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A STUDY OF RELATIONSHIP BETWEEN SERUM T3, T4 AND TSH WITH LIVER ENZYMES AST, ALT AND ALP IN PATIENTS OF CHRONIC LIVER DISEASES

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ABSTRACT

Objective: The present study is aimed to show the relationship between serum level of markers of thyroid function and chronic liver disease (CLD). **Materials and Methods:** This study was conducted on 80 subjects attending index medical college and Hospital. Statistical analysis was done using SPSS 20.0. **Results:** The mean value of activity of AST, ALT and ALP enzymes was significantly higher compared to healthy controls whereas the serum values of T3, T4 and TSH was found to be low in CLD patients. **Conclusion:** In this study we assessed that the levels of T3 and T4 in CLD patients were significantly decreased to healthy controls. Although the values varied still there was no significant cause effective relationship observed. Therefore, this study confirms the existence of several abnormalities in thyroid function test in CLD.

KEYWORDS: AST, ALT and ALP.

INTRODUCTION

Liver plays a major role in the formation of carrier proteins as well as metabolism of various hormones. It manages metabolism of thyroid hormones and helps in the peripheral

conversion of tetraiodothyronine (T4) to T3).[1] Type I deiodinase is an enzyme present in the liver which accounts for nearly 30%–40% of extra thyroidal production of T3; it also helps in the deiodination of T4 to T3. Furthermore, the liver is heavily involved in conjugation and excretion of thyroid hormone, as well as the production of thyroid binding globulin T4 and T3 regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function. The liver metabolizes the THS and regulates their systemic endocrine effects. Thyroid diseases may perturb liver function; liver disease modulates thyroid hormone metabolism; and a variety of systemic diseases affect both the organs. There are clinical and laboratory associations between thyroid and liver diseases. Patients with chronic liver disease may have thyroiditis, hyperthyroidism, or hypothyroidism.[2] Patients with sub acute thyroiditis or hyperthyroidism may have abnormalities in liver function tests, which return to normal as the thyroid condition improves. Studies have also shown that it is associated with various endocrine disturbances.[3,4] Chronic liver disease is widespread all over the world and the incidence of liver diseases is likely to increase in future.[5] In liver failure the circulating endotoxins and proinflammatory mediators, results in impaired functioning of endocrinal glands like sick euthyroid syndrome which is also known as nonthyroidal illness syndrome.[6]

Iodine containing hormones triiodothyronine and thyroxine are synthesized by the thyroid gland. Thyroxine (T4) and tri-iodothyronine(T3) are required for normal development and function of organs. These play a significant role in regulating of basal metabolic rate of all cells, including hepatocytes, and therefore they affect the functioning of liver. The metabolism of thyroid hormones is well controlled by liver. It plays a vital role in involved in conjugation, emission, peripheral deiodination and in the formation of thyroid binding globulin. TSH –releasing hormone secreted by hypothalamus controls the secretion of TSH by anterior pituitary which is turn controls the production of thyroid hormones.[7] Increase level of unbound T3 and T4 decrease release of TSH and TRH in order to maintain circulating thyroid hormone levels within the required range through negative feedback.[7] Dysfunctioning of the thyroid may disturb liver function. Thyroid hormone metabolism is affected by liver disease while different systemic diseases affect both organs. All the patients with liver disease are usually clinically euthyroid, but some studies have shown abnormalities in the circulating hormone concentrations in patients with liver disease.

The levels of total and free thyroxine may be normal, increased or decreased in various liver diseases; Abnormalities in thyroxine binding globulin serum concentration and a reduced

thyroid hormone binding capacity, perhaps because of a hypothetical circulating inhibitor, have also been reported. The total and free triiodothyronine concentrations may be decreased, and their levels correlate well with severity of liver dysfunction. Usually all the patients with liver disease are clinically euthyroid, but some have shown abnormal concentrations of circulating hormone in previous studies.[8,9] These data, however, may be controversial as results collected may depend on the different analytical procedure used as well as the different groups of patients taken as subjects. Studies have reported that the concentration of serum thyroxine (T4) is normal, increased or decreased in various liver diseases.[10-14] Moreover, the concentration triiodothyronine (T3) is decreased, intensely and their levels correlate well with the severity of liver dysfunction.[11-16] Therefore this study is intended to evaluate the thyroid function in chronic liver disease.

AIM AND OBJECTIVES

The present study was intended to evaluate the thyroid function by measuring serum level of T3, T4 & TSH in subjects of chronic liver disease to asses CLD we evaluated circulating enzymes concerned with liver function (serum ALT, AST & ALP).

MATERIALS AND METHODS

The study was conducted on patients with Chronic Liver Disease attending the OPD and IPD of Department of Medicine and Central Biochemistry Laboratory in Index Medical College Hospital and Research Center, Indore. The study comprised total 80 individuals of which 40 were diagnosed patients of CLD and 40 were normal healthy individuals.

INCLUSION CRITERIA

The participants of 18 to 60 years with diagnosed cases of Chronic Liver Disease were enrolled as study population.

EXCLUSION CRITERIA

Patients having Pregnancy malignancy, COPD, known case of thyroid diseases were excluded from the study.

Individuals who fulfilled the inclusion criteria for the present study, 40 individuals were selected randomly by using simple random sampling technique (Lottery method) that deemed fit as a sample and were consequently selected as subjects for the present experimental study.

SAMPLE COLLECTION

Under strict aseptic precautions, 5ml of venous blood was collected from the median cubital vein and dispensed into plain vials for estimation of following biochemical test:

Serum T3, T4 and TSH and the enzyme activity of serum AST, ALT and ALP in Chronic Liver Disease. Blood samples were kept at room temperature for 30-40 minutes for clotting and then centrifuged at 3000 revolutions per minute for 10 minutes.

The following investigations were then carried out:

The serum total T3, T4, TSH for thyroid confirmation were estimated by enzyme immunoassay competition method with ELFA technique (Enzyme linked fluorescent assay) by using fully automated ViDAs®

Estimation of Serum Alanine Transaminase (ALT), Serum Aspartate Transaminase (AST) and Serum Alkaline Phosphatase (ALP) was done by Kinetic Method using kits and auto analyzer as per manufacturer's instructions.

RESULT

All the statistical analysis was performed using SPSS software (20th version). Table 1 reveals the distribution of age of studied samples of two groups. Research showed that more than one third (37.5%) patients of chronic liver disease were of 51- 60 year age group while only 10% of CLD patients were of 18 -30 year age group.

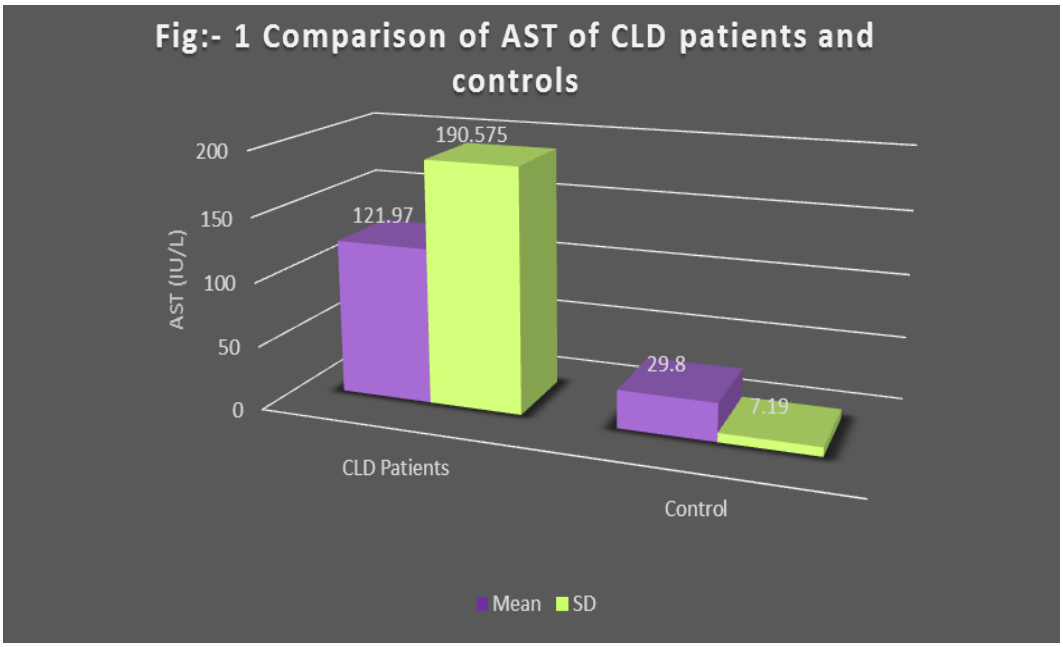
Table 1: Distribution of age among CLD patients and controls.

Age group (in years)	CLD patients		Control	
	Number	Percentage	Number	Percentages
18 – 30	4	10	2	5
31 – 40	10	25	9	22.5
41 – 50	11	27.5	14	35
51 – 60	15	37.5	15	37.5

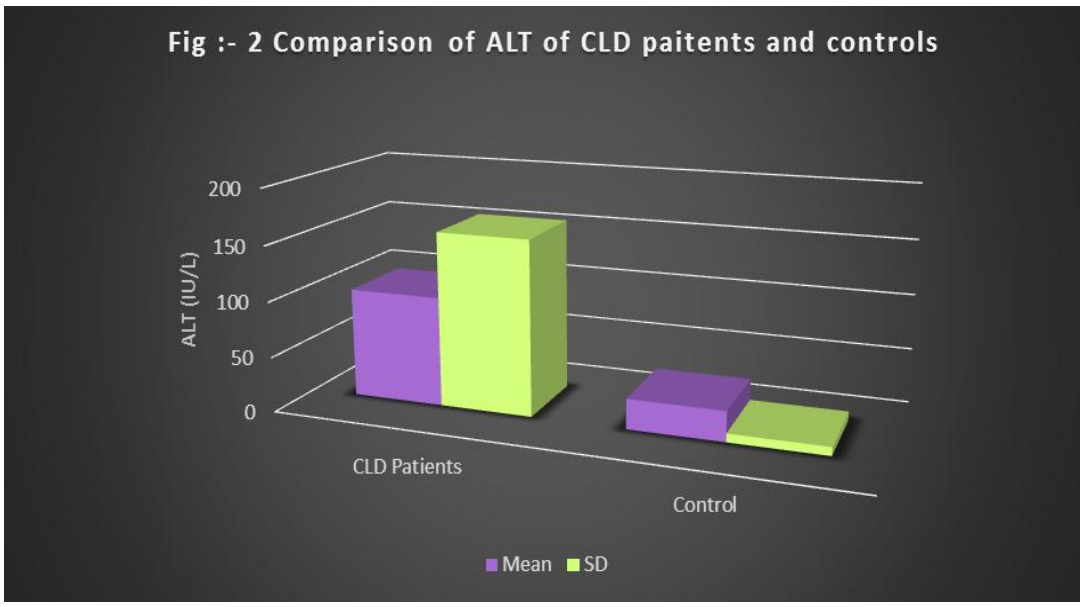
The mean value of activity of Aspartate aminotransferase in CLD patients were 121.97 ± 190.57 IU/L and controls were 29.80 ± 7.190 IU/L. There was a statistically significant increase in AST activity in CLD patient as compared to controls; p-value < 0.003.

Table 2: Comparison of various liver enzymes between cases and controls.

Analyte	Cases (Mean±SD)	Controls (Mean±SD)	P-Value
AST	121.97±190.575	29.80±7.190	.003
ALT	99.13±158.357	27.25±7.551	.005
ALP	173.282±93.653	109.65±41.253	.000



The mean value of activity of Alanine Aminotransferase in CLD patients were 99.13 ± 158.35 IU/L and controls were 27.25 ± 7.55 IU/L. There was a statistically significant increase in ALT activity in CLD patient as compared to controls; p-value < 0.005.



The mean value of activity of Alanine Alkaline Phosphatase in CLD patients were 173.282 ± 93.653 IU/L and controls were 109.65±41.253 IU/L. There was a statistically significant increase in ALT activity in CLD patient as compared to controls; p-value < 0.000.

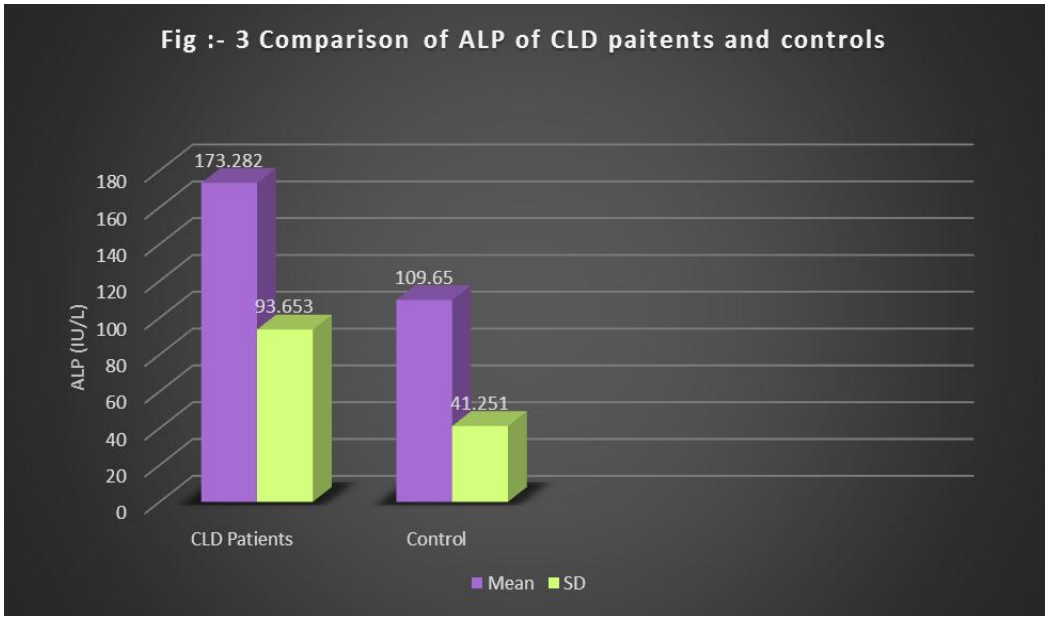
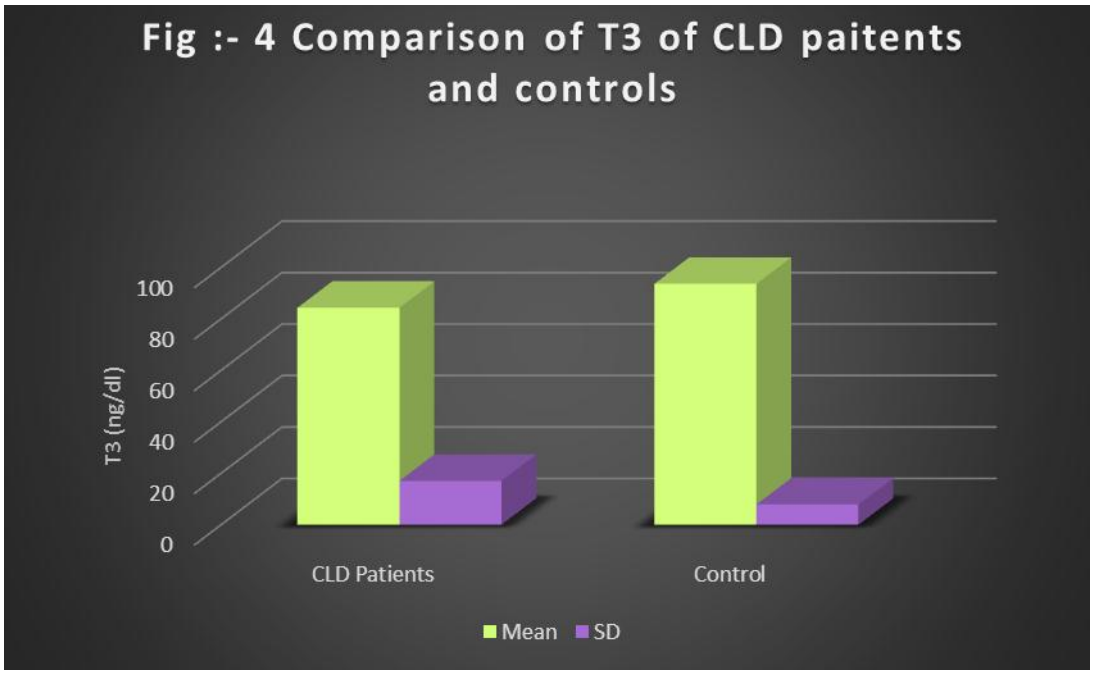
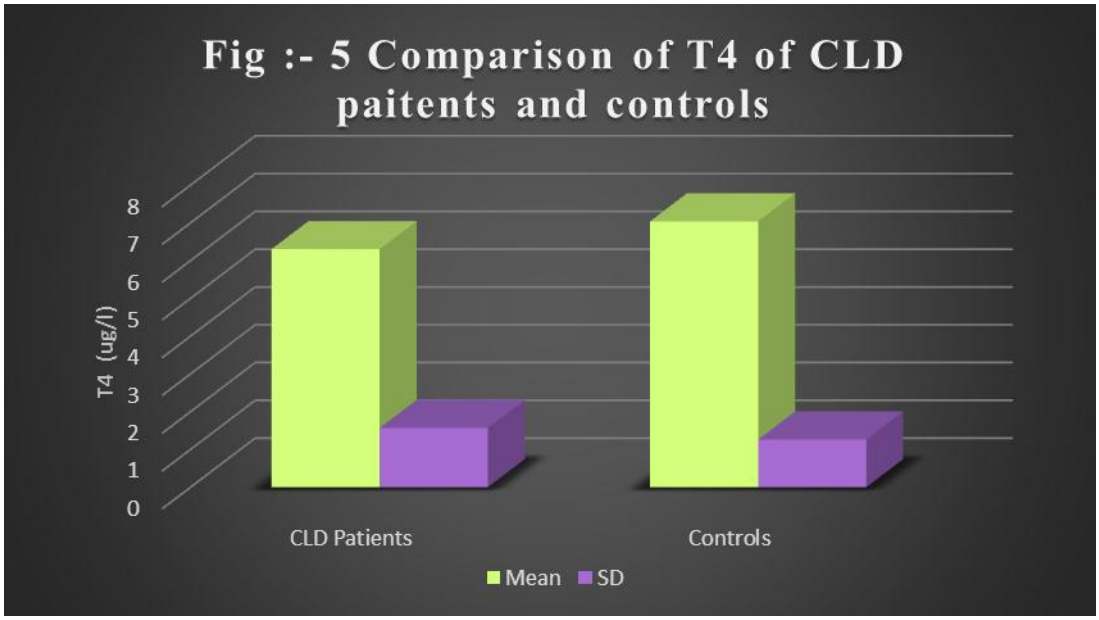


Table 3: Comparison of various Thyroid markers between cases and controls.

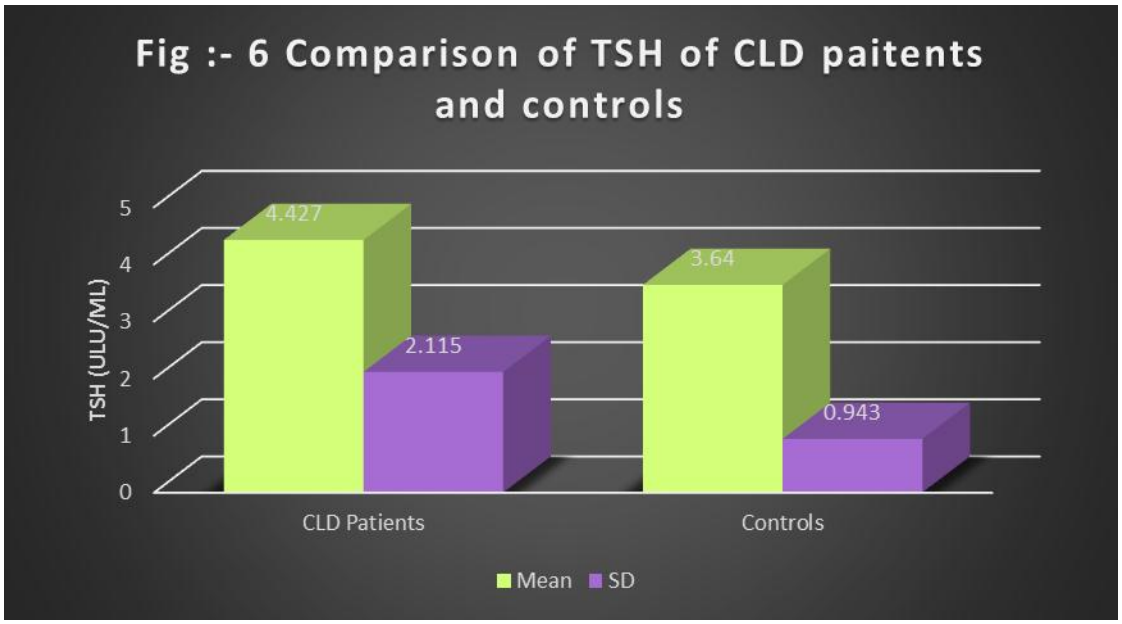
Analyte	Cases (Mean±SD)	Controls (Mean±SD)	P-Value
T_3	84.340±17.063	93.65±7.902	.004
T_4	6.305±1.571	7.04±1.264	.024
TSH	4.427±2.115	3.64±.943	.036



The mean value of T_3 in CLD patients were 84.340 ± 17.063 ng/dl and in controls were 93.65 ± 7.902 ng/dl. Thus was found to be statistically less significant when compared to that of controls; p-value < 0.024.



The mean values of serum T4 is 6.305 ± 1.571 µg/dl in CLD patients are less as compared to that of healthy individual 7.04 ± 1.264 µg/dl which is statistically significant with p value < 0.004.



The mean value of TSH was 4.427±2.115 µlU/mL significantly higher in patients with CLD as compared to healthy controls with mean values being 3.64±.943 µlU/mL which is statistically significant (p = 0.036).

DISCUSSION

Chronic liver diseases remain as one of the most serious health issues universally, which has affected more than 10% of the world population. Chronic hepatic diseases in the clinical context describe hepatic pathological processes that involve a process of progressive destruction and regeneration of the hepatic parenchyma, which eventually leads to cirrhosis and hepatocellular carcinoma if not treated. Among the various forms of chronic liver disease, the most common types include viral hepatitis, alcoholic or non-alcoholic fatty liver disease, autoimmune hepatitis, and cirrhosis and hepatocellular carcinoma.

The metabolism of thyroid hormones is well controlled by liver. It plays a vital role in involved in conjugation, emission, peripheral deiodination and in the formation of thyroid binding globulin. TSH – Thyroid releasing hormone secreted by hypothalamus controls the secretion of TSH by anterior pituitary which is turn controls the production of thyroid hormones.

Several studies in the past years have been carried out to find about the disturbances in metabolism of thyroid hormones in CLD and beneficial approaches to avoid complications associated with it. But the extent of relationship has not been well defined.

Therefore, in this study we evaluated these parameters to see if early recognition of these can avoid complications and improve the living standards.

In the present study, 40 patients diagnosed as chronic liver disease and 40 healthy individuals as controls, of age group 18-60 years, who attended the OPD and IPD of index medical college Hospital & Research Centre, Indore were taken. Out of 40 which 30 were males and 10 were females in CLD patients as well as healthy controls.

The results from this study have shown that the liver enzymes of Chronic Liver Disease patients are significantly higher as compared to control groups. We also found that serum enzymes have been elevated above their normal reference levels compared control subjects.

The mean value of serum AST activity in patients with CLD which was 121.97±190.575 IU/L was found to be higher as compared to that of healthy controls 29.80±7.190 IU/L. The mean difference in serum AST activity between the study groups was statistically significant (p = 0.003). Similarly, serum ALT activity in patients with CLD 99.13±158.357 was seen to be higher as compared to that of controls 27.25±7.551 IU/L was statistically significant (p = 0.005). The mean value of serum ALP activity in CLD patients 3.282±93.653 IU/L was significantly higher compared to that of controls 109.65±41.253(p = 0.00). G. Deepika et al[17] observed that the mean of serum AST, ALT and ALP activity were significantly higher in cases as compare to controls which is similar to our findings. The liver plays an important role in the metabolism of thyroid hormones, as it is the most important organ in the peripheral conversion of T4 to T3 by D1. Moreover, it is involved in conjugation and circulation of thyroid hormones by synthesis of thyroid binding protein.

In this study we observed that the mean value of TSH is 4.427±2.115 µlU/mL significantly higher in patients with CLD as compared to healthy controls with mean values being 3.64±.943 µlU/mL (p = 0.036). Antonelli et al.[18] found that the level of TSH was significantly higher in patients with cirrhosis. Serum TSH is released from anterior pituitary gland in response to Thyroid releasing hormone (TRH) which regulates the production of thyroid hormones. Increase levels of T3 and T4 exert a negative feedback on the synthesis and release of TSH and TRH in order to maintain circulating thyroid hormone levels within the required range.

P. Punekar et al, have shown a statistically highly significant increase in TSH levels in all cirrhosis patients compared to healthy controls. Our results are consistent with many studies.

Further in this study we observed that the mean value of serum T3 is 84.340±17.063 ng/dl in patients with CLD were lower as compared to that of healthy controls 84.340±17.063 ng/dl which is statistically significant (p = 0.024). Similarly mean values of serum T4 is 6.305±1.571 µg/dl in CLD patients are less as compared to that of healthy individual 7.04±1.264 µg/dl which is statistically significant (p = 0.004). M BORZIO et al[19] results indicate low total T3 and T4 concentrations in the patients with chronic liver disease. G. Deepika et al[17] studied thyroid function tests in chronic liver disease and confirmed the existence of several abnormalities of thyroid function tests in patients with chronic liver disease, thereby showing that levels of T3 and T4 are low and TSH elevated. Thyroid hormones are key regulators of metabolism and development and are known to have

pleiotropic effects in many different organs. The thyroid gland synthesises and releases triiodothyronine (T3) and thyroxine (T4), which represent the only iodine-containing hormones in vertebrates. T4 is the main product of thyroid secretion and local deiodination in peripheral tissues produces T3, the biologically active thyroid hormone.

The mean level of serum T3 in CLD patients were 84.340±17.063 ng/dl and that serum T4 are 6.305±1.571 µg/dl. The level are slightly decrease as compared to healthy controls. TSH is release from Anterior pituitary in response to low level of these hormones. Therefore we have observed that the mean value of TSH in CLD more than healthy controls but the value were within reference range 0.39 – 6.10 µlU/mL, an important point to note that the patients were clinically euthyroid. But it is also possible there levels may further increase leading to hypothyroidism if CLD untreared.

In are study be also observed that the serum T4 was negatively correlated with serum AST with r = -188 and p =0.096, but it shown no correlation with serum AST and ALP. There is no significant correlation of serum T3 and TSH with serum AST, ALT and ALP.

In our study we observed that there are certain limitations.

This study is a cross - sectional study therefore we were not able to show casual relationship between abnormalities of thyroid hormone and liver disease. In future this study should be multicentered for better results. The sample size of the study is also not adequate to support our finding. Detailed evaluation of thyroid profile example reverse T3 and thyroid antibodies are also not being carried out.

CONCLUSION

Chronic Liver Disease is a worldwide health problem associated with many complication, hormonal imbalance mainly of T3, T4 and TSH is one of them. The aim of our study was to measure the levels of T3, T4 and TSH in patients with CLD and to correlate there parameters with liver enzymes ALT, AST and ALP.

In this study we assessed that the levels of T3 and T4 in CLD patients were significantly decreased to healthy controls. Although the values varied still there was no significant cause effective relationship observed. Therefore, this study confirms the existence of several abnormalities in thyroid function test in CLD.

Furthermore, Serum T3 concentration appears to be parallel to the severity of liver dysfunction. As liver place an important role in metabolism of thyroid hormones therefore chronic liver diseases like hepatitis, alcoholic liver disease, and cirrhosis can result in alteration of levels of these hormones to such an extent that it may result in complications increasing the risk for liver transplant and motility. Therefore it is advisable to measure the levels of these hormones periodically show as to prevent complications and improve the quality of life.

Authors Contribution

All Authors contributed equally in this study.

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