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Thyroid disorders in Hepatitis C virus infected untreated patients

Muhammad Adnan Saeed*, Muhammad Sadiq**, Asim Zulfiqar***, Javed Irfan*, Samina Jalali
*NORI, G-8/3, Islamabad, **Islamic International Medical College, Rawalpindi, ***Railway Hospital, Rawalpindi, Quaid-e-Azam University, Islamabad

Abstract

Background: To determine the association of thyroid disorders with chronic hepatitis C virus infection in patients who are not getting any antiviral treatment.

Methods: Fifty patients without pre-existing thyroid abnormality having positive Hepatitis C Virus (HCV) infection (confirmed on PCR) and not willing for getting anti-viral treatment (interferon) were included in the study. Blood samples from 50 patients were collected at base line, 03 months, 06 months, 09 months and at 12 months. The level of thyroid stimulating hormone (TSH) and thyroid antibodies was measured in these samples.

Results: Eleven patients (22%) developed thyroid disorder during the study period. Majority of the patients (73%) developed thyroid disorder on the basis of change in TSH level whereas 18% developed thyroid disorder on the basis of alteration in thyroid antibodies levels and 9% patients abnormality both in TSH levels and change in thyroid antibody titre.

Conclusion: A close association of thyroid disorder and chronic HCV infection is noted in the study population.

Key Words: Chronic hepatitis C; Thyroid antibodies; TSH

Introduction

Hepatitis C, discovered in 1988, is one of the important causes of chronic liver disease[1]. It possesses six genotypes with more than 50 subtypes so far known. The viral genotypes have epidemiological clinical and therapeutic significance[2]. It has a frequent association of hepatocellular cancer[3]. A broad spectrum of extrahepatic syndromes has been observed in chronic hepatitis C. Autoimmune manifestation ranges from non-organ-specific autoantibody seropositivity and cryoglobulins to immunological diseases such as glomerulonephritis, vasculitis, lichen planus, and mixed cryoglobulinemia[4-7]. As a secondary event, autoreactivity is detected in liver disorders associated with a variety of etiological factors (e.g. drug- and chemical-induced autoimmunity, viral and microbial infection-induced autoimmunity)[8,9]. The combination of hepatitis C virus (HCV) infection and thyroid diseases raises several issues that are the prevalence of thyroid autoimmunity in patients with chronic hepatitis C, the prevalence of HCV infection in patients with autoimmune thyroid diseases, and the effects of interferon alpha treatment on thyroid function in chronic HCV hepatitis. The prevalence of anti-thyroid auto-antibodies ranges from 4.6 to 15% in HCV infection, which is considered as significant by various authors[10].

The association of thyroid dysfunction with HCV infected patients, who are on interferon therapy, is well established. But thyroid dysfunction in HCV patients, who are not receiving interferon therapy and not having pre- existing thyroid abnormalities is an aspect which the present study intended to explore..

Patients and Methods

It was a cross sectional observational study

Inclusion Criteria: Diagnosed cases of HCV infection, who were not willing to get anti-HCV treatment (interferon). HCV positivity was defined as persistently raised serum aminotransferase (ALT) level associated with confirmation of positive anti HCV RNA antibody on PCR.

Exclusion Criteria: Patients with pre-existing thyroid abnormality. Patients who started treatment during follow up period and patients with advanced liver disease

A total of 50 patients were included in the study. The follow up of the patients was carried out for one year after every three months.

Investigations:

The following investigations were carried out in all patients at baseline i.e. at the time of induction in study and in their quarterly follow up visits till one year i.e. at 3, 6, 9 and 12 months.

Thyroid Stimulating Hormone (TSH:The estimation of TSH was carried out on Immulite using chemiluminescence technique. The normal limits are between 0.4 to 4.0 IU/ml. The readings between this range were considered as normal and any value

above or below this range abnormal and labeled as high or low TSH value. If TSH value was above the normal range, no thyroxine replacement was given except when the level of TSH was above 8.5 IU/ml or there were gross clinical symptoms.

***Autoantibodies*:**Sera were investigated for the presence of thyroid microsomal antibodies. For autoantibody detection, standard indirect immunofluorescence tests on unfixed 4 μm cryostate sections from a composite block of mouse as well as from hyperplastic human (blood group 0) thyroid gland were used. The sera were diluted 1:10 and 1:100.

Criteria of thyroid abnormality

The following points were used to label a patient that he/she is developing thyroid abnormality during the follow up period of the study.

(i)Alteration in TSH level beyond its normal limits either low or high

(ii)Positive thyroid antibodies

Statistical analysis

The mean TSH levels were calculated at each follow up visit. The frequency and percentages of different thyroid abnormalities was calculated. The statistical analysis (χ^2 test) was performed to determine the significant difference in number of male and female patient population as well as gender difference in development of thyroid abnormality. $P<0.05$ was considered statistically significant.

Results

The mean age of the study population was 37.2 ± 1.09 years. The number of male patients was 31 with a mean age of 37.6 ± 1.40 years. The female patients were 19 with mean age of 36.3 ± 1.68 years.

According to the criteria defined, 11 patients (22%) developed thyroid abnormalities during the study period. Out of these 11 patients, 73% showed abnormality in TSH levels, 18% developed positive thyroid antibody and 9% showed change in both TSH levels and positive thyroid antibody.

The baseline mean TSH level of the study population was 4.17 ± 0.38 μIU/ml. During follow up period, eight patients showed change in TSH levels beyond normal limits. Out of these, 7 developed hypothyroidism and 1 hyperthyroidism. The patients who developed hypothyroidism were treated with oral thyroxine tablets and TSH level reverted to normal within three months in all patients (Table 1).

Considering the gender difference, out of 11 patients, 45% were females and 55% were males. Among females, 3 patients developed rise in TSH level, and 2 developed positive thyroid antibody during study period. Whereas in males, 4 patients, had raised TSH level, one developed hyperthyroidism and one male patient showed changes both in TSH level and positive thyroid antibody.

Table 1: Patients developing thyroid abnormalities at quarterly follow up

	Baseline	03 months	06 months	09 months	12 months
No. of patients	50				
Mean TSH level	4.17±0.38	3.91±0.38	3.78±0.34	3.61±0.21	3.07±0.33
Hypothyroid	-	1	3	2	1
Hyperthyroid	-	-	-	1	-
Positive thyroid antibody	-	1	2	-	-

No significant difference was observed in the development of thyroid abnormalities on the basis of gender (male vs females; p=0.122).

Discussion

The criteria laid down in our study for positive thyroid disorder was either a positive thyroid antibody and/or a change (raised or low) in TSH value (normal value 0.4 to 4.0 μIU/ml). . About 22% of the study population showed development of thyroid disorders during the study period. These results are well matched with those already mentioned in the literature[11,13].

The most frequent clinical manifestation was hypothyroidism (Table 1). The patients, who developed hypothyroidism (High TSH) were not given specific treatment until the appearance of clinical symptoms.

The number of male patients in the present study was significantly higher than the female patients (p=0.029). The same was found in the study of Dalgard et al (male patients 60%; n=153 vs. female patients 40%; n=101) and Tran et al[14] (male patients 55%; n=150 vs. female patients 45%; n=122) [13] .

The results of this study corroborate with the findings of Antonelli et al and Ploix et al , who observed that both hypothyroidism and thyroid

autoimmunity are more common in patients with chronic hepatitis C even in the absence of interferon treatment [11,12].

In present study , no gender difference was observed in the development of thyroid abnormalities. This observation differs from the findings of Prummel et al[15], who explained that whatever the underlying pathophysiologic process , the major factor contributing to hypothyroidism includes the female gender with a relative risk ranging between 3-7 times and the presence of anti TPO antibodies. Moreover, Hsieh et al concluded in their study that female gender is a predisposing factor for development of thyroid abnormality in patients with HCV infection and getting α-interferon treatment [16].

In the present study viral genotypes were not considered for the patients. Several studies in this field have shown that the serological pattern of autoantibodies does not correlate with a particular genotype of HCV[11, 17]

The clinical significance of the serological markers of autoimmunity is still an object of discussion. But it seems that there are no significant differences in clinical and biochemical parameters between chronic hepatitis C patients with and without autoimmune features[11,18]. A recent study on the general population showed that in the absence of active liver disease the prevalence of non-organ specific auto antibodies was similar in HCV positive individuals and negative controls[18].

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Conclusion

Thyroid abnormalities can develop in HCV patients without pre-existing thyroid abnormality

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