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ASSESSING THE PRESENCE OF ANTI-THYROID PEROXIDASE (ANTI-TPO) AND ANTI-THYROGLOBULIN (ANTI-TG) AUTOANTIBODIES IN INDIVIDUALS INFECTED WITH THE HEPATITIS C VIRUS.

Junaid Mahmood Alam[1*], Amna Hussain[2], Syed Riaz Mahmood[3]

Department of Clinical Biochemistry lab services and Chemical Pathology, Liaquat National Hospital and Medical College, Karachi-Pakistan.[1]
Pathology Laboratories, Jinnah medical college and Sohail University Hospital, Karachi.[2]
Department of Pathology, Lyari General Hospital, Karachi[3]

Abstract: Thyroid autoimmunity is designated as one of the most recurrent endocrine ailment associated with chronic HCV infection. Numerous research studies noted the prevalence of thyroid dysfunction and production of anti-thyroid antibodies (ATAb) such as anti-thyroid peroxidase (AntiTPO) and anti-thyroglobulin (AntiTG) in patients with HCV. Present study was designed to determine the existence and prevalence pattern thyroid antibodies in hepatitis C infected patients. Thyroid autoimmunity is designated as one of the most recurrent endocrine ailment associated with chronic HCV infection. Numerous research studies noted the prevalence of thyroid dysfunction and production of anti-thyroid antibodies (ATAb) such as anti-thyroid peroxidase (AntiTPO) and anti-thyroglobulin (AntiTG) in patients with HCV. Aim: Therefore, present study was designed to determine the existence and prevalence pattern thyroid antibodies in hepatitis C infected patients. Analysis showed the presence of elevated levels of AntiTG in 12 HCV patients (30%), AntiTPO in 15 (37.5%) and both AntiTG & antiTPO in 10 patients (25%). Only 3 patients were found with history of anti-thyroid auto-antibodies (7.5%) and one with parents & relatives with auto-immune disorders (2.5%). Patients that remained untreated were 12 (30%), under treatment 18 (45%) and with complete-course of treatment 10 (25%). Our current study reiterated that thyroid disorders and/or autoimmunity in HCV patients existed with complex underlying mechanisms where chronic infections carries noteworthy role. Moreover, treatments with IFN also plays significant intriguer in instigating auto-immunity that more likely to encompass thyroid disorders specially related to development of either of thyroid auto-antibodies.

Key words: Anti thyroid peroxidase (Anti TPO), Anti-thyroglobulin (Anti Tg) autoantibodies, Hepatitis C viral infections

INTRODUCTION

Several recent and past studies have reported a notable prevalence of thyroid dysfunction and the presence of anti-thyroid antibodies (ATAb), such as anti-thyroid peroxidase (Anti-TPO) and anti-thyroglobulin (Anti-Tg), in patients with HCV (Mazur, 2021;Ludgate *et al*, 2024; Indolfi *et al*, 2008; Antonelli, 2004). Furthermore, interferon therapy, commonly used to treat HCV infections, has been linked to the development or exacerbation of thyroid disorders, including
autoimmune conditions like Graves' disease and Hashimoto's thyroiditis (Li and Li 2025; Wang *et al*. 2021; Jadali, 2013; Gregorio *et al*. 1998; Shen *et al*. 2016; Antonell *et al*. 2006). A review of the literature, including meta-analyses and cross-sectional studies of selected cohorts, indicates that thyroid disorders are among the most frequent endocrine complications associated with chronic HCV infection (Jadali, 2013; Gregorio *et al.* 1998; Shen *et al.* 2016; Antonelli *et al.* 2006) These thyroid abnormalities are also considered part of the extrahepatic manifestations within the spectrum of HCV-related diseases. Moreover, the prevalence of anti-thyroid antibodies, including antithyroid microsomal antibodies (ATMA), has been reported to vary widely from less than 3% up to 48% among HCV patients undergoing interferon-alpha treatment (Shen *et al*. 2016; Fernandez *et al.* 1998; Quaranta *et al*. 1993). In light of this,

the present study aims to determine the presence and prevalence patterns of thyroid antibodies in patients infected with hepatitis C.

MATERIALS AND METHODS

Patient's selection

Current study is case-control study carried out at Department of Clinical Biochemistry lab services and Chemical pathology, LNH & Medical College, Karachi in collaboration with Department of Pathology, Lyari General Hospital, Karachi (Jan 2023-Dec 2024). Study includes two control groups for comparison purpose,

Control group 1, without HCV infection and with thyroid disorders (n = 20)

Control group 2, with HCV infection and without thyroid disorders (n = 20), whereas HCV infected were patients n = 40 where more than half were noted to be positive for either of HCV IgG and Ag.

Mean age in **control group 1**, 56.50 ± 3.60,

control group 2, 55.45 ± 6.55 and HCV infected patients = 56.10 ± 9.85.

Inclusion criteria for HCV infected patients 1) vertical HCV infection; (2) no previous or ongoing surgical treatments and (3) the availability of at least two of stated lab tests results, HCV either of HCV IgG and Ag, and/or alanine transaminase (ALT) and viraemia tests in last 7-8 months. Medical records were carefully investigated with other human immunodeficiency syndromes and/or hepatitis B virus co-infections were not included.

Determination of thyroid function and auto-antibodies

Those patients either in control groups I and II and in infected group, if doesn't already have thyroid function results, were tested for thyroid function (TSH, T3, T4, FT4, FT3) and thyroid autoimmunity [anti-thyroglobulin (TgA) and anti-thyroperoxidase (TPOA) antibodies]. Similarly, they were also tested for HCV viral load (if not already available); in addition to complete liver function tests. To define thyroid disorders and autoimmunity, protocols described by Indolfi were followed (Indolfi *et al*. 2008). Subclinical hypothyroidism was defined as TSH level > 4•0 mU/l together with normal serum thyroid hormone levels. Overt hypothyroidism was defined as raised TSH together with a decreased serum thyroid hormone level (Stagi *et al*. 2005). Autoimmune thyroiditis was defined by elevated Anti-TPO and/or Anti-Tg values, and elevated TSH levels and/or typical hypoechogenicity of the thyroid ultrasound (Stagi *et al*. 2005).

Analytical methods and processes

All analytical methods were standardized according to AACC, IFCC and CLSI protocols. HCV antibodies were detected by a third-generation enzyme-linked immunosorbent assay (Roche Diagnostic and Abbott Laboratories) whereas HCV RNA was determined by RT-PCR with nested primers (Roche Diagnostics). Liver function test components were determined by methodsdescribed earlier18 on Modular chemistry analyzer c501 Cobas 6000. Thyroid profile tests (TSH, T3, T4, FT3, FT4) were determined by electrochemiluminescence (ECL) technology on Immunoassay analyzer e411 using 3rd generation principles (Roche Diagnostics). Anti-Tg and Anti-TPO antibodies were determined by ECL enzymatic immunoassays using pre-analytical systems p471 p512 integrated with e411 e801. Normal adult reference ranges for thyroid function tests are T3 = 0.80-2.00 ng/ml; T4 = 5.1-14.10 μg/ml; TSH = 0.27-4.2 μIU/ml; FT3 = 1.90-5.10 pg/ml; FT4 = 0.9-1.7 ng/ml; AntiTG Ab = <115 IU/ml; AntiTPO = <34 IU/ml/.

Statistical analysis

The statistical program SPSS (SPSS 15•0) (SPSS Inc., Chicago, IL) was used to analyse all results and comparative data. P-values< 0.05 were deemed statistically significant in the two-tailed test. The association between the independent variable, thyroid profile elements, and auto-antibody levels was examined using a straightforward linear regression analysis. Standard deviations and mean levels are used to express the findings.

RESULTS

Results are summarized in Table 1 and 2. In HCV group, Patients with existing sub-clinical hypothyroidism and clinical hyperthyroidism were less than 5%. Analysis showed the presence of elevated levels of AntiTG in 12 HCV patients (30%), AntiTPO in 15 (37.5%) and both AntiTG & antiTPO in 10 patients (25%). Only 3 patients were found with history of anti-thyroid auto-antibodies (7.5%) and one with parents and relatives with auto-immune disorders (2.5%).Twelve patients (30%) remained untreated, eighteen patients (45%) were receiving treatment, and ten patients (25%) were receiving the full course of treatment. Anti-Tg and Anti-TPO antibody levels varied by clinical condition category, with subclinical hypothyroidism patients having Anti TG levels of 134.70±26.85 IU/ml and Anti TPO levels of 56.30±15.75 IU/ml, one patient having Anti TPO levels of 55.80 IU/ml, patients with a history of anti-thyroid auto-antibodies = Anti TG 120.25±25.65 IU/ml and AntiTPO 65.60±20.55 IU/ml, and one parent or family with auto-immune disorders having Anti TG levels of 123.45 IU/ml and Anti TPO levels of 30.45 IU/ml.

DISCUSSION

Thyroid disorders or dysfunctions were identified as one of the most common endocrine conditions, strongly associated with chronic HCV infection, by a review of the literature

Table 1: Characteristics of patients' thyroid and Hepatitis C (HCV) infection status, HCV antigen and antibody profile and treatments

Categories	Control group 1	Control group 2	HCV infected patients	*HCV IgG Levels	**HCV Ag Levels
Number of patients	20	20	40	37	35
Patients with sub-clinical hypothyroidism	05 (25%)	01 (5%)	02 (5%)	Positive 21 (56.75%)	Positive 26 (74.28%)
Patients with sub-clinical hyperthyroidism	07 (35%)	00	01 (2.5%)		

Presence of AntiTG	05 (25%)	Nil	12 (30%)		
Presence of AntiTPO	04 (16%)	Nil	15 (37.5%)		
Presence of AntiTG + antiTPO	03 (15%)	Nil	10 (25%)		
Previous history of anti-thyroid auto-antibodies	05 (25%)	01 (5%)	03 (7.5%)		
Parents or relatives with auto-immune disorders	06 (30%)	01 (5%)	01 (2.5%)		
HCV infections	nil	07 (35%)	40		
-Untreated		06 (30%)	12 (30%)	17 (80.95%)	20 (76.92%)
-Under treatment		11 (55%)	18 (45%)	02 (9.52%)	06 (23.07%)
-Treated		03 (15%)	10 (25%)	02 (9.52%)	00

Control group 1 = without HCV infection and with thyroid disorders
Control group2 = with HCV infection and without thyroid disorders
*patients with HCV IgG out of n = 40 HCV infected patients
**patients with HCV IgG out of n = 40 HCV infected patients

that included recent and previous studies, statistical evaluations, current data, and cross-sectional comparative studies (Li and Li. 2025; Indolfi, *et al*. 2008; Jadali, 2013; Fernandez, *et al*. 1998). More specifically, in a sequence of HCV infection development, it also presents with an extrahepatic disease or syndrome. Additionally, endocrine disorders, skin conditions, and musculopathies are examples of extrahepatic manifestations linked to HCV (Li and Li, 2025; Pastore *et al*., 2016; Jadali, 2012; Jadali and Alavian, 2010). Additionally, it was noted that every patient with an HCV infection had at least one extra-hepatic disorder during the course of their illness. Thyroid disorders may be caused by a variety of factors, most of which are genetic or environmental (Jadali, 2013; Shen *et al*. 2016; Akeno *et al*. 2008; Blackard *et al*. 2013). Infectious agents received more attention than any other environmental agent, and one of the most compelling findings was the presence of HCV infection (May 2010; Minelli *et al.* 1997; 21. Akeno, Blackrad, and Tomer, 2008; Minelli, *et al*. 1997). Thyroid

Table 2: Prevalence of thyroid auto-antibodies in patients with Hepatitis C infections

Categories	HCV infected patients	TSH (µIU/ml	FT4 (ng/dl)	Anti TG (IU/ml)	Anti TPO (IU/ml)
Number of patients	N = 40				
Patients with sub-clinical hypothyroidism	02 (5%)	21.45±11.65	6.20±1.40	134.70±26.85	56.30±15.75
Patients with sub-clinical hyperthyroidim	01 (2.5%)	0.70	4.50	--	55.80
Presence of AntiTG	12 (30%)	6.10±1.20	1.7±0.45	230.45±55.70	----
Presence of AntiTPO	15 (37.5%)	10.35±3.55	3.40±0.90	----	117.20±30.65
Presence of AntiTG + antiTPO	10 (25%)	8.75±3.45	2.80±1.10	141.15±20.65	78.80±21.45
Previous history of anti-thyroid auto-antibodies	03 (7.5%)	7.25±3.3 0	3.55±1.25	120.25±25.65	65.60±20.55
Parents or relatives with auto-immune disorders	01 (2.5%)	4.50	2.10	123.45	30.45

Results are expressed as mean ± SD

complications were also reported in a number of studies involving patients receiving interferon (IFN-) therapy (Shen *et al*. 2016;Chen, Shao, and Shen, 2015).Kesavachandran (2013)evaluated the fundamentals of the relationship between IFN-therapy and thyroid autoimmune disorders and linked them to the activation of the innate and adaptive immune response, molecular mechanism, and polymorphism in IFN-signaling pathways. Thyroid autoimmunity was confirmed by the significant proportion of HCV-infected patients in our study who showed signs of ATAb. Of these, 30% had high levels of AntiTg, 37.05% had AntiTPO, and 25% had both AntiTg and AntiTPO. Autoimmunity and increased AtAb levels were also observed in patients receiving IFN-a treatment (45%) and those not receiving treatment (30%), indicating a combination of underlying factors that contributed to the autoimmune response. According to earlier research, the prevalence of ATAb in chronic HCV cases ranged from4.5% to 25%1, while AntiTPO ranged from 5.4% to 30% and AntiTg was negligible to 30.7% (Paterson *et al.* 1992; Yang, *et al*. 2011; Floreano *et al*. 2006). 4.5% to 25%, while AntiTPO ranged from 5.4% to 30% and AntiTg was negligible to 30.7% (Paterson *et al.* 1992; Yang, *et al*. 2011; Floreano *et al*. 2006). The precise pathophysiology and aetiology of thyroid disorders and autoimmunity linked to HCV were revealed by additional recent and previous research, which also proposed an underlying mechanism (Patrice et al. 2016). The mechanisms could include cytokine-activation of auto-reactive T-cells, self-antigen response brought on by viral infections, molecular mimicry, and aberrant thyrocyte expression of MHC class II molecules (Martocchia and Falaschi, 2007; Tomer and Villanueva, 2004).

CONCLUSIONS

The occurrence of thyroid disorders and/or autoimmunity in HCV patients is thought to have complex underlying mechanisms, with genetic susceptibility and environmental factors (like the infection itself) playing a significant role. Additionally, IFN-induced therapies are important in triggering autoimmunity, which is more likely to include thyroid conditions, particularly those associated with the development of either ATAb or both antiTG and antiTPO**.**

Conflict of interest

Authors declare no conflict of interest.

REFERENCES

Akeno, N., J.T. Blackrad and Y. Tomer (2008) HCV E2 protein binds directly to thyroid cells and induces IL-8

production: A new mechanism for HCV induced thyroid autoimmunity. *J. Autoimmune*. 31, 339-344.

Antonelli A, C. Ferri, A. Pampana, P. Fallahi, C. Nesti, M. Pasquini, M. Santino, and E. Ferrannini (2004) Thyroid disorders in chronic hepatitis C. *Am. J. Med*. 117, 10-13

Antonelli A, C. Ferri, P. Fallahi, S.M. Ferrari, A. Ghinoi, M. Rotondi and E. Ferrannini (2006) Thyroid disorders in chronic hepatitis C virus infection. Thyroid, 16,: 563-572.

Blackard, J.T., L. Kong, A.K. Huber andY Tomer (2013) Hepatitis C virus infection of a thyroid cell line implication for pathogenesis of hepatitis C virus and thyroiditis. *Thyroid* 7, 863-870.

Chen, Z.X., J.G. Shao and Y. Shen (2015) Prognostic implication of antibodies to soluble liver antigen in autoimmune hepatitis. A PRISMA. Compliant meta analysis. Medicine, 94, e953.

Fernandez, S.J., A, Gonzalez, J..F. Escobar, R. Vazquez, E. Ocete, N. Olea and J. Salmeron (1998).Increased risk of autoimmune thyroid disorder disease in hepatitis C vs hepatitis B before, during, and after discontinuing interferon therapy. *Arch. Intern. Med*. 158, 1445-1448.

Floreano A., C. Betterle, I. Carden, F. Presotto, B. Pedini, A. Muscon. O. Andrea, and M. Chiarammonte (2006) Is hepatitis C virus a risk factor for thyroid autoimmunity? *J. Viral Hepat*. 13, 272-277.

Gregorio,, G.V., P. Pensati, R. Jorio, A. Vegnente, G. Mieli-Vergani and D. Vergani (1998) Autoantibody prevalence in children with liver disease due to chronic hepatitis C virus (HCV) infection. *Clin. Exp. Immunol*. 112, 471-476.

Indolfi, G., Stagi, S., Bartolini, E., Salti, R., de Martino, M., Azzari, C. *et al*. (2008) Thyroid function and anti-thyroid auto-antibodies in untreated children with vertically acquired chronic hepatitis C virus infection. *Clin. Endocrinol*. 68, 117-121.Jadali Z, S.M. Alavian (2010) Autoimmune diseases co-existing with hepatitis C virus infection. *Iran J. Allergy Asthma Immunol*. 9, 191-206.

Jadali Z. (2013) Autoimmune thyroid disorders in hepatitis C virus infection: Effect of interferon therapy. *Indian J. Encrocrinol. Metab*., 17, 69-75.

Jadali, Z. (2012) Dermatologic manifestation of hepatitis C infection and the effect of interferon therapy: A literature review. *Arch. Iran. Med.* 15, 43-48.

Kesavachandran, C.N., F. Haamann and A. Nienhaus (2013) Frequency of Thyroid Dysfunctions during Interferon alpha treatment of single and combination therapy in Hepatitis C Virus-Infected Patients: A Systematic Review Based Analysis. *PLoS One.* 8, e55364. https://doi.org/10.1371/journal.pone.0055364

Li Y and W. Li (2025) Viral infection and thyroid disorders: a narrative review. *Front. Microbiol*. 16:1625179.

Ludgate, M. E., G. Masetti, and P. Soares (2024) The relationship between the gut microbiota and thyroid disorders. *Nat. Rev. Endocrinol*. 20, 511-525.

Mazur L. (2021) Prevalence of thyroid dysfunction in untreated chronic hepatitis C Endocrine Abstracts 73 AEP684, DOI: 10.1530/ endoabs.73. AEP684, ECE2021

Minelli, R., L. E, Braverman, T. Giuberti, C. Schianchi, E. Gardini, M. Salvi, et al. (1997) Effects of excess iodine administration on thyroid function in euthyroid patients with a previous episode of thyroid dysfunction induced by interferon-alpha treatment. *Clin. Endocrinol.* 47, 357-361.

Narciso-Schiavon, J.L. and L.L. Schiavon (2015) Autoantibodies in chronic hepatitis: A clinical perspective. *World J. Hepatol*. 7, 1074-1085.

Pastore F., A. Martocchia, M. Stefanelli, P. Prunas, S. Giordano, L. Toussan, *et al.* (2016) Hepatitis C virus infection and thyroid autoimmune disorders: A model of interaction between the host and the environment. *World J Hepatol*. 8, 83-91.

Paterson D, D.J. Hartman, J.C. Duclos-Vallee, H. M. Jouanolle, Beaugrand. (1992) Latent autoimmune thyroid disease in patients with chronic HCV hepatitis. J, *Hepatolo*. 16, 244-245.

Patrice, C., C. Comarmond, F. Domont, L. Savey, A.C. Desbois and D. Saadoun (2016) Extrahepatic manifestations of chronic hepatitis C virus infection. *Ther. Adv. Infect. Dis*. 3, 3-14.

Quaranta, J. F., A. Tran, D. Regnier. R. Letestu, C. Beusnel, J.G. Fuzibet, V. Thiers, and P. Rampal (1993) High prevalance of antibodies to hepatitis C virus (HCV) in patients with anti-thyroid autoantibodies. *J. Hepato*. 18, 136-138.

Shen Y, X-L. Wang, J-P. Xie, J-G. Shao, Lu, Y-H., Zhang, S., Qin, G. (2016) Thyroid disturbance in patients with Chronic Hepatitis C infection: A systemic review and Meta-analysis. *J Gastrointestin Liver Dis*. 25, 227-234.

Stagi S, T, Giani, G, Simonini and F. Falcini (2005) Thyroid function, autoimmune thyroiditis and coeliac disease in juvenile idiopathic arthritis. *Rheumatology*, 44, 517-520

Stagi S., G. Bindi, A.S. Neri, E, Lapi, S, Losi, R, Jenuso, R. Salti and F. Chiarelli (2005) Thyroid function and morphology in patients affected by Williams syndrome. *Clin. Endocrinol*., 63, 456-460.

Wang H, Y. Liu and Y. Zhao (2021) The association of hepatitis C virus infection and thyroid disease: A systematic review and meta-analysis. *Int. J. Biol. Markers*, 36, 3-9.

Yang, R., Z. Shan, Y. Li, C. Fan, C. Li and W Teng (2011)Prevalence of thyroid autoantibodies in Hepatitis C and Hepatitis B infecton in China. *Intern Med.*, 50, 811-815.

Corresponding Author:
Junaid Mahmood Alam,
Department of Clinical Biochemistry lab services and Chemical Pathology, LNH and Medical College, Karachi-Pakistan.
E mail: dr_jmalam@hotmail.com

Submitted on 30-09-2025
Revised on 08-10-2025
Accepted on 12-10-2025