# A Prospective Study on Prevalence of Thyroid Disorders in Hepatitis C Virus Infected Patients in a Tertiary Care Teaching Hospital.

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## ABSTRACT

**Background:** Hepatitis C virus (HCV) infection has been associated with thyroid abnormalities. Therefore this study was conducted to determine the association of thyroid disorders with chronic hepatitis C virus infection in patients who are not getting any antiviral treatment. **Methods:** Sixty-five 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 our study. Blood samples from 65 patients were collected at base line, 04 months, 08 months and at 12 months. The level of thyroid stimulating hormone (TSH) and thyroid antibodies was measured in these samples. **Results:** Nine patients (13.84%) developed thyroid disorder during the study period. Female patients (66.66%) mostly affected than males (33.33%). Among n=9 affected cases, 66.66% developed hyperthyroidism, 22.22% developed hypothyroidism and 11.11% developed positive thyroid antibody. **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, T3, T4.

## INTRODUCTION

Hepatitis C virus (HCV) infection, being the second most common chronic viral infection in the world, having a global prevalence of approximately 3%, responsible for major global health problem in the world.[1] It is estimated that 170 million persons in the world are infected with HCV. Every year 3 to 4 million new cases of infection are seen due to transfusion contamination, contaminated injection needles, and parenteral exposure.[2]

HCV is both a hepatotropic as well as a lymphotropic virus and therefore chronic infection is known to be responsible for both hepatic and extrahepatic diseases.[2,3] A high prevalence of thyroid autoimmunity and hypothyroidism,[4,5] as well as of papillary thyroid carcinoma,[6] has been seen in patients suffering from chronic HCV infection.

There are many extrahepatic diseases caused by chronic HCV infection and, in most cases, viral infection is the main culprit responsible for causing these manifestations like: hematologic diseases such as cryoglobulinemia and lymphoma, autoimmune disorders such as thyroiditis and the presence of autoantibodies, renal disease, dermatologic conditions such as lichen planus and porphyria cutanea tarda.[7-10]

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Previous literature revealed that the thyroid disorders are common in patients with chronic HCV, particularly women. Anti-thyroid antibodies are present in 5% to 17% of patients with HCV infection, and thyroid disease, primarily hypothyroidism, occurs in 2% to 13% of patients and up to 25% have thyroid antibodies.[5,11] The highest prevalence of both thyroid antibodies and thyroid disease is mainly seen in cases of older women. Most HCV patients with thyroid dysfunction are middle-aged women with asymptomatic hypothyroidism and do not require specific treatment. However, whether or not the prevalence is higher than in age and sex-matched controls is controversial.[12,13]

Thyroid autoantibodies and disorders have been reported in patients with chronic hepatitis both before and after IFN-alpha treatment, but the prevalence appears greater in those with chronic HCV virus infection.[14,15]

Hepatitis C (HCV) is now the main cause of chronic hepatic disease, cirrhosis and hepatocellular carcinoma.

Some patients with chronic hepatitis C experience thyroid problems, and thyroid dysfunction may also be a side effect of interferon (IFN)-based treatment. Also 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. Therefore this study was carried out to know the prevalence of thyroid disorders in Hepatitis C infected patients who were not treated with interferons.

## MATERIALS AND METHODS

This was prospective observational study was conducted on Hepatitis C virus infected patients visited the hospital from Feb 2012 to April 2013 at Gujrat Adani Institute of Medical Sciences, Bhuj, Gujarat. On the basis of inclusion and exclusion criteria, total of n=65 patients Diagnosed with HCV infection with normal thyroid function, who were not willing to get anti-HCV treatment (interferon) were included in our study. After then patients were followed for 1 year at every 4 months interval. Patients with pre-existing thyroid abnormality were excluded from our study.

A written informed was taken from each patient before the commencement of the study. Approval from Institutional Ethical Committee was also granted before starting the study.

The present study was conducted in the department of Biochemistry and Microbiology at Gujrat Adani Institute of Medical Sciences, Bhuj, Gujarat.

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 4, 8 and 12 months.

Thyroid Stimulating Hormone (TSH): The normal limits are between 0.4 to 4.0 IU/ml.

Autoantibodies: Sera were investigated for the presence of thyroid microsomal antibodies.

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.

Positive anti-TPO antibodies (>35 IU/ml) and anti-Tg antibodies (>40 IU/ml) were indications for complicated chronic thyroiditis.

Thyroid abnormality confirmed when TSH level of either more than 4.0 (hypothyroidism) or less than 0.1 (hyperthyroidism) mU/L, irrespective of FT3/FT4 levels.

## RESULTS

Among n=65 patients enrolled in our study, most of the patients were female (n=36, 55.38%) in comparison to male (n=29, 44.61%) [Table 1]. Out of 65 patients, only n=9 (13.84%) patients were found to have thyroid abnormalities. Females patients (n=6, 66.66%) were found mostly affected with thyroid abnormalities than males (n=3, 33.33%) [Table 1]. Most of the patients were found in 20-40 age group (n=37) followed by 41-60 age group (n=25) and least in 61-80 age group (n=3). Percentage of patients developing thyroid disorders were more in 20-40 age group (n=6) and least in 41-60 age group (n=3) [Table 1].

Among females, n=4 patients developed Hypothyroidism with rise in TSH level, and n=1 developed positive thyroid antibody during study period and n=1 patient developed hyperthyroidism. Whereas in males, n=2 patient had raised TSH level, n=1 developed hyperthyroidism.

According to the above defined criteria defined, 9 patients (13.8%) developed thyroid abnormalities during the study period. Out of these 9 patients, 66.66% developed hyperthyroidism, 22.22% developed hypothyroidism and 11.11% developed positive thyroid antibody.

The baseline average TSH level of the study population who developed thyroid disorder was 4.75 µIU/ml. During follow up period, eight patients showed change in TSH levels beyond normal limits. Out of these, n=6 developed hypothyroidism and n=2 hyperthyroidism. The patients who developed hypothyroidism were treated with Levothyroxine tablets and TSH level reverted to normal within three months in all patients [Table 2].

**Table 1**: Demographic details of patients enrolled (n=65).

| Age Group | Males n=29 (44.61%) | | Females n=36 (55.38%) | | Total n=65 | |
|---|---|---|---|---|---|---|
| | Infected (n=3) | Not-infected (n=26) | Infected (n=6) | Not-infected (n=30) | Infected (n=9) | Not-infected (n=56) |
| 20-40 | 2 | 14 | 4 | 17 | 6 | 31 |
| 41-60 | 1 | 10 | 2 | 12 | 3 | 22 |
| 61-80 | - | 2 | - | 1 | - | 3 |

**Table 2:** Patients developing thyroid abnormalities at follow up

| | Baseline | 4 months | 8 months | 12 months |
|---|---|---|---|---|
| Mean TSH level (IU/ml) | 4.7 | 3.61 | 3.22 | 3. 17 |
| Hypothyroid | - | 1 | 4 | 1 |
| Hyperthyroid | - | - | 2 | - |
| Positive thyroid antibody | - | - | 1 | |

## 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 13.84% of the study population showed development of thyroid disorders during the study period. These results are contradictory to the results showed in the similar study conducted by Antonelli A. 2004, Dalgard O. 2002[16,17] revealing higher percentage of conversion of euthyroid to Thyroid disorders. 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 present study clearly showed the possibility of association of thyroid disorders in patients infected with Hepatitis C Virus and the results of our 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.[16,18]

In our study, Prevalence of thyroid disorders were higher in women (n=6, 66.6%) than in men (n=3, 33.3%), which contradicts the similar study conducted by 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).[17,19] But our findings were in accordance with the study conducted by Hsieh et al, who 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.[20] Similarly Vezali E et al, 2009 showed that the incidence of Thyroid disorders in women (nine of 13, 69.2%) was higher than that observed in men (four of 13, 30.8%). In the present study viral genotypes were not accounted as previous similar studies showed that the serological pattern of autoantibodies does not correlate with a particular genotype of HCV.[21]

Our study revealed that the among thyroid disorders due to Hepatitis C infection, Hypothyroidism is most commonly found than Hyperthyroidism. These findings were in accordance with study conducted by Vezali E et al, 2009.[21]

The results of the study conducted by Antonelli A et al, 2004 also revealed that both hypothyroidism and thyroid autoimmunity are more common in patients with Chronic Hepatitis C, even in the absence of cirrhosis, hepatocellular carcinoma, or interferon treatment, than in HCV-negative controls or in patients with chronic hepatitis B infection.[5]

## CONCLUSION

The abovementioned results showed a high prevalence of Thyroid abnormality in patients with Chronic Hepatitis C infection. The presence of a higher risk of thyroid disorders in female gender, increased circulating levels of thyroid antibodies, and increased risk of hypothyroidism in female gender and Ab-positive subjects suggested the pattern of thyroid disorders observed in HCV infection. Therefore according to our study patients affected with Hepatitis C virus should be carefully monitored for thyroid abnormalities.

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