ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 07 | July - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF THYROID FUNCTION ABNORMALITY IN PATIENTS OF CIRRHOSIS OF LIVER: TERTIARY CARE CENTRE STUDY

Biochemistry

Vandana Sharma Ph.D Scholar, Department of Biochemistry, SMS Medical College and Hospitals, Jaipur, India (Rajasthan University of Health Sciences).

Kamlesh Kumar Sharma Assistant Professor, Department of Gastroenterology, SMS Medical College and Hospitals, Jaipur, India (Rajasthan University of Health Sciences).

Sandhya Mishra* Senior Professor, Department of Biochemistry, SMS Medical College and Hospitals, Jaipur, India (Rajasthan University of Health Sciences)*Corresponding Author

Sandeep Nijhawan Senior Professor, Department of Gastroenterology, SMS Medical College and Hospitals, Jaipur, India (Rajasthan University of Health Sciences)

ABSTRACT

Introduction: Chronic liver disease is characterized by chronic inflammation and fibrosis with clinical feature of portal hypertension. Liver is major site for synthesis of thyroid hormone binding proteins and peripheral conversion of FT4 to FT3. Therefore chronic liver disease leads to alterations in thyroid functions.

Material and methods: We enrolled 50 patients of chronic liver disease as case group and 50 healthy controls. Blood sample for routine blood investigations and hormonal analysis were taken in morning and FT3, FT4 and TSH levels were measured using electrochemiluminesece immunoassay. All data analysed and compared with control group. Statistical analysis was done by SPSS software version 20. A statistical value of <0.05 was considered significant. Majority of patients had decompensated cirrhosis.

Results: Ethanol was most common cause of CLD in 64% patients. Ascitis and oligurea were major presenting features in 86% and 76% patients respectively. The prevalence of abnormal thyroid function in cirrhotic patients was 70%. Among these patients 44% had sick euthyroid syndrome, 8% subclinical hypothyroidism and 12% had overt hypothyroidism. Hyperthyroidism was present in 4% patients. Serum levels of FT3 and FT4 were significantly low in case group as compared to control group. ($p<0.001$). Mean serum TSH level was 3.33± 2.77.Conclusion: Alterations in thyroid hormone functions were common in cirrhotic patients .Majority of patients had sick euthyroid syndrome. The mean serum FT3 and serum FT4 levels were significantly low in case group as compared to control group.

KEYWORDS

Liver Cirrhosis; TSH; FT3; FT4; Thyroid Hormone Binding Protein

INTRODUCTION

Chronic liver disease characterized by chronic inflammation, regeneration and fibrosis, which converts the liver architecture into regenerating nodules with varying degree of fibrosis. Cirrhosis is the common end stage of chronic liver damage. Alcoholic liver disease, chronic hepatitis B, chronic hepatitis C, and non alcoholic steatohepatitis (NASH) are most common causes of CLD. Non alcoholic steatohepatitis (NASH) is going to become the leading cause of liver cirrhosis in near future among all populations in parallel with the global increase in diabetes, obesity and metabolic syndrome[1]

Endocrine system is a complex, sophisticated system which works by release of various hormones in blood which acts at distant site and involved in multiple metabolic processes. Liver is involved in production of various hormones, proteins, cytokines and interleukins synthesis and destruction. Liver plays a major role in synthesis and metabolism of thyroid binding proteins. Liver is also major site for peripheral conversion of tetraiodothyronine (T4) into triiodothyronine (T3).[2]

Eighty percent of daily T3 production occurs through iodothyronine deiodinase type 1 (D1) and deiodinase type 2 (D2) conversion in liver [3]. Hepatic dysfunction occurring in patients with cirrhosis can result in decreased D1 activity and in turn inadequate free T3 levels.[4,5,6] Almost all of these patients remain euthyroid but progressive hepatic dysfunction can lead to further decrease in free T3 levels and its clinical manifestations.[7,8] Thus in patients with chronic liver disease , decreased total T4 and T3 levels are reflection of both decrease in D1 activity and TBG synthesis .[9,10] Aim of our study is to find out abnormalities of thyroid Functions in patients with chronic liver disease. Secondary aim was to classify these thyroid disorders and to correlate with disease severity.

MATERIAL AND METHODS

This case control study was conducted at Sawai Man Singh medical college and hospital, Jaipur which is one of the largest tertiary care centres of north India. We enrolled 50 patients of diagnosed chronic liver disease admitted in gastroenterology department and taken as case group. 50 healthy subjects were enrolled as control group. Cirrhosis was diagnosed based on biochemical, radiological and clinical features and liver biopsy if needed. Cirrhotic patients who are critically ill, hepatocellular carcinoma, associated endocrine disorders such as diabetes mellitus and thyroid disorder, pregnancy, post organ transplant were excluded. The study period was from September 2018 to August 2020.The study protocol was approved by the ethical and research committee of the institute. Data were collected after the patient's informed and written consent. Patients were categorized into groups based on functional severity of the liver disease. Severity of liver cirrhosis was graded on the basis of the Child Pugh Turcotte score (CTP) and model for end stage liver disease score (MELD). Normal values of TSH 0.35 - 5.5 µIU/ml, FT3 2.3 – 4.2 pg/l and FT4 0.89 –1.76ng/dl. Selection of subjects is done on the basis of inclusion and exclusion criteria. Detailed clinical history related to demographic parameters and liver disease along with anthropometry was taken at the time of enrolment. Patient's blood samples were collected for routine laboratory investigations along with samples for serum hormonal assay after an overnight fasting in appropriate vials from ante-cubital vein puncture. Collected samples were analysed for hemogram , renal function tests, prothrombin time (PT).Standard liver function tests like serum albumin, serum bilirubin (total/direct), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and serum alkaline phosphatase were measured on the same day on AU 680 auto-analyser using IFCC approved methods. Rest sample used for measurement of hormonal analysis including serum TSH, FT3 and Ft4.

STATISTICAL ANALYSIS

Detailed data of all subjects of case and control group were collected. After complete evaluation all findings were expressed in terms of Mean ± SD. Comparison between case group and control group was done using paired "t" test. All statistical analysis was done using SPSS software version 20. A statistical value of $p<0.05$ was considered significant.

RESULTS

As per study protocol we took 50 patients of chronic liver disease as case group and 50 healthy subjects as control. Mean age of patients was 40.98±5.05 years. Out of 50 patients most common cause of CLD was ethanol intake in 64% patients followed by HBV, HCV and autoimmune hepatitis in 20%, 8%, 4% patients respectively. Ascitis

(86% patients) and oligourea (76% patients) were major presenting features. Most of the patients (72%) had decompensated cirrhosis.

When we analysis all investigations we found that:

1. Majority of patients in case group (86%) were anaemic with mean Hb level was 8.09 ±1.44 gm/dl, most common type of anaemia was macrocytic.
2. Serum calcium levels were significantly lower in case group as compared to control group ($p<0.001$).
3. Serum bilirubin and serum AST level were significantly high in case group as compared to control group ($p<0.001$).
4. on assessment of endocrinal assessment we found that majority of endocrinal function were affected up to variable extent.
5. Prevalence of thyroid hormone abnormalities was 70% in case group. Serum TSH levels were found high in 20% patients in case group with mean serum TSH level was 3.33±2.77 µ IU/ml.
6. Mean serum FT3 levels were significantly low in case group (2.17±1.37 pg/ml) as compared to control group(2.91±0.66 pg/ml) ($p<0.001$).
7. Mean serum FT4 levels were significantly low in case group (0.96±0.53 ng/dl) as compared to control group (1.21±0.32 ng/ml) with $p<0.001$.
8. Sick euthyroid syndrome was most common abnormality found in 44% patients followed by overt hypothyroidism, sub clinical hypothyroidism and secondary hypothyroidism in 12%, 8% and 2% patients respectively .Hyperthyroidism was seen in 4% patients.

OBSERVATION TABLES

Table no. 1: Demographic Profile & Clinical Characteristics of Patients

	N	Mean	SD	Median	Min.	Max.
Age (years)	50	40.98	5.05	41	28	55
Dose per week	32	53.91	10.22	50	40	80
Duration	32	15.75	3.42	15	10	25
Duration of CLD	50	3.07	1.24	3	1	6
PT/INR	50	2.06	0.70	1.85	1.1	4
GGT	50	107.60	26.18	103	62	175
Total Cell N/L	49	521.18	683.46	150	85	2650
MELD	50	23.30	6.40	24.5	11	32
APRI	50	3.16	1.25	2.85	1.02	6.74
GPRI	50	2.13	0.77	2.055	0.88	4.64
oesophageal Vx grade	49	2.25	0.66	2	1	3
Duration of hospital stay (in days)	50	5.92	1.85	6	3	10

Table No. 2: Thyroid Function Tests

TSH	Case		Control		Total	
	No.	%	No.	%	No.	%
Low	4	8.00	1	2.00	5	5.00
Normal	36	72.00	37	74.00	73	73.00
High	10	20.00	12	24.00	22	22.00
Total	50	100.00	50	100.00	100	100.00

Chi-square = 1.996 with 2 degrees of freedom; P = 0.369

Ft3	Case		Control		Total	
	No.	%	No.	%	No.	%
Low	32	64.00	6	12.00	38	38.00
Normal	15	30.00	43	86.00	58	58.00
High	3	6.00	1	2.00	4	4.00
Total	50	100.00	50	100.00	100	100.00

Chi-square= 32.307 with 2 degrees of freedom; P<0.001

Ft4	Case		Control		Total	
	No.	%	No.	%	No.	%
Low	27	54.00	5	10.00	32	32.00
Normal	21	42.00	44	88.00	65	65.00
High	2	4.00	1	2.00	3	3.00
Total	50	100.00	50	100.00	100	100.00

Chi-square= 23.597 with 2 degrees of freedom; P<0.001

Table No. 3: Classification of Thyroid Function Abnormalities in Case & Control Group

S. No.	Thyroid Function Abnormalities	Total No of Cases (50)		Total No of Control (50)	
		Subject	Percentage	Subject	Percentage
1	Overt Hypothyroidism	6	12	3	6
2	Sub-clinical Hypothyroidism	4	8	9	18
3	Sick Euthyroid Syndrome	22	44	3	6
4	Secondary Hypothyroidism	1	2	0	0
5	Hyperthyroidism	2	4	1	2
6	Normal Thyroid Function	15	30	34	68
7	**Total Number**	**50**	**100**	**50**	**100**

DISCUSSION

Cirrhosis is end stage of all chronic liver disease, progression of which depends on aetiology and duration of illness. Several abnormal alterations in thyroid gland have been found in patients with liver cirrhosis which may range from altered size and morphology of thyroid gland to alteration in thyroid hormone and its metabolism. Liver is the main organ involved in peripheral conversion of FT4 to FT3 and synthesis of various thyroid binding Proteins [11]. Therefore dysfunctions of thyroid hormone are common in patients with cirrhosis.

The prevalence of thyroid hormone abnormalities ranged from 13% to 61% in various studies. In a study done by Tas etal on 106 patients of CLD, the prevalence of thyroid hormone abnormalities was 61% [12]. Another study done by Caregaro et al showed prevalence of 30% of thyroid disease in CLD[13].

In our study we found that prevalence of abnormal thyroid function in CLD patients was 70%. Among these patients 44% had sick euthyroid syndrome, 12% overt hypothyroidism, 8% subclinical hypothyroidism and 2% had secondary hypothyroidism. . Hyperthyroidism was present in 4% patients of CLD.

Serum FT3 and FT4 levels were low in 64% and 54% patients of CLD respectively. Mean serum FT3 levels were significantly low in case group (2.17±1.37 pg/ml) as compared to control group (2.91±0.66 pg/ml) with $p<0.001$. Similarly mean serum FT4 levels were significantly low in case group (0.96±0.53 ng/dl) as compared to control group (1.21±0.32 ng/ml) with $p<0.001$.

In previous studies done by D,Costa and Dhume [14] , Saleem and Waden [15] the levels of FT3 were significantly low in liver cirrhotic patients. In another study done by Mobin et al [16] reported that majority of CLD patients had low serum T3 levels (76%) and low serum T4 levels (14.4%).

In several studies, most common abnormalities of thyroid functions in cirrhotic patients were low serum T3 levels, low serum T4 levels and normal or raised TSH levels. In patients with cirrhosis decreased synthesis of thyroid binding proteins, impaired hepatic clearance of reverse T3 and reduced conversion of T4 to T3 in liver are responsible for these thyroid function abnormalities. When we compared results of our study with previous studies, we found that these results were consistent. We tried to find out all abnormalities of thyroid hormones in cirrhotic patients so that these can be managed accordingly.

CONCLUSION

Thyroid hormone function abnormalities were common in cirrhotic patients with prevalence of 70. Out of these, majority of patients (44%) had sick euthyroid syndrome. Mean serum FT3 and serum FT4 levels were significantly low in CLD patients of case group as compared to control group ($p<0.001$). Therefore, serum FT3, FT4 and TSH are good indicator of disease severity in cirrhotic patients. Early diagnosis and treatment of these thyroid hormone abnormalities will improve survival as well as quality of life of cirrhotic patients.

DISCLOSURE STATEMENT

This study is investigator initiated. The authors declare that they have no competing/conflict of interests in relation to this article.

ACKNOWLEDGEMENT

This work was supported by Dr.Sudhir Bhandari, Principal & Controller, SMS Medical College, & Hospital, Jaipur.

Dr. Sandhya Mishra, Sr. Professor, Guide & the study principal investigator.The authors are grateful to Sr. Professor for her helps in scientific discussion and takes responsibility for the integrity of the data and the accuracy of the data analysis.

FUNDING

No financial support from an external agency was used for this study.

CONSENT FOR PUBLICATION

- Not applicable.
- Ethics approval and consent to participate.
- The study protocol was approved by the medical ethics committee of the Rajasthan University of Health Sciences, Jaipur, Rajasthan(State), India.

REFERENCES:

[1] Starr SP, Raines D. Cirrhosis: diagnosis, management, and prevention. Am Fam Physician. 2011; 84: 1353 – 1359.
[2] Huang MJ, Liaw YF. Clinical associations between thyroid and liver diseases. J Gastroenterol Hepatol. 1995; 10: 344 – 350.
[3] Penteado KR, Coelho JC, Parolin MB, et al. The influence of end-stage liver disease and liver transplantation on thyroid hormones. Arq Gastroenterol 2015; 52(2):124–8.
[4] Borzio M, Caldara R, Borzio F, et al. Thyroid function tests in chronic liver disease: evidence for multiple abnormalities despite clinical euthyroidism. Gut 1983;24(7): 631–6.
[5] Green JR, Snitcher EJ, Mowat NA, et al. Thyroid function and thyroid regulation in euthyroid men with chronic liver disease: evidence of multiple abnormalities. Clin Endocrinol 1977;7(6):453–61.
[6] L'Age M, Meinhold H, Wenzel KW, et al. Relations between serum levels of TSH, TBG, T4, T3, rT3 and various histologically classified chronic liver diseases. J Endocrinol Invest 1980;3(4):379–83.
[7] Guven K, Kelestimur F, Yucesoy M. Thyroid function tests in non-alcoholic cirrhotic patients with hepatic encephalopathy. Eur J Med 1993;2(2):83–5.
[8] Kayacetin E, Kisakol G, Kaya A. Low serum total thyroxine and free triiodothyronine in patients with hepatic encephalopathy due to non-alcoholic cirrhosis. Swiss Med Wkly 2003; 133(13–14):210–3.
[9] Kostopanagiotou G, Kalimeris K, Mourouzis I, et al. Thyroid hormones alterations during acute liver failure: possible underlying mechanisms and consequences. Endocrine 2009;36(2):198–204.10
[10] A, Köklü S, Beyazit Y, Kurt M, Sayilir A, et al. Thyroid hormone levels predict mortality in intensive care patients with cirrhosis. Am J Med Sci. 2012; 344: 175 – 179.
[11] Huang MJ, Liaw YF. Clinical associations between thyroid and liver diseases. J Gastroenterol Hepatol. 1995; 10: 344 – 350.
[12] Tas A, Köklü S, Beyazit Y, Kurt M, Sayilir A, Yesil Y, et al. Thyroid hormone levels predict mortality in intensive care patients with cirrhosis. Am J Med Sci. 2012; 344: 175 – 179.
[13] Caregaro L, Alberino F, Amodio P, Merkel C, Angeli P, Plebani M, et al. Nutritional and prognostic of serum hypothyroxinemia in hospitalized patients with liver cirrhosis. J Hepatol. 1998; 28: 115 – 121.
[14] D'costa L, Dhume CY. Assessment of thyroid parameters in alcoholic liver disease. Int J Pharm Biosci. 2016; 7:771–6.
[15] Saleem WM, Wadea FM. Evaluation of thyroid dysfunction in Egyptian chronic hepatitis c virus cirrhotic patients complicated with portal hypertension. Int J Sci Res. 2016; 5:595–600.
[16] Mobin A, Haroon H, Shaikh H, Qureshi F, Ali M. Decompensated cirrhosis; Thyroid hormone levels in patients. Prof Med J. 2016; 23:34–8.