Prevalence of Anti-Thyroid Peroxidaes Antibodies in Patients with Chronic Hepatitis C Virus Infection
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Abstract

Background and aim: Chronic hepatitis C virus infection is associated with many autoimmune thyroid antibodies and thyroid dysfunction. The frequency of anti-thyroid peroxidaes antibodies among chronic Hepatitis C patients has been reported in many studies with different result. The aim of this study is to determine the frequency of thyroid peroxidaes antibodies among chronic hepatitis C patients in Benghazi before treatment with Interferon.

Methods: Thyroid peroxidaes antibodies concentration evaluated in 120 chronic hepatitis C infected patients in addition TSH level, HCV-RNA concentration and genotype for HCV has been evaluated. Patients on Interferon therapy, coinfected with HBV, HIV, Type 1 DM, history of thyroid disease and autoimmune diseases has been excluded.

Results: Out of 120 patients, 50% were males with mean age group 44±8 year. The most frequent genotype reported was genotype 4 (91.7%). Twenty four patient (20%) has high Anti-TPO, there was no statistical Difference among males and females (P = 0.702). High TSH (> 4.2 muI/ml) found in 15 patient (12.5%) in the age group above 45year (P = 0.002).

Conclusion: We found high prevalence of anti-TPO in chronic HCV infected patients (20%). The tendency to develop thyroid dysfunction after initiation of Interferon based therapy proven in many studies, this implies the need for screening of those patients for the presence of such antibodies and cooperation with endocrinologist for optimal patient care.

Keywords: TPO, HCV, Prevalence, Libya.

Introduction: Hepatitis C virus infection (HCV) is the major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma worldwide, it is estimated that more than 170 million person in the world are chronically infected with HCV (1,2). The frequency of HCV antibodies reported to be positive in 11.6% of patients with autoimmune thyroid disease (3,4). Extrahepatic manifestations of chronic HCV infection are clinically evident in nearly 40% of patients including hematologic diseases such as cryoglobulinemia and B-cell non-Hodgkin's lymphoma, autoimmune disorders such as thyroiditis, Membranoproliferative,
glomerulonephritis, and dermatologic diseases such as lichen planus, porphyria cutanea tarda and the presence of end organ autoantibodies which frequently associated with HCV infection\(^{(3,5,8)}\). Autoimmune disease like autoimmune thyroiditis and auto antibodies like antithyroid peroxidaes (Anti-TPO) and antithyroglobulin (Anti-TG) antibodies are reported to be high in HCV patients\(^{5-7}\). Thyroid disorders (TD) are common in patients with chronic HCV, anti-thyroid antibodies are present in 5-17% of patients with HCV infection, and thyroid disease, primarily hypothyroidism, occurs in 2-13% of patients, middle age women seems to be more vulnerable to develop thyroid dysfunction than males\(^{9}\). The prevalence of anti-TPO varies between 2-15% in different studies \(^{10,12}\). Autoimmune thyroid disease is the result of a complex interaction between genetic, endogenous and environmental factors, recent studies have shown a high prevalence of antithyroid antibodies in patients with HCV before Interferon treatment, once combined pegelyted Interferon alpha and ribavirin therapy is initiated, the frequency of patients with TD goes up to 15–20% suggesting that autoimmune thyroid disease could be induced by HCV infection as well as by Interferon therapy\(^{13,14}\). Patients with severe fibrosis have more TD events at baseline and during treatment with Interferon alpha and for this reason patients with advanced hepatic fibrosis require careful attention to diagnose and manage TD \(^{15}\).

**Aims and objectives:**

The aim of this study is to determine the frequency of thyroid peroxidaes antibodies among chronic HCV patients before treatment with Interferon.

**Subjects and Method:**

The cohort of this study were chronic HCV infected patients who were referred to the clinic of viral hepatitis at Aljomhoria hospital in Benghazi city which is considered the main referral center for management of HCV infected patient in eastern part of Libya with more than fifteen year experience. The Period of the study extended from June 2009 till the end of 2010. At the entry to the clinic all patients were initially diagnosed using a third generation ELISA. All patients were interviewed by an experienced specialist, a complete clinical history was taken and a full physical examination was performed. Patients who met one or more of the following criteria were excluded from the study; patients with history of coinfection with hepatitis B virus or HIV, patients with thyroid autoimmune disorders, patients with positive family history of Grave's disease, type 1 diabetes mellitus or goiter, and patients who previously received interferon therapy.

HCV-RNA-quantitative assay was done by COBAS-AMPLICOR Roche diagnostic with lower threshold of detections of less than 600 IU/ml and the level of viremia was defined as; low viremia when PCR level is log 4 or less, intermediate viremia when PCR level is log 5 and high viremia when PCR level is log 6 or more. HCV genotype assay done by the same technique; The thyroid stimulating hormone (TSH)
measurement was performed by using electro chemical immunoassay Kit-200 tests Elecsys 2010, Roche, USA for TSH with normal range between 0.270-4.20 IU/ml while Anti-TPO level was determined by using immune assay Kit-100 tests Elecsys 2010 Roche, USA with upper normal range of 34mIU/ml. All of these tests were performed at the central laboratory at Aljomhoria hospital. Regarding the age variable the patients were classified into two groups (≤ 45 years and > 45 years).

**Statistical analysis** was performed using the SPSS program version 11.5. Demographic and diseases specific variables were examined by t-Test, Chi-Square test, correlation coefficients and Fisher Exact to assess the relationships between the different variables and the presence of anti TPO with 95% CIs. P value of < 0.05 was considered statistically significant.

**Result:**
The total number of the patients included in this study was 120 patients. Half of the patients (50%) were males, their ages range from 17 to 71 years with mean age 44±8 years. The majority of patients (36.7%) were between 50 and 59 year old table1. The duration of HCV infection since the diagnosis ranged from 2 to 10 years. According to the patients’ past history the possible (although not certain) risk factors for acquiring HCV infection were dental procedures 35% followed by blood transfusion 21.66% and surgery 13.33%, while in 21.66% of the patients we were not able to identify any possible risk factor. Mild viremia was found in 28.33% of patients while 38.33% had an intermediate viremia and 33.33% had high viremia. The most predominant viral genotype was genotype 4 (91.7%) followed by genotype 1 (5%), genotype 2 (1.7%), genotype 5 (0.83%) and genotype 3 (0.83%) table 2. Twenty four patient (20%) has Anti-TPO level above cut-off value (> 34mIU/ml), and there was no statistical significant difference between males and females (15% vs. 25%) (P = 0.171) figure . The relation between the age and the anti-TPO level was not statistically significant (19.6% vs. 20.3%, P = 0.927). There was no significant difference in the frequency of high anti-TPO levels between patients with low, intermediate or high viremia (17.6% vs. 19.5% vs. 22.5%, p= 0.87). Cases with TSH more than 4.2 IU/ml found in 15 patient (12.5%) and it was significantly more prominent among the age group older than 45 year (21.87 vs. 1.78, P =0.002).

<table>
<thead>
<tr>
<th>Table 1. Distribution of cases a according to sex</th>
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<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
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</tr>
<tr>
<td>Male</td>
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<tr>
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Table 2. Distribution of cases according to genotype.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>1a</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>1b</td>
<td>3</td>
<td>2.5%</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1.7%</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0.8%</td>
</tr>
<tr>
<td>4</td>
<td>110</td>
<td>91.7%</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0.8%</td>
</tr>
<tr>
<td>Total</td>
<td>120</td>
<td>100</td>
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</table>

Figure. Distribution of cases according to anti-TPO level

Discussion: Autoimmune thyroid disease and autoantibodies against thyroid tissue are frequently reported in patients with chronic HCV infection (16-18). Thyroid dysfunction in those groups of patients tends to be higher in middle aged females and genetic susceptibility may play a role in the development of such disorder (19,20). Hypothyroidism and high titer of anti-TG and anti-TPO are the most frequently reported thyroid disorders among patients with chronic HCV infection; however some studies found no epidemiological evidence regarding the association between thyroid autoantibodies and HCV infection (12,21-23). The prevalence of anti-TPO in our study is 20% which is considerably high when compared to other studies (16, 17,21,22). We did not find any significant deference in the prevalence of anti-TPO between males and females although in most of the previous studies, middle aged females were more susceptible to develop thyroid disorders before and during interferon therapy (20). Also we did not find any statistically significant association between the level of virimia and the presence of high level of anti-TPO which is noted in other similar studies (24). Although we noticed a trend toward increasing the frequency of high anti TPO with the increased level of viremia. The level of TSH was higher in the age group above 45 years old regardless the sex of the patients which was statistically significant.

Study limitations: The study sample was large enough to fulfill our aims; however a larger sample would be more suitable to compare minor differences between subgroups.

Since about 92% of the viral genotypes were genotype 4, it was not possible to make a valid comparison between different genotypes regarding the level of anti-TPO.

The comparison between the prevalence of high anti TPO levels and high TSH levels in patients with chronic HCV infection and the general Libyan population was not possible in this study because of the lack of data regarding the frequency of such disorders among general population.
The relationship between liver fibrosis and anti-TPO level was not explored in this study, which worthy further studies.

**Conclusion:** The anti-TPO antibodies are highly prevalent among our patients with chronic HCV infection (20%), and it seems that there is no any statistically significant difference in the prevalence among males and females. The prevalence of high TSH was significantly higher in patients who were older than 45 years.

**References:**


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