

# Thyroid Autoantibodies in Chronic Hepatitis C Patients Treated With Interferon Alpha Therapy

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## ABSTRACT

The aim of study is to study the thyroid auto antibodies in chronic hepatitis C patients treated with interferon alpha therapy. 70 cases of chronic hepatitis C disease were selected for the study. They were divided into two groups Group A included 35 patients of chronic hepatitis C with positive HCV, RNA on PCR who have received 06 months combined therapy of interferon alpha and ribavirin. Group B included 35 patients of chronic hepatitis C with positive HCV RNA on PCR, not taking any therapy. The subjects were selected from different hospitals. Biochemical parameters i.e. Anti-TG antibodies and anti-TPO antibodies were done by commercially available kits by ELISA methods. Sign test is applied for the level of significance. Following conclusions are drawn: Females are more prone to develop thyroid dysfunctions i.e. 4/35 (11.5%) as compared to males. Anti-TPO antibodies were increased i.e. 03/35 (8.6%) in hepatitis C patients after interferon and Ribavirin Therapy. Anti-TG antibodies were increased i.e. 02(5.7%) in hepatitis C patients after interferon alpha and Ribavirin Therapy.

**Key words:** Hepatitis C, anti TPO antibodies

## INTRODUCTION

In recent years, it has been established that the combination of IFN- $\alpha$  with ribavirin (RIBA) may increase the biochemical and virological response rates in chronic hepatitis C (CHC) patients to about 40%<sup>1</sup>. Currently the combination therapy IFN- $\alpha$  and RIBA is the first line treatment in patients<sup>2</sup>. Interferon is a low molecular weight glycoprotein cytokines produced by host cells in response to viral infections. Interferon bind to specific cell surface receptors and effect viral replication at multiple steps: viral penetration, synthesis of viral mRNA, assembly of viral particles and their release, but the most widespread effect is direct or indirect suppression of viral protein synthesis<sup>3</sup>.

## MATERIALS AND METHODS

It was a cross sectional comparative study done in department of Pathology, Quaid -i- Azam Medical College, Bahawalpur.

**Groupings:** A total of 70 patients of chronic hepatitis C with positive HCV RNA on PCR were included in this study. Two different groups of patients were made.

**Group A:** It comprised 35 patients of chronic hepatitis C with HCV RNA positive on PCR, who have received six months combined therapy of interferon alpha and ribavirin. Before start of therapy, their baseline values regarding thyroid dysfunction were also taken. Group A is further divided into two sub groups: **Group A1:** Patients of Chronic hepatitis C before interferon therapy. **Group A2:** Patients of Chronic hepatitis C after interferon therapy.

**Group B:** It comprised 35 patients of chronic hepatitis C with positive HCV RNA on PCR, not taking any therapy. They were also followed for thyroid dysfunction for the same period of time. Group B is further divided into two sub groups: **Group B1:** Patients of Chronic hepatitis C before study. **Group B2:** Patients of Chronic hepatitis C after study.

**Inclusion Criteria:** Both male and female adult cases of Chronic hepatitis C with positive HCV antibody, elevated ALT level and positive HCV RNA on PCR with normal thyroid function tests.

**Exclusion Criteria:** Patients having history of thyroid disease confirmed by investigations i.e. TSH, T3, T4.

## RESULTS

The detail of results is given in tables 1, 2 and 3

Table 1: Comparison of anti-TPO in group A before and after therapy

Anti TPO	Group A (with therapy)	
	A1 Vs A2	p <0.05 ( Significant)
Negative signs	31	
Positive signs	04	

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Difference	27	
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**Sign test is applied.**

**Key: Group A1:** Patients of Chronic hepatitis C before interferon therapy

**Group A2:** Patients of Chronic hepatitis C After interferon therapy

Table 2: Comparison of anti-TG in group A before and after therapy

Anti TG	Group A (with therapy)	
	A1 Vs A2	
Negative signs	28	p <0.05 (Significant)
Positive signs	07	
Difference	21	

**Sign test is applied.**

Table 3: Different markers in group A

Parameters	Patients with positive markers	Patients with negative markers
TSH	06 (17.2%)	29(82.8%)
Anti-TPO	03(8.6%)	32(91.4%)
Anti-TG	02(5.7%)	33(74.3%)

## DISCUSSION

Regarding Anti-TG antibodies in this study, out of 35 patients, 03/35 (8.6%) patients were with increased levels of anti-TG antibodies. This study is in favor of the results of Kee et al (2006)<sup>4</sup> i.e., 9.2% and Mandac et al (2006)<sup>5</sup> i.e. 9.8% who also observed increased levels of anti-TG in patients with IFN and Ribavirin therapy.

In other studies, the development of thyroid dysfunction during interferon alpha monotherapy with HCV have been well described, and the incidence ranges from 2.5% to 34.3%<sup>6</sup>. These studies have shown that hypothyroidism was more common than hyperthyroidism (3.8% vs 2.8%), and thyroid dysfunction occurred more often in females than males (13.0% vs 3.0%)<sup>7</sup>. The strongest risk factors that were associated with an increased risk of development of thyroid disease during interferon alpha therapy were female sex and the presence of thyroid auto antibodies (particularly thyroid peroxidase antibodies) before the initiation of therapy.<sup>8</sup> Thyroid disease is less likely to develop in patients with chronic hepatitis B infection who are treated with interferon alpha only than in those with chronic HCV infection, despite the use of higher doses of interferon alpha for the treatment of hepatitis B virus.<sup>100</sup> This finding suggests that HCV and interferon alpha may have a synergistic role in inducing thyroid disease during antiviral therapy.

In this study, out of 35 patients, 02(5.7%) patients were with increased levels of Anti-TPO Antibodies. This study is consistent with the results of Dalgard et al (2002)<sup>9</sup> i.e. 6.2% and Manns et al

(2001)<sup>10</sup> i.e., 6.8% who also observed increased levels of anti-TPO antibodies in patients of CHC after interferon and Ribavirin therapy. In another study, Huang et al (2006)<sup>11</sup> showed 11.6% anti TPO antibodies among CHC patients receiving combined INF/ribavirin therapy while 14.7% patients developed TD after six months of treatment. In another study, the prevalence of thyroid auto-antibodies among Taiwanese CHC patients with normal base-line thyroid function is approximately 8.4%, and female patients had slightly higher prevalence of both thyroid anti-bodies than those of male patients (8.6% vs. 6.7%)<sup>12</sup>

Edmund et al (2004)<sup>13</sup> observed that out of 225 patients, 12(5.8%) patients showed hypothyroidism. Anti thyroglobulin antibodies were present in 10 (4.4%) patients while anti TPO were present in 11(4.9%) cases. Kwong et al (2006)<sup>14</sup> observed that at the end of treatment, anti-TPO were observed in 12 patients (12/116, 10.3%) while our study showed 2/35 i.e. 5.7% anti TPO antibodies in patients of CHC disease with interferon/Ribavirin therapy. Vezali et al (2009)<sup>15</sup> studied 94 patients with CHC and normal thyroid functions were evaluated. 13 (21.3%) patients developed TD and 11 of these were with hypothyroidism.

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