

A Cross Sectional Study of Thyroid Function Abnormalities in Liver Diseases in a General Hospital

Dr.Panuganti Ratnachary¹, Dr.K.Sudha Rani^{2*} Dr.Panuganti Raveen³

¹Assistant Professor, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

^{2*} Professor and HOD, Department of Anatomy, Kakatiya Medical College, Warangal.

³MBBS

Corresponding Author: Dr.K.Sudha Rani

Abstract

Introduction: A complex relationship exists between the thyroid gland and the liver in both health and disease. Many studies have been carried out on liver disease patients assessing their thyroid status, mostly in European countries. Most of these studies are limited by the number of patients in these studies. This study tries to find out the relationship between thyroid function and chronic liver disease in a general hospital in India.

Materials and methods: This hospital-based cross-sectional study was conducted in patients admitted in the ward under the Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad. A total of 200 subjects were selected after explaining the purpose of the study and the procedure in detail and after obtaining their consent in written format. Data collection was done by history, clinical examination and investigations. With physical examination aided by abdominal imaging, patients who had ascites were graded into mild, moderate and severe refractory ascites. Hepatic encephalopathy was graded into grade 0 to 4 according to West Haven criteria.

Results: 24.6% of the study population showed abnormalities in thyroid function tests. The commonest was sick euthyroid syndrome in 18% of patients. Subclinical hypothyroidism was present in 4.7% of patients. Thyroid hormone levels had significant correlation with various liver function indices. Serum levels of total T3 and free T3 had significant positive correlation with serum albumin level and negative correlation with serum bilirubin and INR value. Free T4 had a weak negative correlation with serum bilirubin. Serum T3 and Free T3 were found to be decreased in patients with hepatic encephalopathy and ascites according to the severity. When severity of liver dysfunction was assessed using Child-Pugh score, it was found that there was statistically significant decrease in serum T3 and FT3 levels as the severity of liver dysfunction increased.

Conclusion: Chronic liver diseases were associated with abnormalities in thyroid function tests, although most of the patients remained clinically euthyroid. Serum T3 and FT3 levels had an inverse correlation with the severity of liver dysfunction.

Key words: thyroid function, chronic liver disease, West Haven criteria, refractory ascites.

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I. Introduction

Thyroid disorders vary according to the geographic location, environmental factors, major radio nuclear events, factors affecting the onset and persistence of iodine-deficiency as well as iodine excess in diet and the population studied [1]. It is a spectrum of disorders of the thyroid gland which manifests either as hyper - or hypothyroidism and is reflected in the circulating levels of thyroid stimulating hormone (TSH). Thyroid hormones, namely Tri-iodothyronine (T3) and Thyroxine (T4); either or both of which may be elevated or reduced have both direct and indirect effects on blood glucose homeostasis. Elevated levels of free circulating thyroid hormones (hyperthyroidism) produce hyperglycaemia by causing polyphagia, enhancing glucose absorption from the gastro-intestinal tract, accelerating insulin degradation and stimulating glycogenolysis. Reduced levels of the hormones (hypothyroidism) may cause hypoglycaemia[2]. The prevalence of thyroid disorders has been found to increase linearly with age and virtually all thyroid diseases are common in women [1]. The WHO estimate of diabetes prevalence for all age groups worldwide was 2.8% in 2000 and 4.4% in 2030. The total no. of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. Factors such as sedentary lifestyle, dietary modifications, ethnicity, hypertension and obesity have led to a dramatic increase in the incidence of diabetes mellitus, especially in the 21st century. Thyroid disorders are also very common in the general population and it is second only to diabetes as the most common condition to affect the endocrine system. As a result it is common for an individual to be affected by both thyroid diseases and diabetes. The first report showing the association between diabetes and thyroid dysfunction were published in

1979. Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17 %. However, fewer studies have estimated much higher prevalence of thyroid dysfunction in diabetes i.e. 31 % and 46.5% respectively.

Thyroid hormone is associated with basal metabolic rate, and low total and free T3 levels may reflect adaptive hypothyroid state, which may help to preserve hepatocytes and liver function by reducing the basal metabolic rate. Occurrence of hypothyroidism in cirrhotic patients has been shown to be associated with a biochemical improvement in liver function and decreased rate of decompensation in cirrhosis.

II. Materials And Methods

This study was conducted in the Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad. The study population were the patients with chronic liver diseases admitted in the Kamineni Academy of Medical Sciences and Research Centre, Hyderabad. This hospital-based cross-sectional study was conducted in inpatients of the Department of General Medicine. A total of 150 subjects were selected after explaining the purpose of the study and procedure in detail and after obtaining their consent. Data collection was done by history taking, clinical examination and investigations. With physical examination aided by imaging, patients who had ascites were graded into mild, moderate and severe refractory ascites. Hepatic encephalopathy was graded into grade 0 to 4 according to West Haven criteria. Serum bilirubin, SGOT, SGPT, albumin, ALP, prothrombin time and value were estimated. TFT including TSH, T3, T4, FT3 and FT4 were estimated using chemiluminescence method.

Inclusion Criteria

All patients admitted in medicine wards with chronic liver diseases. Diagnosis of chronic liver disease was based on clinical grounds, impaired liver function tests and ultrasonographic features consistent with chronic liver disease.

Exclusion Criteria

1. Patients with preexisting thyroid disorder, chronic renal failure, congestive heart failure, malignancy.
2. Patients on medications

Statistical Analysis: Data from the study case sheets were entered in Microsoft Excel. SPSS version 20.0 was used for data analysis. Continuous variables were described by Mean, SD, Minimum and Maximum. Qualitative variables were described by percentage distribution between groups. Parametric data were expressed as mean values \pm standard deviation (SD) and categorical variables as percentages. Categorical data were analysed by Chi-square tests for statistical significance.

III. Results

Study population was categorised into 3 groups according to the severity of hepatic encephalopathy. In each group, number of patients having T3 level lower than normal range (0.80 - 1.81 ng/mL) were found out. Out of the 100 patients who did not show any evidence of HE, 10 had $T3 \leq 0.8$ while 90 patients had $T3 > 0.8$. Of the total of 40 patients with grade 1 - 2 HE, 13 patients (32.5%) had $T3 \leq 0.8$ and 27 patients had $T3 > 0.8$ (67.5%), while 4 out of the 10 patients (40%) with grade 3 - 4 HE had $T3 \leq 0.8$ and 6 patients had $T3 > 0.8$ (60%). $T3 \leq 0.8$ was present in 10% of patients without HE and 32.5% of patients with grade 1 - 2 HE and 40% of patients with grade 3 - 4 HE. This difference was statistically significant with a P value of 0.001.

Similarly, in each of the above group, number of patients having Free T3 level lower than normal range (2.50 - 3.90 pg/mL) were also found out. Of the total 100 patients without HE, 11 (11%) had $FT3 \leq 2.5$, while 89 (89%) had $FT3 > 2.5$. Out of the 40 patients with grade 1 - 2 HE, 13 patients (32.5%) had $FT3 \leq 2.5$ and 27 patients had $FT3 > 2.5$ (67.5%) $FT3 \leq 2.5$ was present in 4 patients (40%) with grade 3 - 4 HE and $FT3 > 2.5$ in 6 patients (60%) with grade 3 - 4 HE.

$FT3 \leq 2.5$ was present in 11% of patients without HE and 32.5% of patients with grade 1 - 2 HE and 40% of patients with grade 3 - 4 HE. This difference was statistically significant with a P value of 0.003.

Parameter	Minimum	Maximum	Mean	SD
TB	1.2	10.9	4.15	2.43
ALB	2.2	4.6	3.25	0.46
SGOT	23	289	67.34	38.45
SGPT	15	198	43.24	23.65
ALP	49	238	107.5	32.20
PT	14	37	23.3	5.21
INR	1.0	2.75	1.611	0.41

Table 1: Liver function Tests

Parameter	Minimum	Maximum	Mean	SD
TSH	0.18	18.6	2.67	2.04
T3	0.35	2.02	1.05	0.27
T4	3.07	10.67	7.47	1.34
FT3	1.43	4.16	2.67	0.52
FT4	0.56	2.07	0.98	0.18

Table 2: Thyroid function tests

	Liver size	Spleen size	Portal vein size
Mean	14.76±1.23	11.02±0.80	12.06±1.01

Table 3: USG findings

Parameter	No hepatic encephalopathy	Grade 1-2 hepatic encephalopathy	Grade 3-4 hepatic encephalopathy
TSH	2.83±2.36	2.54±1.20	2.67±0.78
T3	1.12±0.20	0.80±0.20	0.76±0.17
T4	7.65±1.34	7.35±1.28	7.16±1.57
FT3	2.87±1.42	2.39±0.43	2.26±0.45
FT4	1.02±0.21	0.85±0.18	0.84±0.18

Table 4: Comparison between Thyroid Functions and Hepatic Encephalopathy

Thyroid function parameters in patients with no evidence of hepatic encephalopathy and those with grade 1 - 2 and grade 3 - 4 hepatic encephalopathy were compared using ANOVA. Means of T3 in no hepatic encephalopathy, grade 1 - 2 hepatic encephalopathy and grade 3 - 4 hepatic encephalopathy were 1.13 ± 0.30 , 0.82 ± 0.20 and 0.77 ± 0.19 respectively and the difference in means was statistically significant with a p value of 0.001. Means of FT3 in each above groups were 2.97 ± 1.43 , 2.46 ± 0.45 and 2.21 ± 0.55 respectively and the difference in mean value was found to be significant with a p value of 0.001.

Parameter	No Escites	Mild Escites	Moderate to severe Ascites
TSH	2.50±1.39	3.02±2.60	3.16±1.12
T3	1.09±0.20	0.83±0.23	0.79±0.21
T4	7.45±1.35	7.42±1.35	7.10±1.62
FT3	3.02±0.30	2.42±0.42	2.25±0.50
FT4	1.02±0.23	0.98±0.21	0.90±0.20

Table 5: Comparison between Thyroid Functions and Ascites

Thyroid function parameters in ascites were compared using ANOVA. Means of T3 in no ascites, mild ascites and moderate-to-severe ascites group were 1.18 ± 0.30 , 0.88 ± 0.23 and 0.79 ± 0.21 respectively and the difference in means was statistically significant with a p value of 0.001. Means of FT3 in each of the above groups were 3.08 ± 0.40 , 2.55 ± 0.43 , 2.25 ± 0.50 respectively and the difference in mean value was found to be significant with a p value of 0.001.

IV. Discussion

The liver has an important role in thyroid hormone metabolism and the level of thyroid hormones is also important to normal hepatic function and bilirubin metabolism. Besides the associations between thyroid and liver diseases of an autoimmune nature, such as that between primary biliary cirrhosis and hypothyroidism, thyroid diseases are frequently associated with liver injuries or biochemical test abnormalities. Liver diseases are also frequently associated with thyroid test abnormalities or dysfunctions, particularly elevation of thyroxine-binding globulin and thyroxine. According to Takahashi et al, The abnormalities of serum levels of thyroid hormones are frequently found in liver diseases. The pattern of abnormalities may be observed according to the type of disease and its severity. The estimation of free thyroid hormones level is important in liver dysfunction because of the changes of the binding protein in blood. Serum FT4 concentration is decreased only in cirrhosis of liver. It is observed that the decrease of serum FT4 concentration was noted in critical stages of liver diseases as in other diseases. Hence serum FT4 concentration is presumed to be a useful index for prognosis and has a different significance from serum FT3 level. Hepner and Walfish observed a significant inverse correlation between serum T3 value and the severity of liver dysfunction. A progressive fall in T3 concentration in cirrhosis of liver was shown as an indicator of poor prognosis. Hitomi et al studied on changes of thyroid hormones in various liver diseases which showed usefulness of free thyroid hormones as liver function test.

Hodgson et al studied the relationship between the thyroid gland and the liver. He observed that thyroxine and tri-iodothyronine hormones modulate hepatic function. The liver metabolizes the thyroid hormones and in turn regulates their systemic and endocrine effects. Thyroid dysfunction may affect liver function, liver disease in turn modulates thyroid hormone metabolism, and many systemic diseases affect both organs.

V. Conclusion

Chronic liver diseases were associated with abnormalities in thyroid function tests, although most of the patients remained clinically euthyroid. Serum T3 and FT3 levels had an inverse correlation with the severity of liver dysfunction.

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