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DECOMPENSATED CIRRHOSIS;
THYROID HORMONE LEVELS IN PATIENTS

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ABSTRACT… Objective: The objective of the study is to find out, the levels of thyroid hormones in serum of the patients having decompensate cirrhosis and to determine the frequency of signs and symptoms of thyroid dysfunctions in such patients. **Study design:** Prospective descriptive study. **Setting:** All medical wards of Civil Hospital and Ojha campus, Dow University of Health Sciences, Karachi, Pakistan. **Period:** May 2013 to January 2015. **Methodology:** 76 patients having decompensated liver cirrhosis with various presentations, which were fulfilling the inclusion and exclusion criteria and were admitted in medical wards during the study period, were included in this study. Detailed history and examination of each case was performed. Thyroid hormone levels were performed along with other relative laboratory investigations and the results were obtained. **Results:** Out of 76 patients 58 patients had low serum T3 levels, whereas 18 had normal T3 levels. 65 patients had normal T4 levels and 11 had low serum T4 levels. The TSH levels were found normal in 74 patients and two patients had raised TSH levels. **Conclusion:** It is concluded that T3 levels is low in cirrhotic patients but at the same time T4 and TSH levels remains normal in majority of cases and the patients remain euthyroid. As far as the clinical scenario is concern, no significance was found in the frequency of sign and symptoms of thyroid dysfunction. Most of the patients did not show signs and symptoms of hyper and hypothyroids.

Key words: Liver cirrhosis, Decompensated cirrhosis, Hypothyroids

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INTRODUCTION

Liver cirrhosis is one of the most common diseases affecting Pakistani population and viral hepatitis is the most common etiological factor causing hepatic cirrhosis.[1] Among the hepatitis viruses, Hepatitis C virus appears to be more common cause of liver cirrhosis. Cirrhosis is characterized pathologically by inflammation of hepatocytes, fibrosis and nodule formation with loss of liver architecture and re-organization of vascular architecture.[2] Clinically cirrhosis may be compensated or de-compensated, depending upon the absence or presence of the complication of cirrhosis.[3] Patients with decompensated cirrhosis usually present to different medical wards with moderate to severe ascites, variceal bleeding, hepatic encephalopathy, hepatorenal or hepatopulmonary syndrome or with hepatocellular carcinoma.[4] Liver is the major organ concerned with the body metabolism, therefore any condition causing acute or sub-acute or chronic liver injury is bound to produce metabolic abnormalities. Of these metabolic abnormalities, thyroid hormone dysfunction is one of the most common abnormalities. Other abnormalities include hyper glucagonemia, alterations in testosterone levels etc.[5,6] There are many factors that accounts for these abnormalities of thyroid hormone levels. These includes, alteration in plasma levels of thyroid binding proteins, altered binding of T_3 and T_4 to their carrier proteins, impaired

hepatic clearance of RT_3, hyperglucagonemia and decreased extra thyroidal conversion of T_4 to T_3.[7,8] The most consistent finding regarding thyroid levels in decompensated cirrhosis is a decrease in serum concentration of T_3. Serum T_4 levels either remain normal or slightly low. However serum TSH levels remain normal. These changes in thyroid hormone levels are so well established that some workers have advocated its use as a sensitive index of liver function.[9,10]

SUBJECTS AND METHODS

This study was conducted in different medical wards of Civil Hospital Karachi. Study started from 12th of May 2013, continued for about eight months and ends in January 2015. Patients are admitted in different medical wards either through casualty or from the outpatient department. The hospital is equipped with a central laboratory having arrangements of all routine tests. The laboratory also provides facility of all hormonal assays including thyroid hormone assay by Elisa technique. All patients of either sex, having 12 year or more age, and having signs and symptoms of decompensated liver cirrhosis were included in this study. Patients who were a known case of thyroid dysfunction or a known case of pituitary dysfunction or renal failure were excluded from this study.

After this, a detailed history was obtained from each patient with special emphasis on symptoms suggesting decompensated cirrhosis and symptoms suggesting thyroid dysfunctions such as, history of Jaundice, Pedal Edema, haemetemesis, Spleenomegaly, tremors, heat intolerance, exopthalmos, weight gain, goiter etc. Patients were also inquired about histories of blood transfusions, repeated use of syringes, sharing of razors and toothbrushes. After taking history, a detailed and thorough examination was performed. Firstly, pulse blood pressure and temperature were noted then general physical examination was performed with special emphasis on the presence of jaundice, anemia, spider naevi, palmer erythema, leukonychia, pedal edema and gynaecomastia. Then abdominal examination was performed for measurements of hepatic size, presence of Spleenomegaly, ascites and superficial abdominal veins. Only those cases were selected which shows signs and symptoms of decompensated cirrhosis. These cases were investigated for their complete blood counts, liver function tests, serum protein and A/G ratio, urea creatinine and electrolytes, ultrasound of abdomen, random blood sugar, viral markers and in selected cases upper gastro-intestinal endoscopies. Thyroid hormone profiles were performed for each case. The data of all the seventy-five cases was collected and was analyzed to compute results.

RESULTS

Out of the 76 patients, the majority was found to be male. 50(60.83%) males and 26(34.22 %) females. Ratio between the male and female is 1.92:1. Mean age was found to be 50.57 ± 12.54 years. During the study Ascites was found as the commonest complication in all 76 (100%) patients, followed by Spleenomegaly in 54 (71.1%) patients, jaundice in 53 (69.7%) patients, variceal bleed in 22 (28.9%) patients, weight gain in 20 (26.3%) patients, constipation in 7 (9.2%), somnolence in 3 (3.9%) patients and tremors in only one patient. It is also found that out of these 76 cases, none of the patients had heat intolerance, exopthalmos, husky voice or goiter (Table-I).

According to the finding or the results total bilirubin was found normal (0-2.5) in 29 (3.8%) patients while significant proportion (61.8%) had raised total bilirubin. Significant number of patients ($n=72$, 94.7%) had raised level of direct bilirubin (>0.25). The same pattern of significance was observed in SGPT ($p<0.01$). Alkaline phosphate level was found normal (30- 300) in significant majority (82.9%). A low level of serum albumin (<3.8) was observed in significant number of patients (92.1%). Raised (>16 seconds) prothrombin time was found in significant number of patients ($n = 67$, 88.2 %), while only 09 (11%) had a normal PT (Table-II).

Significant number of patients had low T3 levels that was observed in 58 (76.3 %) patients, while 18 (23.7%) had normal T3 [0.8-2.2], normal levels of T4. Normal levels of T4 and TSH were found in

significantly in high number of patients; i.e. 85.5 % and 97.4 % respectively, the details of which are furnished in Table 2. HBsAg was found positive in 16 (21.1%) patients while it was negative in 60 (78.9%) patients. HCV Antibodies was found positive in significantly high number of patients (64.5%, $p<0.01$) (Table-I).

Variable	No. Patients	Percentage
Gender		
Male	50	60.83%
Female	26	34.22%
Age		
20-30 years	4	5.26%
31-40 years	16	21.05%
41-50 years	24	31.57%
51-60 years	23	30.26%
61-70 years	8	10.52%
Sign and symptoms		
Ascites	76	100%
Spleenomegaly	54	71.1%
Jaundice	53	69.7%
Variceal bleed	22	28.9%
Weight gain	20	26.3%
Constipation	7	9.2%
Somnolence	3	3.9%
Tremors	1	1.3%
Hepatitis B Surface Antigen		
Positive	16	21.1%
Negative	60	78.9%
Hepatitis C Virus Antibodies		
Positive	49	64.5%
Negative	27	35.5%

Table-I. Demographic variable

DISCUSSION

Liver is one of the largest organs of the body. It performs a wide variety of functions including storage function, execratory functions, synthetic functions as well as metabolic functions. Liver is the main metabolic organ of the body along with kidneys. It is responsible for the metabolism of not only proteins, carbohydrates, and fats but it also metabolizes various hormones of the body. Therefore, injury to liver parenchyma may produce abnormalities of metabolism of these substances.[11]

Cirrhosis is a chronic liver disease characterized by chronic inflammation of hepatocytes with extensive fibrosis and nodule formation. In cirrhosis, most of the hepatocytes are replaced by fibrous tissue. As the disease progress, the function of the hepatocytes also reduces, especially the synthetic and metabolic functions.[12]

Therefore thyroid hormones level derangements are very common in cirrhosis. The most commonly noted abnormality of serum thyroid hormone concentration in cirrhotic patients are, low serum T3 level, raised rT3 level and a normal Thyroid Stimulating Hormone (TSH) level.[13] There are many factors that may be responsible for these abnormalities. These includes alteration in plasma level of thyroid binding proteins, altered binding of T4 and T3 to there career protein, impaired hepatic clearance of Reverse T3 (rT3), Hyperglucagonemia and reduced extra thyroidal conversion of T4 to T3. In Cirrhotic patients, because of extensive hepatic inflammation and

Parameter	Normal	Raised	Low
Distribution of biochemical parameters of patients having decompensate cirrhosis			
Total bilirubin [0-2.5]	29 (38.2)	47 (61.8)	
Direct bilirubin [0-0.25]	04 (5.3)	72 (94.7)*	-
SGPT [5-50]	27 (35.5)	49 (64.5)*	-
Alkaline phosphate [30-300]	63 (82.9)*	13 (17.1)	-
Serum albumin [3.8-4.4]	4 (5.3)	2 (2.6)	70 (92.1)*
Prothrombin time [14-16]	9 (11.8)	67 (88.2)*	-
Distribution of levels of thyroid hormones in serum of patients having decompensated cirrhosis			
T3 [0.8-2]	18 (23.7)		58 (76.3)
T4 [5-13]	65 (85.5)		11 (14.5)
TSH [0.1-7]	74 (97.4)	2 (2.6)	

Table-II. Laboratory Result

fibrosis, there is inhibition of Type 01 deiodinase enzymes that leads to decreased conversion of T4 to T3.[14] Since the type 02 deiodinase enzymes remain active, now most of the T4 is converted into Reverse T3 (rT3) leading to increase rT3 levels.[15]

In this study, we have taken Seventy Six (76) patients with various presentations of decompensated Cirrhosis and have looked for the signs and symptoms of hyper and hypothyroidism. Of all the 76 patients, 20 patients (26.3%) had shown an increase in weight, seven patients (9.2%) had constipation, three patients had somnolence (3.9 %) and only one patient had complained of tremor. None of the seventy-six patients had signs symptoms of goiter, heat intolerance, exopthalmos or husky voice. These results suggest that despite changes in thyroid hormone profiles, these patients remain euthyroid clinically.[16] Weight gain in twenty patients probably was the result of accumulation of fluid in the intercellular compartment because of hypoalbuminemia. The frequency of somnolence and tremors is non-significant and it is safe to say that these patients / remain euthyroid clinically.

We also performed thyroid hormone assay in all the 76 patients. This assay includes total T3 level (T3), total T4 level (T4) and Thyroid Stimulating Hormone level (TSH). The serum level of T3 in liver cirrhosis varies from 0.51 nm per liter to 1.48 nm per liter.[17] In our study out of 76 patients 58 had a lower T3 level (76.3 percent) whereas 18 had normal T3 values. This is in accordance to a previous study by Schlienger J. L. et al. Published in Ann. Endocrinol in 1980 that also shows a markedly reduced T3 level in patients with alcoholic cirrhosis.[18]

In this study T4 levels were found within normal range in 65 patients (85.5 percent) whereas 11 patients had a low serum T4 level. So, normal level of T4 was found in significant majority cases. The TSH levels were found within normal range in 74 out of 76 cases. Only two patients had a raised TSH levels. This again signifies that TSH levels remain within normal range in significant majority of patient and these patient remains eu-thyroid.

If we compare our results by study performed by Aga F, Qureshi H. and Khan R. A[17] conducted in Pakistan and published in JPMA in July, 1989, we find very much similar pattern of results. They studied 55 patients with liver cirrhosis for their thyroid hormones profiles. In their study 04 out of 55 patients (7.27%), had raised total T4 values and in 14 patients (25.45%), total T4 was below normal while the rest of the 37 cases (67.27%), had normal T4 values. A low T3 was found in 14 patients (25.25%), while free T3 (FT3) was low in 48 patients (87.27%). The TSH levels were normal in nearly all patients (92.72%) except four cases in which TSH levels were above the normal.

The results of our study were much closed to the study of Aga F., Qureshi H. and Khan R. A. study. In our study, T4 levels were found normal in 85.5 percent patients whereas in mentioned study 67.27 percent in normal T4. In Aga F. study showed 92.7 percent had normal TSH levels and in our study 97.4 percent has normal TSH levels. Total T3 levels in Aga F, study were low in 25.45 percent patients while FT3 levels were found low in 87.2 percent. In our study T3 were found low in 76.3 percent of patients and we had not performed FT3 level. The reason of this discrepancy in the T3 level is still unclear.

CONCLUSION

The present data confirm the existence of several abnormalities of thyroid function tests in patients with decompensated cirrhosis of liver. It is concluded that the serum concentration of T3 is found to be low in significant number of patients with cirrhosis, but at the same time T4 and TSH levels remains normal in majority of cases and the patients remain euthyroid. As far as the clinical scenario is concern, no significance was found in the frequency of sign and symptoms of thyroid dysfunction. None of the patients shows any signs and symptom of hyper or hypothyroidism.

REFERENCES

1. Abbas Z, Qureshi M, Hamid S, Jafri W. **Hepatocellular carcinoma in hepatitis D: does it differ from hepatitis**

B monoinfection. Saudi J Gastroenterol 2012; 18:18-22.

2. Singal AG, Volk ML, Jensen D, Di Bisceglie AM, Schoenfeld PS. **A sustained viral response is associated with reduced liver-related morbidity and mortality in patients with hepatitis C virus.** Clin Gastroenterol Hepatol 2010; 8:280-8.

3. Soriano G, Castellote J, Alvarez C, et al. **Secondary bacterial peritonitis in cirrhosis: a retrospective study of clinical and analytical characteristics, diagnosis and management.** J Hepatol 2010;52:39-44.

4. **European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis.** J Hepatol 2010;53:397-417.

5. Pothiwala P, Levine SN. **Analytic review: Thyrotoxicperiodic paralysis: A review**. J Intensive Care Med. 2010;25:71–7.

6. Tyagi P, Sharma P, Sharma BC. **Prevention of hepatorenal syndrome in patients with cirrhosis and ascites: a pilot randomized control trial between pentoxifylline and placebo.** Eur J Gastroenterol Hepatol 2011;23:210-7.

7. Den Brinker M, Joosten KF, Visser TJ et al. **Euthyroid sick syndrome in meningococcal sepsis: The impact of peripheral thyroid hormone metabolism and binding proteins.** J Clin Endocrinol Metab 2005;90:5613-5620.

8. Khan TM, Malik S, Diju I. **Correlation between plasma thyroid hormones and liver enzymes level in thyrotoxic cases and controls in Hazara Division.** J Ayub Med Coll Abbottabad 2010;22(2):76-9.

9. Hasselbalch HC, Bech K, Eskildren PC. **Serum prolectin and TSH responses to TRH in men with alcoholic cirrhosis.** Act Med. 1981; 209: 37-40.

10. Janni A, D Azzo G, Pinzello GB. **The prognostic value of thyroid function tests in liver cirrhosis.** In: Langer M, Chiandurri L, Chopra IJ. The endocrine and the liver. Academic press London, 1982.

11. Singh K. **Evaluation and interpretation of biomarkers of liver diseases.** Int J Resear in Health Scie. 2013;1(3):213-23.

12. O'Shea RS, Dasarathy S. **Alcoholic Liver Disease.** Hepatology 2013;51(1):307-328.

13. Kabadi UM, Kabadi MU, Premchandra BN. **Low serum T3 and raised rT3 levels in hepatic cirrhosis: role of glucagon.** Am J of Gastroenterology. 1991; 86(10): 1504-7.

14. Nomura S, Pittman CS, Chamber's JB, Buck MW, Shimizu T. **Reduced peripheral conversion of thyroxine to tri-iodothyronine in patients with hepatic cirrhosis.** J Clin Invest. 1975; 56: 643-52.

15. Kodding R, Janzen J, Schmidt E, Hesch RD, Letter. **Revese tri-iodothyronine in liver disease.** Lancet 1976; 2:314.

16. Kharb S, Garg M K, Puri P, Brar KS, Pandit A, Srivastava S. **Assessment of thyroid and gonadal function in liver diseases.** Indian J Endocr Metab 2015;19:89-94.

17. Agha F, Qureshi H, Khan RA. **Serum thyroid hormone levels in liver cirrhosis.** JPMA 1989; 39: 179-82.

18. Balhara YPS, Deb KS. **Impact of alcohol use on thyroid function.** Indian J Endocrinol Metab. 2013 Jul-Aug; 17(4): 580–587.

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