FREQUENCY OF THYROID DYSFUNCTION IN PATIENTS WITH CLD (CHRONIC LIVER DISEASE) SECONDARY TO HEPATITIS C VIRUS

Arosha Mansoora Khan[1], Abdul Latif Khattak[1], Mohammad Shabaz Amin[2], Mohammad Anwar[1], Faisal Mehmood[3] Mohammad Khalid Azam Khan[3]

[1]Combined Military Hospital, Kohat Pakistan
[2]Lahore Medical and Dental College, Lahore Pakistan
[3]Combined Military Hospital, Lahore Pakistan

ABSTRACT

Objectives: To establish the rate of thyroid dysfunction in patients with CLD resultant from HCV (Hepatitis C Virus).
Material and Methods: This descriptive, cross-sectional study was held in Medicine Department in CMH (Combined Military Hospital), Kohat from 3rd January 2020 to 2nd July 2020. One hundred patients of chronic HCV causing CLD were selected for the study. Age ranging 18 - 65 years of either gender were included. Patients taking medication that can affect thyroid functions, known thyroid disorders and CKD (Chronic Kidney Disease) were not selected. Blood samples were sent to the laboratory to assess thyroid function tests and thyroid dysfunction was noted.
Results: Age ranging 18 - 65 years with mean age of 37.69 ± 8.72 years. Majority patients 56 (56%) were ranging 18 - 40 years of age whereas 44 (44%) were from 41 - 70 years of age. Out of the 100 patients, 45 (45%) males and 55 (55%) females with ratio 1.1: 4 respectively. Frequency of thyroid dysfunction in patients of CLD from HCV was found in 4 (4%) patients with 01 was hypothyroid and 03 were hyperthyroid.
Conclusion: This study concluded that rate of thyroid disease in CLD patients affected from HCV is not too high in our study.
Key Words: CLD, Thyroid dysfunction, Hepatitis C.

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INTRODUCTION

The thyroid hormone is integral in multisystem functioning of the body. Hence any disorder in the thyroid hormone levels has a varied clinical picture ranging from nonspecific to a specific constellation of signs and symptoms [1].

The liver has a vital function in metabolism of thyroid hormones including conjugation, excretion, peripheral deiodination with the help of type I deiodinase and in the synthesis of thyroxine binding globulin[2] Thyroxine T4 Is monodeiodinated in the liver to 3,3',5 -triiodothyronine before exerting biological activity at the tissue level [3].

To summarize, the liver has a pivotal function in metabolism of thyroid hormone and indirectly in their systemic endocrine effects. As a consequence, liver disease has its impact on thyroid hormone levels and this disturbance in thyroid profile is an extrahepatic manifestation of cirrhosis [4]. The most common abnormality in thyroid function tests found is a reduction in Total T 3 and Free T 3 in proportion to the degree of hepatic damage (hypothyroidism in 26.0% and hyperthyroidism 2%) [5]. As a reference; in another study, low Free T 3 and T 4 were found in 72.5 % and 26.47 % of patients with CLD respectively [6].

A study conducted in Beni Suef University Hospital and Beni Suef General Hospital in Egypt revealed up to 66.7% thyroid dysfunction in CLD, with different percentages in different child groups [7].

Pagadala *et al*. established that NAFLD proven by biopsy (nonalcoholic fatty liver disease) is connected with an increased frequency of hypothyroidism (21% versus 9.5%) as evaluated against controls matched for gender, age, ethnic background and body mass index [8]. Another study conducted in University Hospital of the Federal University of Paraná, Brazil showed a total of 13.3% patients of end-stage CLD had thyroid dysfunction [9].

As the CLD goes on increasing in our population and thyroid dysfunction is associated with CLD, so the purposed significance of my study is to assess the rate of thyroid dysfunction in CLD patients. The above-mentioned studies have shown variability in

Correspondence: Dr Arosha Mansoora Khan, Department of Pathology, Combined Military Hospital, Kohat Pakistan

Email: **arosha23@hotmail.com**

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frequency of thyroid dysfunction in CLD patients among different ethnic groups, so there is a need of a study in our geographical area which will provide the local magnitude of the problem. As routinely thyroid functions in CLD patients are not assessed in our general practice and failure to recognize the presence of abnormal thyroid hormone level in CLD may be a cause of poor prognosis, so the results of my study will assist the medical community to design a proper management protocol for these particular patients in order to reduce the morbidity of our population.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in Medicine Department of CMH, Kohat 3rd January 2020 to 2nd July 2020. After approval from Hospital Ethical Committee, a sample of 100 cases with 6% margin of error, 95% confidence level taking expected percentage of thyroid dysfunction in CLD as 16%[10] through non- probability, consecutive sampling we included patient of both gender from 18 to 70 years of age having CLD due to chronic hepatitis C virus of more than 06 months duration were incorporated in the study. Those patients taking medication that can affect thyroid functions (dopamine antagonists, antiepileptics, oral contraceptives, lithium, glucocorticoids), patients with known thyroid disorders, and patients with CKD (s/creatinine >1.5 mg/dl) assessed on medical record were not included.

100 patients presenting to the outpatient department of Medicine, CMH, Kohat, fulfilling the established criteria were selected. Informed written consent was taken from every patient. Venous blood samples were taken and sent to the laboratory for analysis of thyroid function tests and thyroid dysfunction was noted. All the data including the demographic data (age, gender, duration of HCV, place of living (rural/urban), child pugh class (A/B/C) and thyroid abnormality (present/absent) obtained from patients was endorsed in the template proforma.

Data being endorsed and assessed by SPSS version 25.0. Descriptive statistics were applied to draw certain conclusions i.e. calculation of mean and standard deviation for patients' age, duration of HCV and Thyroid function tests. Rates and percentages were calculated for categorical variables such as gender, place of living (rural/urban), child pugh class (A/B/C) and thyroid abnormality (present/absent). Effect modifiers like age, gender, duration of HCV, place of living (rural/urban) and child pugh class (A/B/C) were controlled by stratification and post stratification and p-value ≤ 0.05 was declared significant.

RESULTS

This study includes age range from 18 - 70 years with mean age of 46.87 ± 13.05 years. Most patients 56 (56%) ranged between 18-40 years. Out of the 100, there were 42 (42%) male patients and 58 (58%) female patients with gender ratio of 1.1:4 respectively. Frequency of thyroid dysfunction in CLD secondary to HCV is shown in Figure-I whereas, division according to child pugh class are shown in Figure-II. Mean duration of disease was 10.01 ± 2.64 months. Occurrence of thyroid abnormalities in CLD patients, secondary to HCV was found in 4 (4%) patients where 03 were hypothyroid and 01 was hyperthyroid. Demographic difference of thyroid dysfunction in age groups, gender, duration of disease, Child pugh class and place of living are shown in Table-I along with their P-values. In our study, insignificant difference between different groups was found as depicted in Table-I which shows the stratification of thyroid abnormalities with respect to sex, age, duration of disease and Child pugh class respectively.

Figure-I: Frequency of thyroid dysfunction in patients with CLD from HCV (n=100).

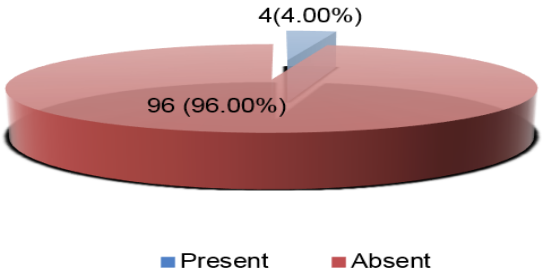

Figure-II: Distribution of patients according to Child Pugh Class(n=100)

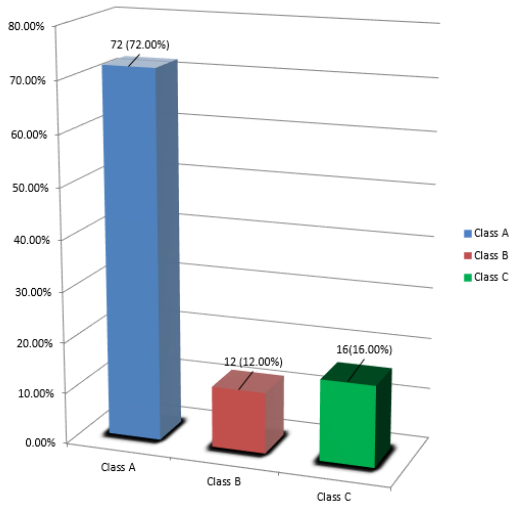

Table-I: Demographic profile of thyroid dysfunction.

Gender	thyroid dysfunction		p-value
	Present	Absent	
Male	1	41	0.5262
Female	3	55	
Age (years)			
18-40	3	53	.4346
41-70	1	43	
Place of Living			
Rural	01	75	0.0148
Urban	03	21	
Duration of Disease			
6- 12 months	2	74	
>12 months	2	22	0.214
Child Pugh Class			
A	72	72%	0.5834
B	12	12%	
C	16	16%	

DISCUSSION

The liver has a pivotal function in thyroid hormone metabolism, being an essential organ in causing peripheral conversion of tetraiodo-thyronine (T 4) to T 3 by Type 1 deiodinase [11,12]. The main enzyme in the liver is Type I deiodinase which causes about 30%–40% of extra-thyroidal synthesis of T3, it causes 5'-and 5-deiodination of T4 to T3. Furthermore, the liver causes conjugation and excretion of thyroid hormone and the production of thyroid binding globulin [11]. The basal metabolic rate of all cells is being controlled by T 3 and T 4 which also includes liver functions and adjusts it accordingly. The THS is metabolized by the liver which controls its endocrine effects. We have conducted this study to determine the rate of thyroid abnormalities in CLD patients secondary to HCV. In the study, frequency of thyroid abnormalities in CLD patients resulting from HCV was established in 4 (4%) patients with 3 were hypothyroid and 1 was hyperthyroid. A cross-sectional study held in Army Hospital in New Dehli, revealed a total thyroid dysfunction of 16%. Among thyroid abnormalities, majority was sick thyroid syndrome in 7% patients with subclinical hypothyroidism in 3.5% patients as second in frequency. Thyrotoxicosis and subclinical hyperthyroidism in 2.3% patients each and hypothyroidism in 1% [10]. A study was held in Civil Hospital in Ojha campus, Dow University of Health Sciences, Karachi, Pakistan from May 2013 to January 2015. In the study, 76% were found to have low T3, 14% low T4 and 0.02 % deranged TSH [13]. Dalgard alongwith fellows ascertain thyroid abnormalities in 11.8% [14], however, Kee *et al*, established thyroid abnormalities in 12.6% of patients [15]. A study was conducted in Civil Hospital in Ojha campus, Dow University of Health Sciences, Karachi, Pakistan from May 2013 to January 2015. In the study, 76% were found to have low T 3, 14% low T4 and 0.02 % deranged TSH [11]. Another study by Goyal *et al*. (2016) found that hypothyroidism developed in 26% patients [16]. Yan *et al*. in 2012, investigated that 11.5% HCV patient who were given treatment with IFN-α and anti-virals (RBV) were affected with thyroid abnormalities [17]. Kee *et al*. in 2006 found that around 2 % patients eventually developed thyroid dysfunction [18]. Latest meta-analysis concluded that patients of HCV have three times more tendency to hypothyroidism in contrast to control subjects [19]. Since there is a high occurrence of TPO-Ab in domestic patients of HCV, it is probable that this hypothyroidism is autoimmune [20]. Jemison et el from India demonstrated high incidence of subclinical hypothyroidism (21.6%) characterized by elevated TSH and low T3 in 50% of the patients with hypothyroidism. Remaining 50% of hypothyroid patients had normal FT3, FT4 raised TSH [21]. It is proposed that the main reason of above-mentioned diseases include environmental and genetic aspects. Few studies showed a link between non-organ specific auto antibodies (NOSA) and the risk involved for autoimmune thyroid abnormalities. The main indicator ascertained was anti- LKM 1 for symptomatic TD and de-novo autoimmune thyroid markers. However, only TPO-Ab was measured in the study, half the patients with TPO-Ab needed thyroid dysfunction management while on PegIFN therapy. The disparity in previous records of thyroid dysfunction at base line may dictate that progression of liver disease which is affected by immune processes, may also cause thyroid dysfunction.

CONCLUSION

This study concluded that the rate of thyroid abnormalities in CLD patients due to HCV is negligible in rural and urban areas of Pakistan. However, we recommend that further studies be conducted in every patient of CLD, and thyroid dysfunction should also be contemplated and its early recognition and management be carried out to decrease the morbidity and mortality of the community.

AUTHORS CONTRIBUTION

Arosha Mansoora Khan: Design concept, Data collection

Abdul Latif Khattak: Writing of the manuscript

Mohammad Shabaz Amin: Data analysis

Mohammad Anwar: Data collection and analysis

Faisal Mehmood: Proof reading and editing of the manuscript

Mohammad Khalid Azam Khan: Overall supervision of the study project

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