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Prevalence of Hepatitis B and C infection in autoimmune thyroid patients

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Abstract
This study investigated the possible relationship between the autoimmune thyroid disorders and hepatitis B and C infections. We studied prospectively 100 patients (78 women and 22 men; mean age: 44.32 ± 11.39 Yrs) and 100 euthyroid (70 men and 30 women; mean age: 40.10 ± 8.95 Yrs) as controls. In all patients HCV and HBV antibodies, TSH, TT4, TT3, and circulating anti-thyroid peroxidase antibodies (TPO-Ab) were measured. HCV antibodies were in 4% and HBV antibodies in 1% of patients and HCV was 1% in control samples (p<0.05). Hepatitis B surface antigen and HBs antibodies were found only in 1% of patients and none in the controls. The difference in thyroid function in both positive and negative HCV and HBV sub groups was insignificant. These results confirms the relation between hepatic viral infections and immune mediated thyroid lesions. Therefore, investigation of TG-Ab and TPO-Ab in hepatic viral infections before interferon therapy, is recommended.

Keywords: Thyroid, Autoimmunity, Thyroperoxidase, Hepatitis C virus

1. Introduction
One of the important organs in human body is the thyroid gland which is highly susceptible to autoimmune thyroid diseases [1]. AITDs are organ specific conditions which are caused by attack of antibodies of human body on its own thyroid follicles, thus disrupting its normal function [1]. Grave's disease (GD) and Hashimoto's thyroiditis (HT) are the main forms of a number of types of AITDs. Causes, symptom and treatment methods of these diseases are different [1]. Several hypotheses have suggested that both environmental factors and genetic predispositions have been involved in the pathogenesis of thyroid autoimmunity. Different environmental triggers like viral infection, smoking, drug exposure, stress, intake of iodine, are involved in the onset of AITDs [1, 2].
In the past studies, the onset of AITDs during the alpha interferon (α-IFN) therapy for chronic hepatitis C virus (HCV) and other diseases have been reported [3]. Studies have also suggested a high prevalence of anti-thyroid antibodies in subjects infected with HCV before INF therapy [4, 5]. Which means that HCV may be included in the list of predisposing triggers for the onset of AITDs [6]. Hepatitis B and C are infectious disease of the liver. Various clinical signs and symptoms like endocrinopathies and different skin diseases are associated with chronic hepatitis C infection [7]. Different extra-hepatic abnormalities like porpyhyria cutanea tarda, cryoglobulinemia and membrano-proliferative glomerulonephritis are associated with hepatitis C infection [8]. Studies carried so far have produced discordant results. Some studies manifest enormous prevalence of HCV antibodies in autoimmune thyroid disease patients, suggesting that this autoimmunity could be induced by HCV infection [9], while in other studies, no prove of an epidemiological link of HCV and thyroid autoantibodies was found [10]. The prevalence of autoantibodies against thyroid, reported so far in HCV positive patients are vary, ranging from 2% to 32% [11].
The aim of this prospective investigation was to evaluate the prevalence of hepatitis B and C viral infection in autoimmune thyroid patients and their impact on the function of thyroid.

2. Materials and Methods
In the present study patients and controls were studied in the institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Khyber Pakhtunkhwa Pakistan from November 2015 to October 2016. A total of 100 AITDs patients have been enrolled (78 women and 22 men; mean age: 44.32 ±11.2 yrs) and 100 euthyroid (70 women and 30 men; mean age: 40.10±8.9 yrs) as control.

The criteria of inclusion of these subjects, were clinical observations, hormonal (total thyroxine-TT4, total triiodothyronine-TT3 and TSH values) and serological (presence of antibodies against thyroid peroxidase, TPO-Ab) of AITDs and controls. The exclusion criteria for the patients were hormonal and clinical AITDs suspects without circulating anti-thyroid antibodies and in the control group having circulating antibodies against thyroid. Similarly, the involvement of environmental triggers that causes AITDs like iodinated drugs and non- iodinated drugs, radioactive iodine, stress, pregnancy and patients treated with interferon (IFN) were also included in exclusion criteria.

Serum TSH (normal range: 0.5-5.0 mIU/L), TT4 (normal range: 62-165 nmol/L and TT3 (normal range: 0.8-2.7nmol/L) were determined by immunoradiometric assay (IRMA) and radioimmunoassay (RIA) respectively. Serum level of anti-thyroid peroxidase antibodies was assessed by ELISA technique, using Elisa kit (Aeskulisa, Germany) [12]. After taking ethical approval from the concerned ethical committee of advance study and research board of the university, informed consent was taken from all subjects. HCV antibodies and HBs Ag were measured by lateral flow chromatographic immunoassay (CTK Biotech, USA). HCV antibodies (IgG, IgM, IgA) were detected by the On-site HCV Ab plus Rapid Test- Cassette (Serum/Plasma, CTK Biotech, USA), while the HBs Ag were detected by On Site HBsAg Rapid Test-Cassette (Serum/ Plasma, CTK Biotech, USA).

Statistical analysis

Using conventional techniques, the frequencies and statistical data were obtained. The values were presented as mean± standard deviation (SD). Using t-test and chi-square test, the data showing differences in groups, were analyzed. The significance of the test statistics is considered if $p<0.05$.

3. Results

Table 1 shows the personal and hormonal data of patients and control. No significant differences in the parameters (table 1) exist between the two groups. In the autoimmune thyroid patients, the TPO Ab was positive in 100% of the AITDs patients.

The antibodies against HCV were positive in 4/100 (4%) of the patients while the hepatitis B surface antigen was positive in 1/100 (1%) and HCV antibodies in controls was positive in 1/100(1%) ($p<0.05$) (Table 2 Figure 1). The value of HCV in the controls was less than the value determined previously by various researchers (nearly 2%). All the HCV and HBV positive cases of AITDs patients had TPO antibodies. The prevalence ratio of HCV positive cases in AITDs was higher in female as compared to male (F/M=3/1) but in control group the HCV positive case was male with age 26. Similarly HBV positive case was male with age 28. The prevalence of HCV positive cases in AITDs was higher with increasing age (44.5±6.67) as compared to the positive case in control (age=28). The prevalence of treating hypothyroidism of HCV positive in AITDs was insignificant as both HCV positive and negative were under the same treatment.

Table 1: The clinical and hormonal data of the AITDs and controls

Parameters	AITDs	Controls
N	100	100
Age(Yrs)	44.32±11.39	40.10±8.95
Sex(M/F)	78/22	70/30
TT4 (nmol/L)	96.4±17.6	95.9±16.8
TT3(nmol/L)	2.38±0.36	2.26±0.37
TSH(µIU/L)	1.75±0.82	1.68±0.79

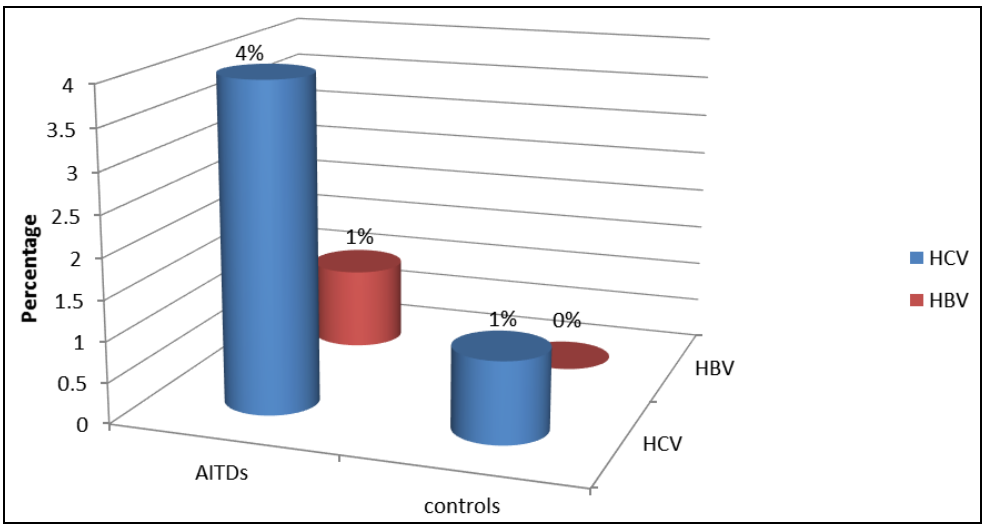

Fig 1: HCV and HBV prevalence in AITDS patients and controls. *P<0.05* between the patients infected with HCV and controls.

4. Discussion

The present analysis implies that the prevalence of HCV and HBV infection was statistically significant ($p<0.05$) in AITDs (4%) as compared to that of control (1%). The same observation has been given by other researches [13, 14]. The prevalence of HCV in controls is slightly less (1%) than the expected value found in the general population (2%) [15]. Similarly, a significant difference of HBV infection was found (1%) in the AITDs patients as compared to the controls (0%) but again less than the already determined value in the general population (2.5%) [16]. Results, similar to this study, were also found in other study conducted in Italy that shows prevalence of HCV and occurrence of anti TPO antibodies [10]. In another study, conducted on 630 HCV positive patients with control group, demonstrated a prevalence of 21% for TPO-Ab and 17% for TG-Ab that suggested a link between HCV and AITDs [11]. Many research have been conducted that demonstrate the relationship between HCV and AITDs [17]. Most of the studies suggest a close link between the HCV infection and AITDs, so HVC may be one of the possible environmental triggers that could breakdown autoimmunity against thyroid. Many logical suggestions have been put

forward for the pathogenetic mechanism [18]. Some of the possible outcomes are the molecular mimicry [19], viral infection that could make the host to induce alpha IFN response [5]. Another study conducted showed that HCV infection was significantly higher in AITDs patients than controls [4]. Very few studies have demonstrated no association between the HCV infection and AITDs [20].

5. Conclusion

The present study, in accordance with many other studies, logically concluded a close link between HCV infection and AITDs, particularly in elderly patients. This study has also shown a high prevalence of HCV infection in female. The present study did not clearly show a close association between HBV and AITDs. It is suggested that the detection of TPO-Ab and TG-Ab should be performed in all HCV positive patients before interferon therapy and screening of HCV in all autoimmune thyroid patients should be done.

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7. References

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