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Original Article

CORRELATION OF THYROID PROFILE WITH GAMMA-GLUTAMYL TRANSFERASE IN PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Introduction: Cirrhosis is a condition in which the liver slowly deteriorates and fails to function properly due to chronic injury. It is an increasing cause of morbidity and mortality in most developed countries. Thyroid profile consists of triiodothyronine (T_3), thyroxine (T_4), and Thyroid Stimulating Hormone (TSH). Only 20% of circulating T_3 is synthesized in the gland and the rest is generated by T_4 in the liver. Gamma-Glutamyl transferase (GGT) is a dimeric glycoprotein and is effective in the diagnosis of Liver Diseases. **Aim:** To evaluate the correlation of Thyroid profile with Gamma-Glutamyl Transferase in Liver Cirrhosis patients. **Materials and Methods:** 100 clinically diagnosed cases of Liver Cirrhosis patients aged between 30-65 years of either gender were enrolled in the study. Patients with prior history of thyroid disease, undergoing thyroid medications and with other chronic disease were excluded. Blood samples were drawn from enrolled patients and estimation of thyroid profile and GGT was done to assess the correlation between them by applying statistic evaluation. **Results:** A strong negative correlation between T_3 and GGT (r-value= -0.3105 and p-value=0.002) in liver cirrhosis patients was observed. **Conclusion:** The present study suggested a strong negative correlation between T_3 and GGT in patients of Liver Cirrhosis. Therefore, serum T_3 levels in association with serum GGT can be a useful marker for the early prognosis of Liver Cirrhosis and can be helpful in better management of patients at risk and in averting the risk of progression to Cirrhosis, End Stage Liver Disease and Hepatocellular Carcinoma

KEYWORDS: Fibrosis, Necrosis, Triiodothyronine, Thyroxine

INTRODUCTION

Cirrhosis is a condition in which the liver slowly deteriorates and fails to function properly due to chronic injury. Liver cirrhosis is characterized by reiterated parenchymal damage which is a frequent consequence of the long clinical course of all chronic liver diseases (CLD). Necrosis of liver cells followed by fibrosis and nodule formation leads to cirrhosis [1]. The healthy tissues of the liver are replaced by the scar tissues leading to the impairment in the liver's ability to control infections; remove bacteria and toxins from the blood; nutrients, hormones and drugs processing; making of proteins that regulate blood clotting; produce bile that helps absorb fats including cholesterol and fat-soluble vitamins. Cirrhosis is an increasing cause of morbidity and mortality in most developed countries, being the 14th most common cause of death in adults worldwide; it results in 1.03 million deaths per year worldwide [2].

Around 10 lakh new patients of liver cirrhosis are diagnosed in India every year. Liver disease is the 10th most common cause of death as per the World Health Organization in India. Every 1 in 5 Indians may get affected by liver disease.

Thyroid profile consists of hormones triiodothyronine (T_3), thyroxine (T_4) and Thyroid Stimulating Hormone (TSH). T_4 is entirely produced by thyroid gland, T_3 is a product of the thyroid as well as all the tissues in which it is produced by deiodination of T_4. Only 20% of circulating T_3 is synthesized in the gland and rest is generated by peripheral conversion of T_4 by the deiodinase expressed in the liver [3]. Liver is one of the major sites involved in the peripheral conversion of T_4 to T_3 [4]. The formation of T_3 from T_4 is catalyzed by iodothyronine-5-deiodinase.

Gamma-Glutamyl Transferase (GGT) (EC 2.3.2.2) is a dimeric glycoprotein consisting of a heavy and a light subunit linked by non-covalent bonds [5]. The serum level of GGT is closely correlated with the state of the liver and is effective in the diagnosis of Liver Diseases. In oxidative stress, the level of oxidized glutathione increases and hepatic GGT is induced [6]. GGT is the most sensitive indicator of hepatobiliary diseases, elevated serum levels of GGT are observed usually in alcoholics, alcohol induced hepatitis, alcoholic liver disease and cirrhosis patients [7]. Thyroid hormones are strong mediators of multiple physiological processes. Liver is a target organ of thyroid hormones; therefore, the alterations of thyroid hormones can affect liver function. GGT is widely used as a marker of excessive alcohol intake in patients with Alcoholic Liver Disease (ALD) and is often increased in patients with Non-alcoholic fatty liver disease (NAFLD). Therefore, serum GGT level is associated with risk of liver cirrhosis and liver cancer. The present study was therefore, planned with the aim to assess the correlation of GGT with Thyroid hormone among Liver Cirrhosis patients.

MATERIALS AND METHODS

After seeking approval from Institutional Ethics Committee (IEC) and consent from enrolled patients, the study was conducted in the Department of Biochemistry in collaboration with the Department of Gastroenterology, Mahatma Gandhi Medical College & Hospital, Jaipur (Rajasthan), India. 100 diagnosed patients of Liver Cirrhosis aged between 30-65 years of either gender were enrolled for the study. Patients with prior history of thyroid disease, undergoing thyroid medications and with any other chronic disease were excluded from the study. Blood samples were collected and analyzed for T_3, T_4 and TSH by Chemiluminescence (CLIA) immunoassay and Gamma Glutamyl Transferase by International Federation of Clinical Chemistry method, Kinetic (IFCC).

Statistical Evaluation

The results obtained during the study were recorded and presented as mean ± SD (standard deviation). Correlation between Serum GGT and Thyroid Profile was analyzed by applying Pearson's Correlation. P value of ≤ 0.05 was considered as statistically significant.

RESULTS

In the present study, among 100 liver cirrhosis patients, the majority of cases were male (86%) when compared with females (14%). Higher percentage (34%) of patients were in the age group 51-60 years, followed by the age group 41-50 years with 31% of patients, when cases were distributed on the basis of age. The mean ± SD for T_3, T_4, TSH and GGT were 0.54±0.15, 6.27±2.48, 3.44±1.53 and 113.23±15.64 respectively. On analyzing the correlation between thyroid profile and

GGT, a strong negative correlation between T_3 and GGT (r-value= -0.3105 and p-value= 0.002) in liver cirrhosis patients was observed by applying Pearson's correlation.

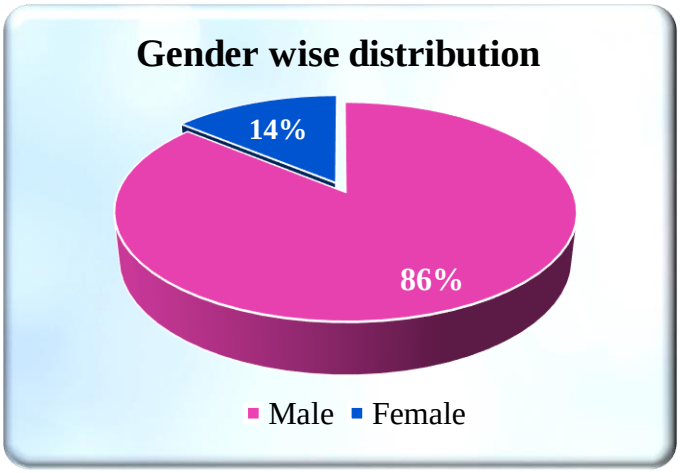

Figure 1: Gender wise distribution of patients with Liver Cirrhosis

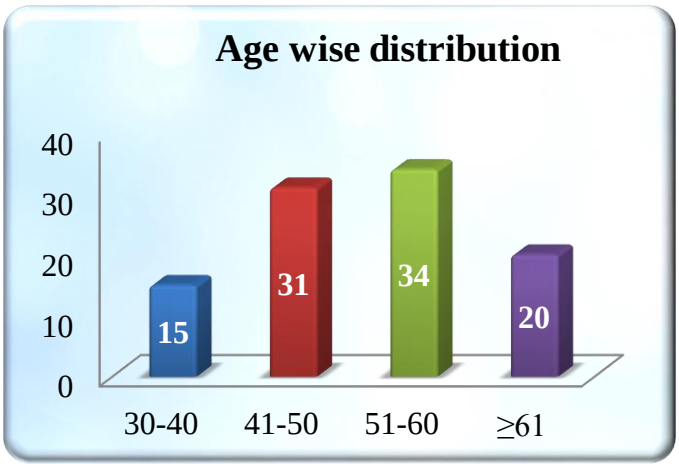

Figure 2: Age wise distribution of patients with Liver Cirrhosis

Correlation between GGT and Thyroid Profile		
	r-value	**p-value**
GGT v/s T_3	-0.3105	0.002
GGT v/s T_4	-0.032	0.75
GGT v/s TSH	-0.0113	0.911

Table 1: Correlation of Thyroid Profile with GGT in patients with Liver Cirrhosis

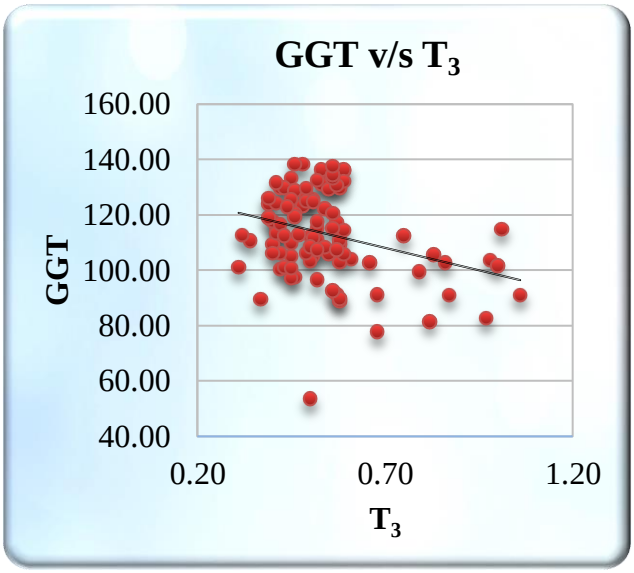

Figure 3: Correlation between T_3 and GGT in patients with Liver Cirrhosis

DISCUSSION

The present study was planned to evaluate the correlation of Thyroid profile with GGT among 100 Liver Cirrhotic patients. Patients were selected on the basis of pre-defined exclusion and inclusion criteria and after obtaining informed consent. Liver Cirrhosis is one of the most common diseases and is characterized pathologically by inflammation of hepatocytes, fibrosis and nodule formation with loss of liver architecture [8]. Cirrhosis in most patients is not a reversible process. In addition to fibrosis, the complications of cirrhosis include portal hypertension, ascites, hepatorenal syndrome and hepatic encephalopathy [9]. Liver is the most important organ in the peripheral conversion of T_4 to T_3 by type I deiodinase resulting to 5' deiodination of T_4 [10]. Moreover, it is involved in conjugation and circulation of thyroid hormones by synthesis of thyroid binding proteins [11,12]. When total cases were distributed on the basis of gender, then it was observed that, majority of cases were males (86%) when compared with females (14%) as shown in **Figure 1**.

Vijay kumar S et al., 2020 [13] also shown the high occurrence of Liver Cirrhosis among males in their study i.e., 78% males out of total 100 cases. **Mobin A et al., 2016** [14] also reported the high occurrence of cirrhosis among male in their study.

Figure 2 exhibits the distribution of cases on the basis of age. Almost similar percentage of cases was in age group of 51-60 and 41-50 years i.e., 34% and 31% respectively, which was followed by 20% in the age group of ≥61 years. The least number of cases (15%) were in the age group of 30-41 years. Similar patterns were reported by **Mobin A et al., 2016** [14]. A study by **Vijay kumar S et al., 2020** [13] also reported the major percentage of patients i.e., 78% above the age of 40 years. Almost similar percentage was found in the present study i.e., 83%.

Thyroid hormones are responsible for regulating the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function. A complex relationship exists between the thyroid gland and the liver in both health and diseased condition. The liver is the major site for cholesterol and triglyceride metabolism and the thyroid hormones play an integral part in lipid homeostasis [15]. GGT is found distinctly in the kidneys, pancreas, liver, intestine and prostate in large amounts [16], but is particularly common in the liver, small intestine, and kidney. In adult liver, GGT is localized in the biliary pole of hepatocytes and in cholangiocytes and hence secreted in bile [17].

Table 1 demonstrated the correlation of GGT with T_3, T_4 and TSH. A strong negative correlation between T_3 and GGT was observed as shown in **figure 3**. **Harischandra P et al., 2020** [18] reported abnormalities in circulating thyroid hormone concentrations and thyroid dysfunction in patients with Liver Cirrhosis and **Anand A K et al., 2019** [19], reported a significant increase in GGT levels and concluded that serum GGT levels are altered in liver diseases and can be useful in differentiating the liver diseases of different etiologies. Similar patterns were reported in our study. A study conducted by **E. Piantanida et al., 2020** [20], concluded that a complex interplay exists between the thyroid and the liver. On one hand, thyroid dysfunction can cause liver function test abnormalities and on the other hand, liver disorders may cause thyroid dysfunction. Therefore, a close interaction between endocrinologists and gastroenterologists is recommended for a proper and correct assessment of the patients with Liver Cirrhosis.

CONCLUSION

The present study was planned to evaluate the correlation of Thyroid Profile with GGT level in patients of Liver Cirrhosis. Finding of the study suggested that there is a strong negative correlation between T_3 and GGT in patients of Liver Cirrhosis. Therefore, serum T_3 levels in association with serum GGT can be a useful marker for the early prognosis of Liver Cirrhosis and can be helpful in better management of patients at risk and in averting the risk of progression to Cirrhosis, End Stage Liver Disease (ESLD) and Hepatocellular Carcinoma (HCC).

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