Does Hepatitis C Virus Infection is a Relevant Factor for Thyroid Dysfunction?

Saad Muhmood Hussain* **MRCS , FICMS, Surgery**

Abdul-Razak Sh. Hasan* **Ph.D. Microbiol**

Abstract

Background: Because hepatitis C virus can replicate in cells other than hepatocytes, more than 5% of infected patients develop during the course of the disease at least one extrahepatic manifestations.

Objective: Determination of the seropositivity rate of anti-HCV antibody among patients with thyroid dysfunction in Diyala province.

Materials and methods: The present study was conducted from September/2008 to October/2009. 122 patients who presented with abnormal thyroid function tests. 29 (23.3%) of them were males with mean age 35.4 ± 19.0 years and 93 (76.7%) were females with mean age 37.5±11.5 years. Additionally, 117 normal healthy blood donors were included as control group, the mean age 32.3 ± 8.7 years. Anti-HCV antibody was detected by ELISA technique. Repeatedly positive sera were confirmed by immunoblot assay. Data were statistically analyzed.

Results: The preliminary results showed that the anti-HCV seropositivity rate among patients was insignificantly higher than controls (1.6% and 0.8%) respectively. Male and female were equally infected (50%). The age of infected male was 56 years, while the age of infected female was 47 years.

Conclusion: Hepatitis C virus infection is not a risk factor for the development of thyroid dysfunction.

Keywords: HCV, Thyroid dysfunction, extrahepatic manifestation.

* **College of Medicine\ Diyala University**

Introduction

Hepatitis C virus (HCV) is a hepatotropic and lymphotropic virus that causes acute and chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma [1]. Upto 3% of the world's population is infected with HCV, and 80% become chronic carriers, making the HCV is the second most common chronic viral infection in the world [2,3]. Due to its ability to replicate in cells other than the hepatocytes, HCV infection is characterized by a panel of extrahepatic manifestations [4,5]. It has been suggested that HCV infection should be regarded as a systemic infectious disease with multiorgan involvement, since more than 5% of infected patients develop during the course of the disease at least one extrahepatic manifestations [6]. The link between HCV infection and cryoglobulinemia, diabetes mellitus, lichen planus, hematological malignancies, and autoreactive antibodies production has been well studied [7,8]. Studies exploring the relationship between HCV infection and thyroid dysfunction have yielded variable results [9,10,11]. Anew proposed mechanism for HCV induced thyroid autoimmunity suggest that HCV envelope glycoprotein E2 can bind to CD81 receptors expressed on thyroid cells and induce a cascade of signaling pathway leading to IL-8 release, an important pro-inflammatory cytokine [12]. However, most of the studies attribute the induction of thyroid dysfunction in HCV infected patients to the interferon-ribavirin combination therapy [13,14,15].

Materials and Methods

This is aprospective study was conducted from September/2008 to October/2009. 122 patients who presented clinically with thyroid gland abnormalities. After sufficient history was taken and clinical examination had been performed on every single patient with either goiter or with signs and symptoms of thyroid dysfunctions who is nongoirouse, ablood sample were aspirated for thyroid function tests which are (T3 ,T4 and TSH) and other sample for Anti-HCV Antibodies had been also aspirated ., Additionally, 117 normal healthy blood donors were included as control group, with mean age 32.3 ± 8.7 years. Anti-HCV antibody was detected by ELISA technique. Repeatedly positive sera were confirmed by immunoblot assay. Data were statistically analyzed.

Results:

29(23.8%) of the patients were males with mean age 35.4 ± 19.0 years, and 93 (76.2%) were females with mean age 37.5±11.5 years

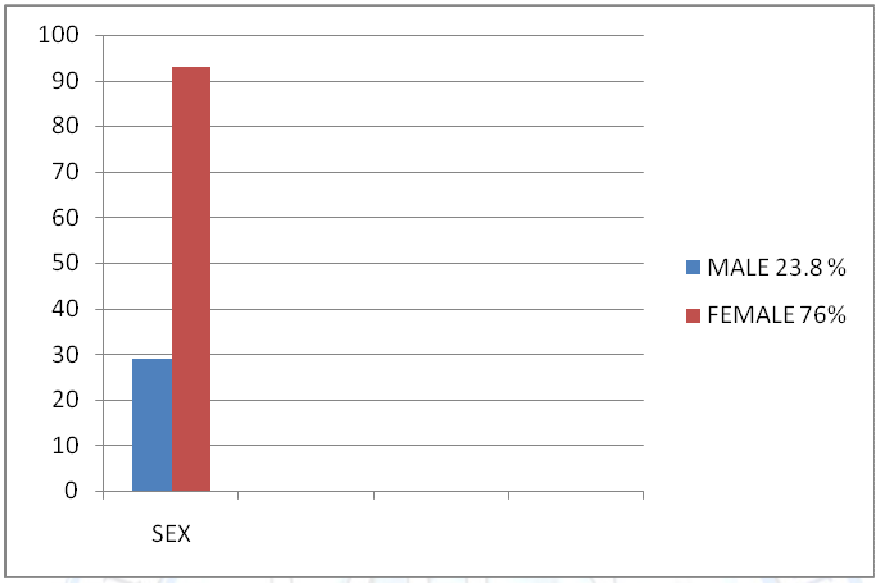


Figure (1): illustrate the gender distribution

According to the interpretation of thyroid function tests (T3, T4, and TSH) [16] , the patients were categorized as follows; 61 (50%) with primary hypothyroidism, 27 (22.1%) with primary hyperthyroidism, 7 (5.7%) with subclinical primary hyperthyroidism ,8(6.5%) with subclinical hypothyroidism, and 19(15.5%) with unusual thyroid function test.

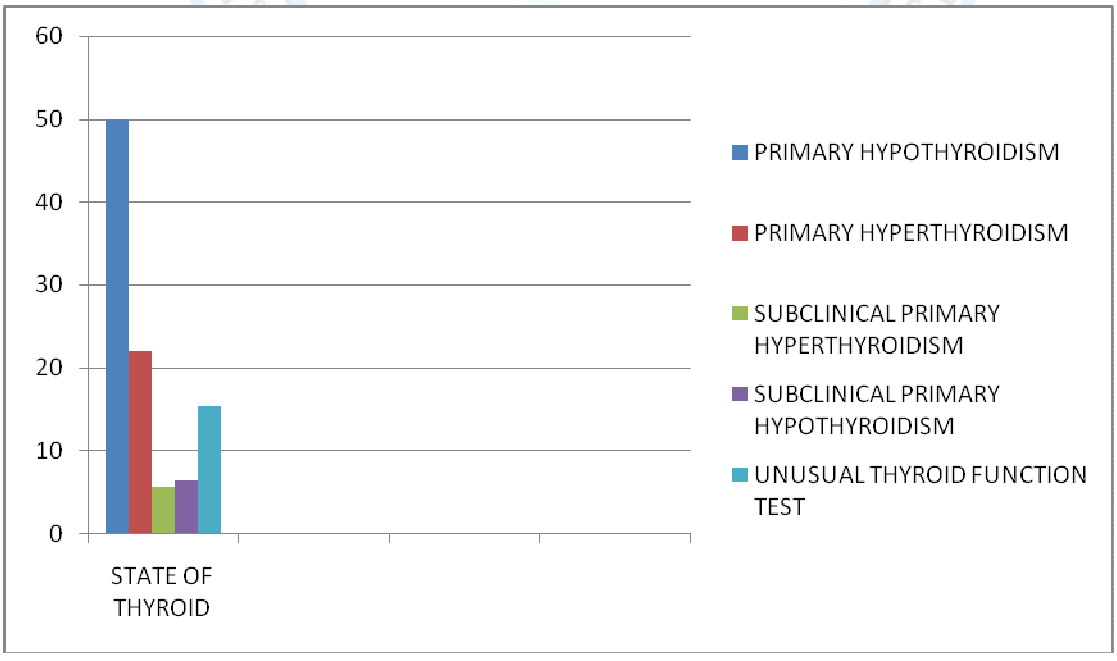


Figure (2): illustrate the thyroid states among the patients

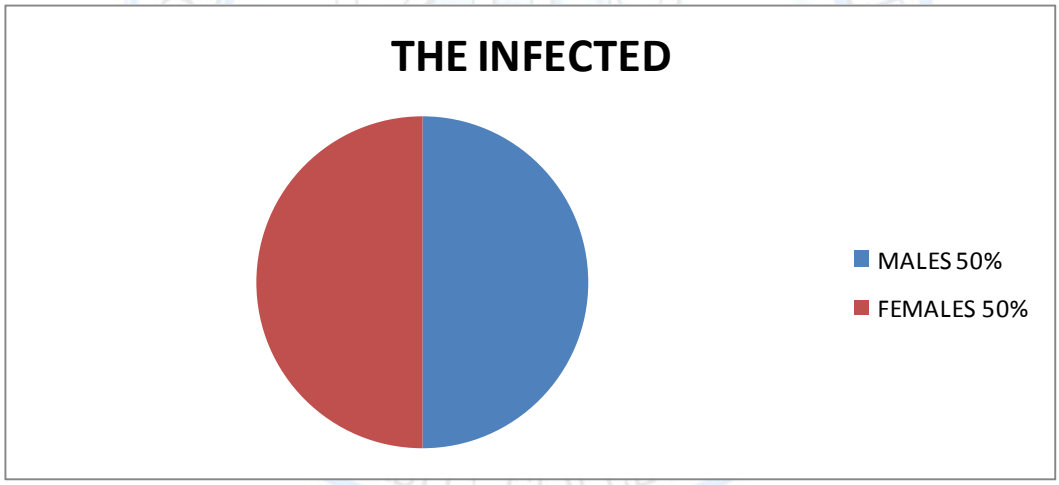
The preliminary results showed that the anti-HCV seropositivity rate among patients and controls was (1.6% and 0.8%) respectively. There was insignificant difference between the two groups ($p > 0.05$).

Table (1): Anti-HCV seropositivity rate among study groups.

Study group	No. tested	Anti- HCV positive		P value
		No.	%	
Patient group	122	2	1.6	P > 0.05 [NS]*
Control group	117	1	0.8	

*NS: not significant

Males and females were equally infected (50%). The age of infected male was 56 years, while the age of infected female was 47 years. And both of them were with hypothyroid state



Figer (3): illustrate the gender distribution of the infection

Discussion

The preliminary results of the present study found insignificant increase of anti-HCV seropositivity among patients with abnormal thyroid function tests compared to healthy blood donors. Previous studies on the relationship between HCV infection and thyroid dysfunction have yielded controversial results [9,10,11,15,17]. In a retrospective study extending from 1995 to 2004 on Australian chronic HCV positive patients, 7% were developed thyroid dysfunction predominantly hypothyroidism after completion of a nti-viral therapy [14]. On

the other hand, it has been reported that patients with chronic HCV infection had significantly higher TSH and significantly lower free T3 and free T4 levels, beside a significant increase in the positivity rate for thyroid peroxidase and anti-thyroglobulin antibodies compared to uninfected controls [13]. Therefore, it has been suggesting that patients with HCV infection should be routinely screened for thyroid disease [18].

It is worth to mention that most of studies document a thyroid dysfunction in chronic HCV positive patients who underwent a treatment with interferon-alfa-2β and ribavirin [10,11]. The current study was oriented in the opposite direction, i.e. we investigate the HCV positivity rate in patients with thyroid dysfunction, and so none of our patients was received treatment for HCV infection. Therefore, our results support the interpretation of other studies which affirm that the thyroid dysfunctions in patient with HCV infection are probably induced by the HCV anti-viral treatment but not by the replication of the virus itself in thyroid tissues [10,11,15,18]. Howver, an association between HCV infection and thyroid cancer has been documented in countries with high prevalence of HCV infection [19].

Reference

[1] Thomson, B.J. and Finch, R.G. Hepatitis C virus infection. Clin. Microbiol. Infect. 2005; 11(2): 86-94.

[2] Seeff, L.B. The natural history of chronic hepatitis C virus infection. Cln. Liver Dis. 1997; 1(13): 587-602.

[3] Flamm, S.L. Chronic hepatitis C infection. JAMA. 2003; 289 (18): 2413-17.

[4] Manns, M.P. and Rambusch, E.G. Autoimmunity and extrahepatic manifestations in hepatitis C virus infection. J. Hepatol. 1999; 31(Suppl.1): 39-42.

[5] Nocente, R.; Ceccanti, M.; Bertazzoni, G.; Gammarota, G.; Silveri, N.G. and Gasbarrini, G. HCV infection and extrahepatic manifestation. Hepatogasteroenterology, 2003; 50(52): 1149-54.

[6] Zignego, A. and Craxi A. Extrahepatic manifestations of hepatitis C virus infection. Clin. Liver Dis. 2008; 12: 611-36.

[7] Persico, M.; De Mario, F.A.; Di Giacomo-Russo, G.; Persico, E.; Mora nte, A.; Palmentieri, B. and Torella, R. Prevalence and incidence of cryoglobulins in hepatitis C virus-related chronic hepatitis patients: a prospective study. Am. J. Gastroenterol. 2003; 98(4): 884-8.

[8] Nago,Y.; Kawasaki, K. and Sata, M. Insulin resistance and lichen planus in patients with HCV infectious liver diseases. J.Gastroenterol. 2008; 23(4): 580-5.

[9] Antonelli, A.; Ferri, C.; Fallahi, P.; Ferrari, S.M.; Ghinol, A.; Rotondi, M. and Ferrannini, E. Thyroid disorders in chronic hepatitis C virus infection. Thyroid, 2006; 16(6): 563-72.

[10] Andrade, L.J.; Atta, A.M.; D'Almeida, J.A. and Parana, R. Thyroid dysfunction in hepatitis C individuals treated with interferon-alpha and ribavirin- a review. Braz. J. Infect. Dis. 2008; 12(2): 144-8.

[11] Huang J.F.; Chuang, W.L.; Dai, C.Y.; Chen, S.C.; Lin, Z.Y.; *et al*. The role of thyroid autoantibodies in the development of thyroid dysfunction in Taiwanese chronic hepatitis C patients with interferon-alpha and ribavirin combination therapy. J. Viral Hepat. 2006; 13(6): 396-401.

[12] Akeno, N.; Blackard, J.T.; Tomer, Y. HCV E2 protein bnds directly to thyroid cells and induces Il-8 production: A new mechanism for HCV induced thyroid autoimmunity. J. Autoimmun. 2008; 31(4): 339-44.

[13] Boggs, W. Thyroid disorders common in patients with chronic hepatitis C. Am.J. Med. 2004;117: 10-17.

[14] Huy, A.T.; Tracey L.J. and Robert G.B. The spectrum of thyroid dysfunction in an Australian hepatitis C population treated with combination interferon- α2 β and ribavirin. BMC Endocr. Disord. 2005; 5:8.

[15] Vezali, E.; Elefsiniotis, I.; Mihas, C.; Konstantinou, E. and Saroglou, G. Thyroid dysfunction in patients with chronic hepatitis C: Virus –or therapy related. J.Gastroenterol. Hepatol. 2009; 24(6): 1024-29.

[16] Dayan, C. Interpretation of thyroid function tests. Lancet, 2001; 357: 619-24.

17. Vallee, D. Hepatitis C virus antibodies and Graves disease. Brit. Med. J. 1995; 310: 128-9.

[18] Bini, E.J. and Mehandru, S. Incidence of thyroid dysfunction during interferon alfa-2b and ribavirin therapy in men with chronic hepatitis C: a prospective cohort study. Arch. Intern. Med. 2004; 164 (21): 2371-6.

[19] Montella, M.; Pezzullo, L.; Crispo, A.; Izzo, F.; Amore, A.; Marone, U.; Tamburini, M.; *et al*. Risk of thyroid cancer and high prevalence of hepatitis c virus. Oncol.Rep. 2003; 10(1): 133-6.