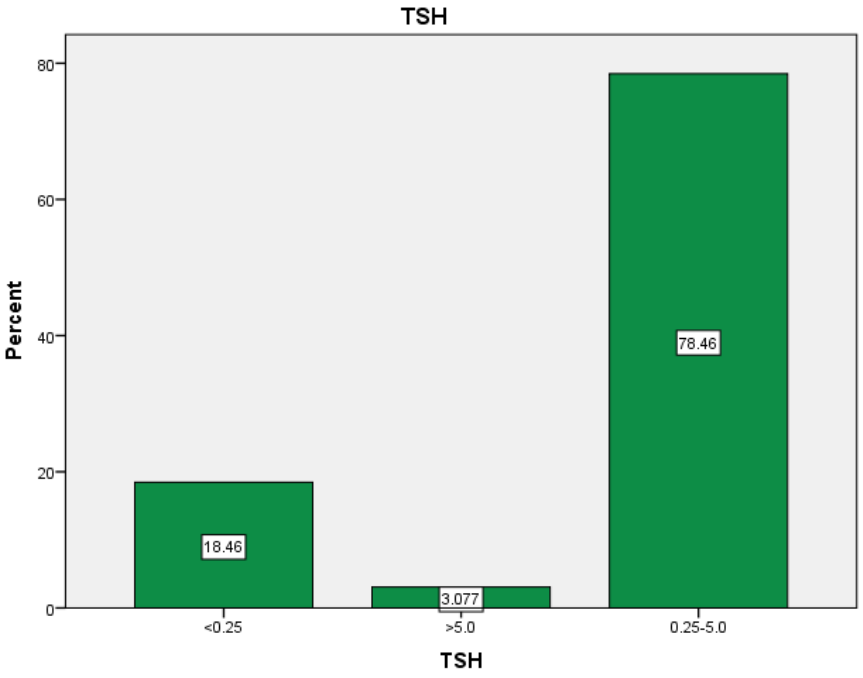


In our study 18.46 percentage of patients were found to have FT 4 value less than 0.8, 13.85 percentage were within the normal range (0.8-1.8) and 67.69percentage were above the normal range.

TSH: TABLE NO 13

	Frequency	Percent
<0.25	12	18.5
>5.0	2	3.1
0.25-5.0	51	78.5
Total	65	100.0

FIGURE NO 13



In our study 18.46 percentage of patients were found to have TSH value less than 0.25, 78.46 percentage were within the normal range (0.25-5.0) and 3.077 percentage were above the normal range.

Table No. 14

Variables	N	Mean	Std. Deviation
AGE	65	46.11	9.996
TOTAL BILIRUBIN	65	8.218462	8.6785996
SGOT	65	100.88	112.639
SGPT	65	71.17	92.975
INR	65	2.294523	1.3491281
FT3	65	4.525754	2.1778535
FT4	65	13.960738	10.2873273

Above table no 11 showing number cases, mean and standard deviation of age, total bilirubin, SGOT, SGPT, INR, FT3, FT4.

Correlations: - Table No 15

		AGE	TOTAL BILIRUBIN	SGOT	SGPT	INR
TOTAL BILIRUBIN	Pearson Correlation (r)	-0.242	1	.303*	0.132	0.593
	P-Value	**0.052**		**0.014**	**0.295**	**0**
	N	65	65	65	65	65
SGOT	Pearson Correlation (r)	-0.193	.303*	1	.668**	0.341
	P-Value	**0.124**	**0.014**		**0**	**0.005**
	N	65	65	65	65	65
SGPT	Pearson Correlation	-0.048	0.132	.668**	1	0.239
	P-Value	**0.704**	**0.295**	**0**		**0.055**
	N	65	65	65	65	65
INR	Pearson Correlation (r)	-.358**	.593**	.341**	0.239	1**
	P-Value	**0.003**	**0**	**0.005**	**0.055**	
	N	65	65	65	65	65
FT3	Pearson Correlation (r)	0.067	-0.204	-0.113	0.04	-0.221
	P-Value	**0.596**	**0.104**	**0.369**	**0.75**	**0.076**
	N	65	65	65	65	65
FT4	Pearson Correlation (r)	-0.04	-0.217	-0.113	0.027	-0.225
	P-Value	**0.755**	**0.082**	**0.369**	**0.828**	**0.071**
	N	65	65	65	65	65
TSH	Pearson Correlation (r)	-0.089	-0.082	-0.075	-0.073	-0.056
	P-Value	**0.481**	**0.515**	**0.551**	**0.564**	**0.658**
	N	65	65	65	65	65
CHILD PUGH SCORE	Pearson Correlation (r)	-0.159	.667**	0.135	0.164	0.467
	P-Value	**0.206**	**0**	**0.285**	**0.192**	**0**
	N	65	65	65	65	65

Above table No 12 showing correlation between age, total bilirubin, SGOT, SGPT, INR, FT3, FT4, TSH, CHILD PUGH SCORE

Positive correlation between total bilirubin, SGOT, SGPT, INR

Negative correlation between FT3, FT4, TSH with total bilirubin, SGOT, SGPT, INR

DISCUSSION: -

In our study, 65 patients with chronic liver disease were enrolled, and they received a full medical history, physical examination, and ultrasonography-based haematological and biochemical tests. The link between free triiodothyronine and Child-pugh and CTP scores, as well as hypothyroidism in the context of chronic liver disease, were examined.

In clinical terms, a diagnosis of chronic liver disease is made when symptoms have been present for more than six months, there are suggestive clinical signs, and serum and imaging results are available. Thus, clinical (signs and symptoms of liver cell failure), biochemical (raised bilirubin, SGOT, SGPT, low albumin) and radiological (absence of thin hyper echoic line, paucity of peripheral hepatic vessels, accentuated echogenic walls of the portal vein, nodular liver cirrhosis, contracted, signs of portal hypertension) tools are critical in the diagnosis of chronic liver disease.

Patient characteristics: This study included 65 individuals with chronic liver disease, with an average age of 46.1 years (range 24-80 years, table no1). Males comprised 90.8 percent (59 patients), while females comprised 9.2 percent (6 patients) [table No.2]

Analysis: In our study 30.77 percentage of patients were found to have hypothyroidism with FT 3 value less than 2.5, 13.85 percentage were within the normal range (2.5-3.9) and 55.38 percentage were above the normal range (Table No. 11). 18.46 percentage of patients were found to have FT 4 value less than 0.8, 13.85 percentage were within the normal range (0.8-1.8) and 67.69 percentage were above the normal range (Table No. 12). 18.46 percentage of patients were found to have TSH value less than 0.25, 78.46 percentage were within the normal range (0.25-5.0) and 3.077 percentage were above the normal range (Table No. 13). About 30.77 percentage were low free T3, 18.46 percentage were low Free T4 and around 78.46 percentage patients TSH within normal range,

This study discovered, first and foremost, that hypothyroidism is common in chronic liver disease patients. Second, free triiodothyronine has a negative relationship with Child-Pugh and CTP scores. The prevalence of thyroid hormone abnormalities has been found to range from 13 percent to 61 percent,

according to various writers. Hypothyroidism was more common in people with cirrhosis. This is owing to a wide range of etiologies and degrees of severity.

Study shows, corelation between age, total bilirubin, SGOT, SGPT, INR FT3, FT4, TSH, child pugh score. Positive corelation between total bilirubin, SGOT, SGPT, INR. Negative corelation between FT3, FT4, TSH with total bilirubin, SGOT, SGPT, INR (Table 12).

In our study there were distributions of cases according to CTP score, **A** mild 3 (4.61%) cases, and **B** moderate 14 (21.53%) cases and **C** severe 48 (73.84%) cases.

4 people (5.33 percent) of 75 individuals with liver disease were found to be hypothyroid in a study by Sandeep kharb et al[52], with 3 (3.5 percent) being subclinical hypothyroid and 1 (1.3 percent) being overt hypothyroid. Subclinical hypothyroidism was observed in 10% (3 patients), central hypothyroidism in 6.66 percent (2 patients), and primary hypothyroidism in 3.3 percent of 30 patients with hepatic cirrhosis in a study conducted by K.V.S. Harikumar et al.[50] (1patient).

In a study of 310 cirrhotic patients, G.Deepika et al [53] colleagues found that cirrhotic patients had a higher prevalence of thyroid dysfunction, particularly hypothyroidism, for a variety of causes. This research also found that none of the findings were statistically significant on their own. However, when hypothyroidism is considered as a unified entity that encompasses all subtypes, it is statistically significant. With P values of 0.001 and 0.008, respectively, this study reveals a statistically significant drop in Mean FT3 and TSH when compared to the control group.

These findings contradict those of Mohamed Abdel-Fattah El-Feki et al[55] who reported that in patients with chronic hepatitis C with cirrhosis, there was a drop in FT3 and FT4 levels and an increase in TSH levels when compared to those with CHC without cirrhosis. This is in line with Hussein Awad Mousa's findings, which showed a considerable decrease in T3 levels and a negligible change in TSH and T4 levels when compared to control groups.[58]

Takahashi et al. [57]found that serum Free T3 (FT3) levels decreased in CLD in the order of CPH, CAH, and LC, and were low in AH to the same extent as LC. Liver illness is also linked to an increase in

inflammatory cytokines that negatively affect the hypothalamic-thyroid axis [71,72,] which could explain why patients with liver disease have lower TSH levels (statistically not significant) than controls. In our investigation, this could be the theory for central hypothyroidism.

I. Ilias et al.[73] discovered that hypothalamic-pituitary suppression is common in cases of chronic sickness. TSH secretion is reduced, and T4 synthesis by the thyroid gland is reduced. Several lines of evidence point to a reduction in dopaminergic tone as a result of the build-up of false neurotransmitters, which could be the cause of elevated baseline TSH concentrations, as dopamine has been found to impede TSH secretion control. Antonelli, A., et aldisagreed with our findings that TSH levels were considerably greater in CHC patients [74]

TBG levels, which are generated as an acute phase reactant, have been found to increase in patients with acute and chronic liver disease. Because of the higher and lower concentrations of TBG, it can be claimed that total T4 production increases in the early stages of acute liver illness and then decreases as liver function deteriorates. This is consistent with the findings of Fariborz Mansour-Ghanaei et al.which showed a negative connection between Child Pugh scores and total serum T3 levels. There was also a link between the two. Patient characteristics: This trial included 65 individuals with chronic liver disease, with an average age of 41.6 years (range 24-62 years). Males made up 90.8 percent (59 patients) while females made up 9.8 percent (06 patients).[55]

TBG levels, which are generated as an acute phase reactant, have been found to increase in patients with acute and chronic liver disease. Because of the higher and lower concentrations of TBG, it can be claimed that total T4 production increases in the early stages of acute liver illness and then decreases as liver function deteriorates.

This is in agreement with Fariborz Mansour-Ghanaei et alreported that a negative correlation was found between ChildPugh scores and total serum T3 level ($r = -0.453$, $P < 0.001$). Also, a reverse correlation was observed between MELD score and T3 levels, indicating that serum T3 concentration is a useful indicator of liver function and decreasing by the severity of liver damage.[55]

Hussein Awad Mousa et al. came to the conclusion that there was a considerable drop in T3 levels.[58]According to this study, decreased total T3 likely reflects a decrease in deinodinase1 activity in the liver of cirrhotic patients[75, 76,]According to multiple studies, the most consistent thyroid hormone profile in people with cirrhosis is low total and free T3 levels and high rT3 levels, which is comparable to what patients with poorly euthyroid syndrome have. As a result, T4 to T3 conversion is lowered. The T3:Rt3 ratio is a liver function measure[60, 61,62-66.]

CONCLUSION

Because it is the producer of protein that binds thyroid hormone, such as thyroid-binding globulin (TBG), prealbumin, and albumin, the liver plays a significant role in thyroid hormone metabolism. It also plays a role in the conjugation, biliary excretion, oxidative deamination, and extra thyroidal deiodination of thyroxin (T4) to triiothyronine (T3) and reverse T3 in thyroid hormone peripheral metabolism. Thyroid hormone levels, on the other hand, are critical for adequate liver function and bilirubin metabolism.

The findings of this investigation demonstrated, about 30.77 percentage were hypothyroids with low Free T3. Free tri iodothyronine has a negative relationship with Child-pugh score and CTP score. The current investigation found that cirrhotic patients had a higher prevalence of thyroid dysfunction particularly hypothyroidism due to peripheral conversion affected.

Low FT3 levels were also attributed to the severity of CTP-related liver damage.

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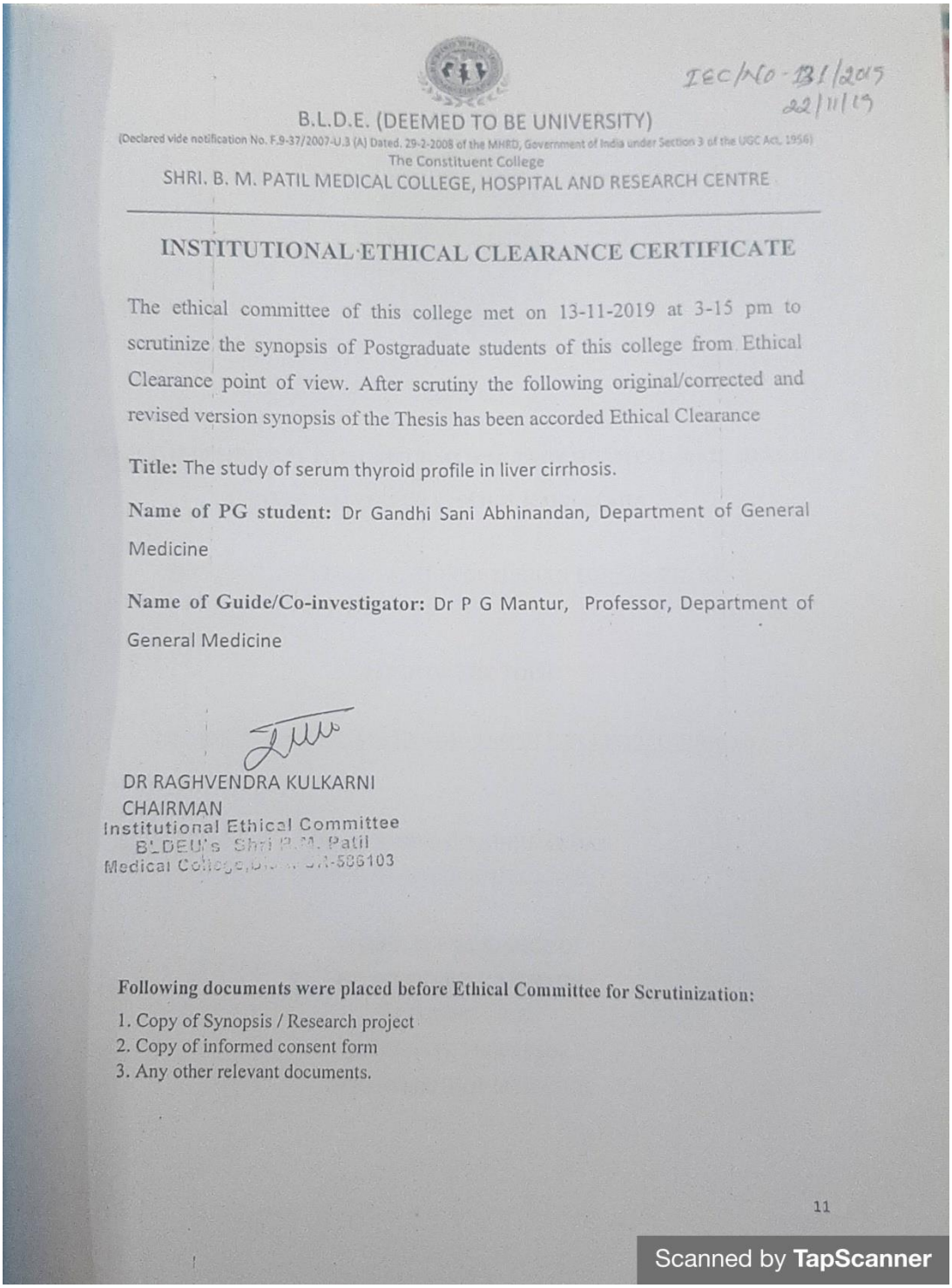
Annexures-I Ethical Clearance Certificate



IEC/NO-B1/2019
22/11/19

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to 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 been accorded Ethical Clearance

Title: The study of serum thyroid profile in liver cirrhosis.

Name of PG student: Dr Gandhi Sani Abhinandan, Department of General Medicine

Name of Guide/Co-investigator: Dr P G Mantur, Professor, Department of General Medicine

DR RAGHVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,Bi... UK-586103

Following documents were placed before Ethical Committee for Scrutinization:

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

11

Scanned by TapScanner

ANNEXURE–II

INFORMEDCONSENTFORM

B.L.D.E. (DU) SHRI B.M. PATIL MEDICAL COLLEGE,

HOSPITALANDRESEARCHCENTRE,

VIJAYAPURA-583106.KARNATAKA

THE STUDY OF SERUM THYROID PROFILE IN LIVER CIRRHOSIS

PRINCIPALINVESTIGATOR - DRGANDHISANIABHINANDAN
7709707975

All aspect soft his consent forma reexplained to the patient in the language understood by him/her.

I) INFORMEDPART

1) PURPOSEOFRESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

3) RISKANDDISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4) BENEFITS:

I understand that my participation in this study will help to patient survival and better outcome.

1) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

2) REQUESTFORMOREINFORMATION:

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

Dr. GANDHI SANI ABHINANDAN is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might in fluence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for care ful reading.

3) REFUSALORWITHDRAWALOFPARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. GANDHI SANI ABHINANDAN may terminate my participation in the study after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if thesis appropriate

4) INJURYSTATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research , the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

DR. GANDHISANIABHINANDAN Date (Investigator)

II) STUDYSUBJECTCONSENTSTATEMENT:

I confirm that DR. GANDHI SANI ABHINANDAN has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant/Guardian Date

_____ _____

Witnesstosignature Date

ANNEXURES -III

B.L.D.E. (DU) SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA - 583106. KARNATAKA

THE STUDY OF SERUM THYROID PROFILE IN LIVER CIRRHOSIS.

Name: **CASE NO:**

Age: **IP NO:**

Sex: **DOA:**

Religion: **DOD:**

Occupation:

Residence:

Presenting complaints with duration:

History of present complaints:

Past History:

Family History:

Personal History:

Diet/appetite Sleep

Bladder and bowel habits:

Addictions

Drug allergy

Treatment History:

General Physical Examination

Height:
Weight:
Body Mass Index:
Vitals

PR:
BP:
RR:
Temp:

Neck:
Upper Limbs:
Chest:
Abdomen:
Lower Limbs:
Skin:

SYSTEMIC EXAMINATION: -

PER ABDOMEN-

RESPIRATORY SYSTEM-

CARDIVASCULAR SYSTEM-

CENTRAL NERVOUS SYSTEM-

INVESTIGATIONS

PATHOLOGY

Complete Blood Count	
Total Count	Cells/cumm
Differencial counts Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
HB	gm%
Platelets	lakhs/cumm
ESR	mm/1st hour
Urine routine	
Urine albumin	
Urine sugar	
RBC	
Epithelial cell	
Pus cell	
Casts	

BIOCHEMISTRY

Serum thyriod profile Serum free T3and T4	Million international unit
Serum Creatinine	mg/dl
Serum liver function test	
Serum Albumin	mg/dl

Child Turcotte pugh score		**patient's score**
1) Encephalopathy		
None 0 grade	**+1**	
Mild to moderate 1 to 2 grade	**+2**	**-------**
Severe 3 to 4 grade	**+3**	
2)Ascites		
None	**+1**	
Mild to moderate	**+2**	**-------**
Severe	**+3**	
3) Bilirubin		
<2 mg/dl	**+1**	
2-3 mg/dl	**+2**	**------**
>3 mg/dl	**+3**	
4) Albumin		
>3.5gm/dl	**+1**	
2.8-3.5 gm/dl	**+2**	**----**
<2.8gm/dl	**+3**	
5)INR		
<1.7	**+1**	
1.7-2.8	**+2**	**-----**
>2.8	**+3**	
	Total score	**-----**

CTP score is obtained by adding the score for each parameter CTP class:

- **A severe = 5-6 points**
- **B moderate = 7-9 points**
- **C mild = 10-15 points**

USG ABDOMEN AND PELVIS

HBV AND HCV

ECG

<u>FINAL DIAGONOSIS</u>

MASTER CHART

SR. NO.	NAME	IP NUMBER	AGE	SEX	PAST HISTORY	TOTAL BILIRUBIN	SGOT	SGPT	INR	HBSAG	HCV	FT3	FT4	TSH	USG ABDOMEN	CHILD PUGH SCORE	CTP SCORE
1	SIDDAPPA ALI	7064	45	MALE	ALCOHOLIC	1	17	14	1.6	NEGATIVE	NEGATIVE	2.56	20.3	1.01	LIVER CIRROHSIS	6	MILD
2	AMAR KHOSE	55	44	MALE	ALCOHOLIC	27	109	22	2.01	NEGATIVE	NEGATIVE	3.76	21.7	1.78	LIVER CIRROHSIS	13	SEVERE
3	BOURAMMA PATIL	7037	80	FEMALE	NON ALCOHOLIC	1.1	20	23	1.1	POSITIVE	NEGATIVE	4.93	16.6	4.34	LIVER CIRROHSIS	9	MODERATE
4	SURAJ JADHAV	44142	39	MALE	ALCOHOLIC	4	46	24	1.9	NEGATIVE	NEGATIVE	4	26	4026	LIVER CIRROHSIS	11	SEVERE
5	LRAJASAHAB PUNEKAR	42321	46	MALE	ALCOHOLIC	12	128	38	2.56	NEGATIVE	NEGATIVE	7.78	18.3	2.77	LIVER CIRROHSIS	13	SEVERE
6	RAJENDRASINGH TAKUR	13173	57	MALE	ALCOHOLIC	3.2	48	34	1.1	NEGATIVE	POSITIVE	5.69	9.59	3.85	LIVER CIRROHSIS	12	SEVERE
7	SUMALA JADHAV	14383	43	FEMALE	ALCOHOLIC	2.8	43	18	1.1	NEGATIVE	NEGATIVE	6.85	23.9	3.64	LIVER CIRROHSIS	11	SEVERE
8	PRAKASH BENJEGATRI	1458	50	MALE	ALCOHOLIC	3.1	133	35	1.7	NEGATIVE	NEGATIVE	7.08	17.6	0.933	LIVER CIRROHSIS	11	SEVERE
9	RAJU	52503	52	MALE	ALCOHOLIC	3	64	20	1.5	NEGATIVE	NEGATIVE	7.1	26.1	3.1	LIVER CIRROHSIS	9	MODERATE
10	RAJAHAMMADA ATTAR	159653	42	MALE	ALCOHOLIC	0.8	28	17	1.6	NEGATIVE	NEGATIVE	5.25	20.35	3.14	LIVER CIRROHSIS	6	MILD
11	PARASAPPA	61268	52	MALE	ALCOHOLIC	10.8	25	52	1.2	NEGATIVE	NEGATIVE	7.1	18.1	1.2	LIVER CIRROHSIS	11	SEVERE
12	SHRIDHAR BENAKANAHALLI	26726	44	MALE	ALCOHOLIC	12.5	55	12	2	NEGATIVE	NEGATIVE	7	22.1	2.1	LIVER CIRROHSIS	11	SEVERE
13	MAHTESH GOWDA	28023	44	MALE	ALCOHOLIC	5.8	12	54	1.5	NEGATIVE	NEGATIVE	6.92	22.2	1.11	LIVER CIRROHSIS	9	MODERATE
14	JAGDISH MOURPPAGORA	28492	39	MALE	ALCOHOLIC	2.8	63	20	1.5	NEGATIVE	NEGATIVE	6.99	25.4	1.88	LIVER CIRROHSIS	6	MILD
15	SHRISHAIL BAGAYAT	25081	48	MALE	ALCOHOLIC	2	12	55	1.5	NEGATIVE	NEGATIVE	7.08	17.6	0.93	LIVER CIRROHSIS	8	MODERATE
16	NIGAPPA PUJARI	21036	35	MALE	ALCOHOLIC	2.5	22	85	1.6	POSITIVE	POSITIVE	5.25	20.35	3.14	LIVER CIRROHSIS	10	SEVERE
17	VEERSANGAPPA KAMAGOND	64637	43	MALE	ALCOHOLIC	4.7	12	58	1.1	NEGATIVE	NEAGTIVE	6.85	23.9	3.64	LIVER CIRROHSIS	11	SEVERE
18	KAMALABI NADAI	23369	50	FEMALE	ALCOHOLIC	21	125	52	4.7	NEGATIVE	NEGATIVE	6.95	29.6	1.15	LIVER CIRROHSIS	13	SEVERE
19	POMU JADHAV	81196	60	MALE	ALCOHOLIC	1.4	22	45	1.86	NEGATIVE	NEGATIVE	6.91	25.9	2.5	LIVER CIRROHSIS	9	MODERATE
20	KAMARUDDIN JAMADAR	47967	45	MALE	ALCOHOLIC	6	111	44	1.5	NEGATIVE	NEGATIVE	6.92	25.2	2.5	LIVER CIRROHSIS	11	SEVERE
21	MALAPPA BANDE	157899	52	MALE	ALCOHOLIC	10	124	46	2.47	NEGATIVE	NEGATIVE	6.91	25.9	2.212	LIVER CIRROHSIS	13	SEVERE
22	MARUTI HIREMATH	109446	54	MALE	ALCOHOLIC	5.5	121	45	1.1	NEGATIVE	NEGATIVE	2.3	0.438	1.1	LIVER CIRROHSIS	10	SEVERE
23	RAJU RANDEVI	14387	51	MALE	ALCOHOLIC	6	38	120	1.2	POSITIVE	POSITIVE	6.9	25.9	2.5	LIVER CIRROHSIS	10	SEVERE
24	MAHTESH MANVEDE	5689	37	MALE	ALCOHOLIC	23.5	117	45	1.83	NEGATIVE	NEAGTIVE	1.44	0.95	0.31	LIVER CIRROHSIS	13	SEVERE
25	KEMNABAI LAMANI	14257	56	FEMALE	NON ALCOHOLIC	8	45	110	1.2	POSITIVE	POSITIVE	6.9	25.4	1.88	LIVER CIRROHSIS	12	SEVERE
26	SIDDALINGA PUJARI	9042	24	MALE	ALCOHOLIC	1	39	32	1.6	NEGATIVE	NEGATIVE	2.59	11.27	6.35	LIVER CIRROHSIS	8	MODERATE
27	KASHINATH ALONI	8571	37	MALE	ALCOHOLIC	19.2	383	204	6.77	NEGATIVE	NEGATIVE	3.58	14.32	0.089	LIVER CIRROHSIS	14	SEVERE
28	BHARAT MITHALE	12024	50	MALE	ALCOHOLIC	8.5	89	48	1.894	NEGATIVE	NEGATIVE	4.58	16.95	1.34	LIVER CIRROHSIS	12	SEVERE
29	SANGAMMA DEVKAR	139486	75	FEMALE	NON ALCOHOLIC	1.9	56	24	1.1	NEGATIVE	NEGATIVE	3.15	14.4	2.54	LIVER CIRROHSIS	8	MODERATE

30	BASAPPA MALI	11323	43	MALE	ALCOHOLIC	4.2	82	28	2.24	NEGATIVE	NEGATIVE	4.3	17.6	1.1	LIVER CIRROHSIS	12	SEVERE
31	UMESH WALI	11147	28	MALE	ALCOHOLIC	3.9	39	20	2.19	NEGATIVE	NEGATIVE	2.594	23.87	1.84	LIVER CIRROHSIS	11	SEVERE
32	SIDDAPPA HOKRANI	13067	42	MALE	ALCOHOLIC	1.6	739	390	1.58	NEGATIVE	NEGATIVE	5.25	20.35	3.14	LIVER CIRROHSIS	7	MODERATE
33	BASAPPA	14560	43	MALE	ALCOHOLIC	6.8	77	35	1.5	POSITIVE	POSITIVE	6.95	29	1.15	LIVER CIRROHSIS	11	SEVERE
34	GURUPPA KUMBHAR	14289	42	MALE	ALCOHOLIC	4.4	43	33	2.27	NEGATIVE	NEGATIVE	6.92	22.2	1.1	LIVER CIRROHSIS	12	SEVERE
35	KASHILING	90684	55	MALE	ALCOHOLIC	4.8	29	40	1.3	NEGATIVE	NEGATIVE	6.55	20.1	1.1	LIVER CIRROHSIS	10	SEVERE
36	VEERANNA Y JALAWADI	17560	45	MALE	ALCOHOLIC	7.3	91	125	3	NEGATIVE	NEGATIVE	6.45	22.1	3.14	LIVER CIRROHSIS	12	SEVERE
37	VITTHAL BIRADAR	39173	50	MALE	ALCOHOLIC	14.9	246	577	2.7	NEGATIVE	NEGATIVE	6.22	21.5	0.114	LIVER CIRROHSIS	13	SEVERE
38	SHANTA RATHOD	19787	46	FEMALE	NON ALCOHOLIC	7.4	43	25	2.4	NEGATIVE	POSITIVE	2.2	1.2	1.2	LIVER CIRROHSIS	10	SEVERE
39	PUNDAPPA KAMBLE	23952	32	MALE	ALCOHOLIC	0.9	81	40	1.1	NEGATIVE	NEGATIVE	6	20.11	12	LIVER CIRROHSIS	8	MODERATE
40	BAPUJI JALAWADI	57747	40	MALE	ALCOHOLIC	5.6	59	29	1.8	NEGATIVE	NEGATIVE	6.2	22.2	0.12	LIVER CIRROHSIS	10	SEVERE
41	VISHAL MASALI	46105	39	MALE	ALCOHOLIC	40.6	116	30	2.7	NEGATIVE	NEGATIVE	2.5	0.8	0.043	LIVER CIRROHSIS	13	SEVERE
42	UMESH BIRADAR	147326	45	MALE	ALCOHOLIC	5.8	55	44	2.2	NEGATIVE	NEGATIVE	6.6	22.2	0.12	LIVER CIRROHSIS	10	SEVERE
43	JANESH KAKKALMELLI	19494	38	MALE	ALCOHOLIC	5.4	48	15	2.47	NEGATIVE	NEGATIVE	6.4	22.1	0.045	LIVER CIRROHSIS	10	SEVERE
44	SURESH BENNUR	44442	52	MALE	ALCOHOLIC	7.1	85	66	3.1	NEGATIVE	NEGATIVE	6.4	19.1	0.21	LIVER CIRROHSIS	11	SEVERE
45	SACHIN SAKATH	20615	29	MALE	ALCOHOLIC	12.4	282	240	3.7	NEGATIVE	NEGATIVE	5.1	18.5	1.1	LIVER CIRROHSIS	12	SEVERE
46	VISHAL KUDE	123042	45	MALE	ALCOHOLIC	12	121	142	5	NEGATIVE	NEGATIVE	6.6	19.1	0.12	LIVER CIRROHSIS	11	SEVERE
47	ABDUL BEPARI	120678	50	MALE	NON ALCOHOLIC	0.4	22	14	1.5	NEGATIVE	POSITIVE	1.9	0.9	2.47	LIVER CIRROHSIS	10	SEVERE
48	RAZAQ KALABURGI	122279	48	MALE	ALCOHOLIC	5.4	63	56	2.2	NEGATIVE	NEGATIVE	1.22	1	0.12	LIVER CIRROHSIS	10	SEVERE
49	SUKHADEV KAHAMANGAL	181845	35	MALE	ALCOHOLIC	11.5	75	53	7.14	NEGATIVE	NEGATIVE	2.5	1.4	1.875	LIVER CIRROHSIS	10	SEVERE
50	SAIFUDDIN NAGHWAN	188300	38	MALE	ALCOHOLIC	10.5	87	56	3.8	NEGATIVE	NEGATIVE	2.5	1.9	1.89	LIVER CIRROHSIS	11	SEVERE
51	BASAVRAJ WADDAR	93481	46	MALE	ALCOHOLIC	0.4	29	33	1.2	NEGATIVE	NEGATIVE	2.7	1.3	737	LIVER CIRROHSIS	8	MODERATE
52	BHIMAPPA ATHANI	98249	45	MALE	ALCOHOLIC	3.4	36	26	2.26	NEGATIVE	NEGATIVE	2.3	0.8	2.107	LIVER CIRROHSIS	10	SEVERE
53	RANGAVVA BUSANNAVARR	41669	48	MALE	ALCOHOLIC	2.1	90	43	2.1	NEGATIVE	NEGATIVE	2.1	0.5	1.4	LIVER CIRROHSIS	8	SEVERE
54	MALEPPA KARANI	81117	35	MALE	ALCOHOLIC	26.9	143	153	5.03	NEGATIVE	NEGATIVE	1.7	0.5	0.22	LIVER CIRROHSIS	13	SEVERE
55	DAVALASAB TAHASILDAR	71378	58	MALE	ALCOHOLIC	17.8	46	18	2.9	NEGATIVE	NEGATIVE	1.2	0.4	1.2	LIVER CIRROHSIS	12	SEVERE
56	SUDHAKAR KOLI	59624	46	MALE	ALCOHOLIC	1.7	88	85	2.1	NEGATIVE	NEGATIVE	1.1	2.2	2.2	LIVER CIRROHSIS	10	SEVERE
57	KENCHAPPA UPPAR	50143	65	MALE	ALCOHOLIC	3.1	64	35	1.3	NEGATIVE	NEGATIVE	2.1	0.8	0.22	LIVER CIRROHSIS	8	MODERATE
58	HAJILAL MULLA	156057	55	MALE	ALCOHOLIC	4.8	186	303	3.1	NEGATIVE	NEGATIVE	2.1	0.6	0.8	LIVER CIRROHSIS	10	SEVERE
59	MALLIKARJUN HIREMATH	153759	68	MALE	ALCOHOLIC	5.5	78	56	1.1	NEGATIVE	NEGATIVE	2.1	0.8	1.2	LIVER CIRROHSIS	8	MODERATE
60	NINGANNA BADIGER	139596	45	MALE	ALCOHOLIC	2.7	33	20	2.74	NEGATIVE	NEGATIVE	2.2	0.8	1.1	LIVER CIRROHSIS	8	MODERATE
61	MAHANTESH HIREMATH	137885	38	MALE	ALCOHOLIC	38.2	370	99	5.4	NEGATIVE	NEGATIVE	2.2	0.7	0.7	LIVER CIRROHSIS	12	SEVERE
62	MALLAPPA GADDAD	130005	42	MALE	ALCOHOLIC	3.7	259	105	1.2	NEGATIVE	NEGATIVE	2.1	1.4	1.8	LIVER CIRROHSIS	8	MODERATE
63	MALLAPPA BANDE	131984	52	MALE	ALCOHOLIC	6.9	204	111	1.7	NEGATIVE	NEGATIVE	2.8	1.1	2.212	LIVER CIRROHSIS	10	SEVERE
64	GURANNAGOUDA ANATHRED	128866	40	MALE	ALCOHOLIC	6.1	188	47	2.3	NEGATIVE	NEGATIVE	3.1	1.5	0.438	LIVER CIRROHSIS	10	SEVERE
65	MALLAPPA KANAMI	81117	35	MALE	ALCOHOLIC	26.9	153	38	5.03	NEGATIVE	NEGATIVE	1.7	0.5	0.22	LIVER CIRROHSIS	13	SEVERE