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ORIGINAL ARTICLE

Thyroid Dysfunction in Patient with Cirrhotic Liver Disease and its Relation to the Severity of Cirrhosis

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ABSTRACT

Background: Liver carries its vital significance due to ability to control over excretion, metabolism and transportation of the thyroid hormone. Peripheral change of T4 to T3 occurs in the live leading to initiation of action and breakdown of the hormones. Any morbidity in the liver can result in the decrease in TSH level and leading to thyroid dysfunction. So it is necessary to determine this impact in cases with liver cirrhosis.

Methodology: 115 cases of chronic liver disease who were not on the any therapy were involved in this research. The age of >18 years and both genders were selected. Data was collected from Department of Medicine, Lahore General Hospital, and Lahore in a duration of one year. All the demographics and baseline information mandatory for the selection of the appropriate sample was recorded. The participants were informed about the purpose of the research and after their consent they were selected for this study. Finally, the collected data was analyzed using SPSS 23.inc.

Practical implication: Thyroid dysfunction in patients with cirrhotic liver disease has practical implications for their management and outcomes. Regular screening and early intervention are important to detect and treat thyroid dysfunction promptly. Managing both cirrhosis and thyroid dysfunction requires a multidisciplinary approach involving hepatologists and endocrinologists. Patient education and support are crucial for raising awareness and ensuring adherence to treatment plans. Further research is needed to understand the relationship between thyroid dysfunction and cirrhosis severity and to explore potential therapeutic targets. Integrating thyroid evaluation into the overall management of cirrhosis can improve patient outcomes and quality of life.

Results: Mean age of 51(9.81) years were involved in this research. The male cases were higher in number 81(70.4%). The body mass index value was 27.5(3.65). Child Pugh A class was noted in 37(32.2%), B in 32(27.8%) & C in 46(40%). Serum T3 level was 2.05, serum T4 level was 8.69, serum FT3 level was 3.06, serum FT4 was 1.24 and TSH level was having a mean value 3.15. A significant inverse relationship noted in the severity of cirrhosis and thyroid profile levels.

Conclusion: Thyroid function depends on the smooth functioning of the liver through its hormones. As the liver compromise some disease, this normal function disturbs and thyroid dysfunction occurs which increase with the harshness of liver disease.

Keywords: Liver Disease, Thyroid Dysfunction, HCV, TSH

INTRODUCTION

Liver is a vital organ as it is involved in multiple important function by its thyroid hormone which is involved in metabolism, conjugation, excretion and production of thyroxine binding globulin. Irrespective of the fact that all the cases of liver disease are found to be euthyroid, previous literature still present that supports that there are hormonal abnormalities that exists in the blood concentrations. But this fact still need to be confirmed and generalized with the help of the careful investigation for the particular method covering all the patients of liver disease[1]

The liver is generally three-sided and comprises of double flaps: a bigger on the right projection and a more modest on the left flap. The flaps are separated by the falciform tendon, a group of tissue that keeps it tied towards stomach[2] .

Glisson's capsule is first protective sheet that covers the liver. Abdominal cavity further convers this capsule and provide it a dual shelter by covering this vital organ Due to it complex function, liver is given two sources for blood. One main artery that is called haptic artery brings the oxygenated blood form heart to liver and other portal vein brings the blood rich with nutrients from the stomach to the liver[3].

The veins partition into little vessels, finishing in a lobule. While the Lobules are the purposeful units of the liver and comprise of masses of cells which are called hepatocytes.

The liver controls the substances levels in the blood and release a juice which is called bile. Which help in to keep away byproducts from the liver. The blood from the stomach and digestion areas goes through the liver. From the liver cycles the blood and separates, balances, and makes the additions and uses it further for drugs into structures that are simpler to use for the rest of the body or that are harmless. At the point when it separated poisonous materials, its results are discharged into the blood.

The Bile by products enters the intestinal system which ultimately excreted as feces. The Blood are filtered in the kidneys, and further discharge as a urine[4] .

Metabolic abnormalities arises from the various functions that are being carried out side by side in the liver which involves cell metabolism, energy utilization and distribution of the fats form the production of the energy through the endocrine hormonal systems. In the processes of the maintenance of body temperature, lipid, carbohydrate breakdown and regulation of the body weight is carried out through thyroid glands[5].

The thyroid yields two-related hormones, thyroxine and triiodothyronine. Through thyroid hormone the receptors α and β, assume a basic part in cell separation during the advancement and help in keeping up thermogenic and metabolic homeostasis in the older children. The T4 is emitted from the thyroid organ in around twenty-crease overabundance on T3[6].

Importance of liver also lies in the fact that it metabolize the thyroid hormones and also it is responsible for the marginal change of (T4) to T3 by the Type 1 deiodinase. Studies has confirmed that up to 40% of extrathyroidal production of T3 is because of type I deiodinase. Furthermore, synthesis of the thyroid binding protein and the thyroid hormone conjugation and excretion is also dependent on liver functioning. Both the T4 and T3 control the basal metabolic rate of cells, plus hepatocytes, and thereby control hepatic purpose[7, 8].

There is considerable difference in the results in the previous studies regarding the change in the thyroid related biochemical parameters. So this study is planned to reach on a decision that

how much chronic liver disease has impact on the thyroid dysfunction.

SUBJECTS AND METHODS

The study was cross sectional by design. Considering the importance of the topic, inclusion criteria was formulated precisely so that biasness could be controlled. The inclusion criteria was consist of the patients of age between 18-65 years of age with the both gender. Patients were selected who have been diagnosed with the liver cirrhosis by the method of liver ultrasound. A coarse liver texture on the report of the ultrasonography was taken as confirmatory criteria for the presence of the liver cirrhosis. To become more precise in the selection of the appropriate cases the exclusion criteria was patients on treatment of HCV, history of surgical procedure related to liver, known cases of thyroid disorder without liver cirrhosis. Patient who faces organ failure, cancer, radio or chemotherapy and individual with active diseases such as bone and muscle disease, cardiac, pancreatic (diabetes), chronic kidney disease, nephrotic syndrome were excluded from this study.

Total 115 cases were studies as a sample. This sample size was estimated using 95% confidence interval using WHO calculator. Patients were selective on the basis on non-probability purposive sampling technique. Once patient is selected, the blood sample was drawn in a sterile syringe. The blood will be evaluated for the presence of the level of the thyroid dysfunction parameters including T3, T4, FT3, FT4 and TSH level. Cases with any etiology of liver cirrhosis like HCV, HBV or unknown etiology were also taken. All the information was recorded on the online proforma developed for this particular purpose.

Data was analyzed using SPSS 23inc. The quantitative data was presented in the form of descriptive stats while qualitative data was presented as frequency and percentages. Chi square and correlation test of analysis was carried out or the determination of the objectives. P-value greater than 0.05 was taken as significant.

RESULTS

All the 115 cases of chronic liver disease with age of 51(9.81) years were studied in this research. The frequency of men were high as 81(70.4%) and lesser number of female case 34(29.6%). Mostly cases has diagnosis of chronic liver disease form last 7.02(3.37) months age. Mean body mass index value was 27.5(3.65). Child Pugh A class was noted in 37(32.2%), & C in 46(40%) (Table#1).

Thyroid parameters when evaluated there was multiple value obtained. Serum T3 level was 2.05, serum T4 level was 8.69, serum FT3 level was 3.06, serum FT4 was 1.24 and TSH level was having a mean value 3.15(Table#2)

It was observed that child Pugh class has inverse correlation with serum T3 Level (r=0.002), serum T4(r=1.47) and serum FT4 level (r=0.001) while it was correlated with Serum FT3 level(r=0.017) (Graph#1).

When the impact of severity of the liver cirrhosis was evaluated, it was observed that FT3(r=0.18) and serum TSH (r=0.081) were positively correlate with Child Pugh Class A. While in Child Pugh Class B serum T3(r=0.059), T4 (0.03) were positively correlated. Child Pugh Class C has positive relationship with T3 (r=0.008) and TSH (r=0.024) levels But all the relationships in the severe cirrhotic disease collectively leads to the decrease thyroid function. (Table#4)

Table 1: Baseline demographical and clinical presentation of the Chronic Liver Disease

	Mean (SD), n (%)
Age	51(9.81) years
Gender(M/F)	81(70.4%)/34(29.6%)
Duration of Chronic liver disease	7.02(3.37) months
Body Mass index	27.5(3.65)
Severity (Child Pugh class A/B/C)	37(32.2%)/ 32(27.8%)/ 46(40%)

Table 2: Thyroid dysfunction parameters in the Chronic Liver Disease Cases

Biochemical parameter	Mean± sd
Serum T3 level	2.05±0.30
Serum T4 level	8.69±0.12
Serum FT3 level	3.06±0.14
Serum FT4 level	1.24±0.10
Serum TSH level	3.15±0.08

Table 3: Impact of Etiology on the Thyroid Dysfunction Parameters

	Etiology of Chronic Liver Disease	Mean	Std. Deviation	P-Value
Serum T3 Level	HCV	2.06	.30	0.73
	Other	2.04	.28	
Serum T4 Level	HCV	8.70	.12	0.22
	Other	8.67	.11	
Serum FT3 level	HCV	3.07	.14	0.18
	Other	3.03	.14	
Serum FT4 level	HCV	1.23	.09	0.09
	Other	1.26	.11	
Serum TSH level	HCV	3.16	.09	0.25
	Other	3.14	.08	

Table 4: Relationship between Severities of the Liver cirrhosis with the Thyroid Parameters level

Child Pugh class		Serum T3	Serum T4	Serum FT3	Serum FT4	Serum TSH
A	Correlation	-.065	-.019	.184	-.095	.081
	Sig.					
B	Correlation	.059	.033	-.139	.126	-.110
	Sig					
C	Correlation	.008	-.012	-.048	-.024	.024
	Sig.					

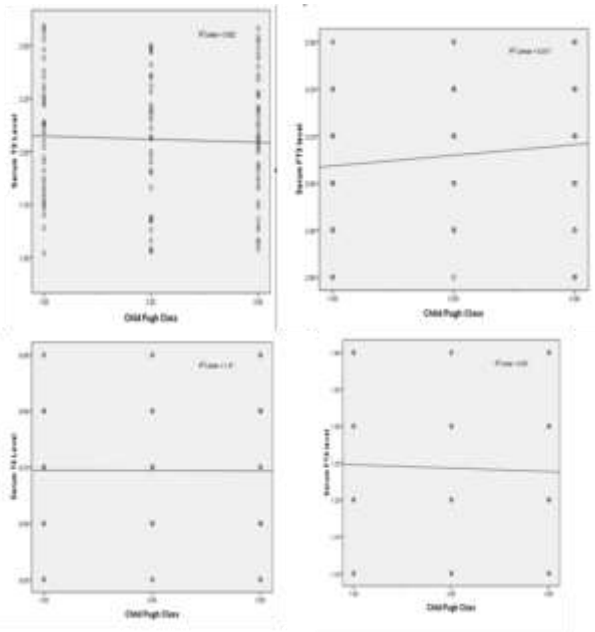

Figure 1: overall impact of the severity of liver disease on the thyroid levels

DISCUSSION

Thyroid dysfunction in the cases with cirrhotic disease is an emerging fact which has attracted the healthcare providers. So multiple studies has been planned and executed but each presented different results that whether the liver cirrhosis has any

impact on thyroid function or not. Therefore, the idea is taken up and this research is executed in a developing country were the patients get their diagnosis confirmed at a later stage.

The thyroid gland produces two hormones, thyroxine and triiodothyronine. Acting through thyroid hormone receptors α and β, these hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult.

It was observed in the current study, most of the cases who were presented in this study were above 50 years and majority were male cases as reported in the previous studies[10, 11].

As studied by Hodgson et al the relationship between the thyroid gland and the liver. He detected that thyroxine and tri-iodothyronine hormones moderate hepatic function. In this research we found that the severity of liver disease increases and the Child Pug score increases the occurrence of thyroid dysfunction growths. And this may have an impact on the endurance of the patients. Neglect of these may result in over of under diagnosis of liver or thyroid diseases and thereby cause problems in patient care[12].

We found that T3 levels were contrariwise associated with the Child-Pugh class and earlier studies also proposed similar results. Several devices have been suggested for this occurrence of lower free T3 levels in patients with cirrhosis of liver and its inverse association with the harshness of liver damage. The hypothesis states that loss of peripheral deiodination as the primary cause of decreased free T3 levels[13-15]. Low nutrition in cases of liver cirrhosis has been linked it. Release of cytokines such as Interleukin-6 (IL-6) might also be accountable for the disease of sick thyroid disease. Additional, alcohol intake has been related directly with diminished hepatic deiodinase activity[16]. All the factors of the thyroid dysfunction levels were not found to be significantly related to Child-Pugh class.

Till date, available studies showed most frequent change in plasma level of thyroid hormones is decreased total T3 and free T3 concentration which is reported to be associated with severity of hepatic dysfunction. But no study clearly mentioned FT4 and thyroid-stimulating hormone (TSH) levels with severity of liver cirrhosis. Serum T4 either remain normal or slightly low. However, serum TSH levels remain normal or slightly raised. These changes in hormone levels are so well recognized that some labors have advocated its use as a sensitive index of liver function[17].

Keeping in view the results of this study and the support from the previous literature, it is recommended that patients who have chronic liver disease should be monitored for the thyroid function. As the changes in the thyroid level could enhance the worse effect of the liver disease. Moreover, patients should be stratified for the any history of the thyroid dysfunction during the course of life so that case could be managed properly.

Current study has also few limitations. Once of the limitation was follow of patients who shifted from mild disease (Child Pugh Class A) to modest (Child Pugh Class B) to (Child Pugh Class C) liver disease. This follow up could inform about the mean change in the secretion of the thyroid hormone as the disease progress. Other limitation was the small sample size and the late presentation of the cases. As this was a single center study carried out at ta public hospital so most of the cases were unaware of healthy life style practices. So majority of them may have develop liver disease at earlier time. So more related studies are needed with larger sample size and multiple type of population involved.

CONCLUSION

Liver cirrhosis has resulted in the mean decrease in T3, T4, FT3, FT4 & TSH levels in the patients which leads towards the thyroid dysfunction. A significant association was noted in the severity of the disease and increase thyroid dysfunction among the cases presenting with liver cirrhosis.

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