Study of thyroid gland dysfunction in hepatitis C patients and Early effect of interferon therapy on thyriod state in chornic hepatitic C patients

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Abstract: Background: HCV is both a hepatotropic as well as a lymphotropic virus and chronic infection is known to be responsible for both hepatic and extrahepatic diseases which treated currently by pegylated IFN and ribavirin. Despite their efficacy, both standard IFN-α and PEG-IFN have a well kdnown side effects profile including thyroid dysfunction (TD), type 2 diabetes mellitus (T2DM) and gonadal dysfunction. **Objectives:** Study the effect of HCV on the thyroid state and highlights the risk factors of these disorders And Study the early effect of interferon therapy on the thyroid gland function in patients with chronic hepatitis C virus**. Methods:** Fifty patients with chronic hepatitis C (CH HCV) genotype 4 were enrolled in this study and equally divided into two groups. The 1st group treated patients with INF and ribavirin (peginterferon alfa- 2a (Pegasys, Hoffmann-La Roche, Nutely, NJ) at fixed dose of 180 mg/week given subcutaneously together with ribavirin 1000 mg to 1200 mg daily, (1000 mg for those who weight less than 75 kg) and (1200 mg for those who weight more75kg). This group was studied before therapy and 3, 6 months after starting therapy. The 2nd group is untreated CH HCV. And 25 healthy persons as a control group, All groups were studied for thyroid function tests (FT3, FT4, and TSH, anti TG, anti TPO). **Results:** There was an increase in thyroid dysfunction and the prevalence of anti-thyroid antibodies in the first group (40%=10/25) versus (16%= 4/25) in the second group and (0%) in control group. Hypothyroidism was more common thyroid dysfunction in the first and second groups. There was significant association between female and occurrence of thyroid disorder. But there was no significant association between age of patients, the viral load and thyroid disorder. **Conclusion:** The frequency of thyroid disorders and anti-thyroid antibodies in hepatitis C infected patients was higher in female and than in healthy persons. Hypothyroidism was significantly more common than hyperthyroidism in thyroid disorders occurring during treatment with interferon.
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Keywords: Chronic Hepatitis C (HCV), Thyroid dysfunction, Hypothyroidism, pegylated interferon alfa-2a. FT3 (Free Triiodothyronin), FT4 (Free Tetraiodothyronin), TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline)

1. Introduction:

Hepatitis C virus infection is endemic worldwide with a global prevalence of 3% affecting 170 million around the world. Egypt has the highest HCV prevalence worldwide [1]. One of the most common phenomena in chronic HCV infection is the appearance of auto antibodies against thyroid gland [2]. Also thyroid disorders (usually hypothyroidism) are more commonly seen in people with HCV than in the general population. Interferon alpha (IFN a) is the cornerstone therapeutic agent for chronic hepatitis C virus infection. Interferon assist the immune response by inhibiting viral replication within host cells, activating natural killer cells, increasing antigen presentation to lymphocytes, and inducing the resistance of host cells to viral infection. Many studies have shown that up to 15% of HCV patients receiving IFN develop clinical thyroid disease, and up to 40% become thyroid antibody positive. In some cases IFN-induced thyroiditis (IIT) may result in discontinuation of interferon therapy; thus, IIT represents a major clinical problem for hepatitis C patients receiving IFN therapy [3].

The mechanism of interferon induced thyroid autoimmunity is MHC class I antigen up regulation and subsequent antibody development. Evidence suggests that interferon up regulates MHC class I antigen expression in the thyroid thereby inducing autoantibody formation [4]. Another possibility is a direct effect of IFN on the thyroid. This hypothesis is supported by data showing IFN induced thyroid dysfunction without TAb's in up to 10% of IFN-treated patients. Some authors hypothesize that interferon cause's autoimmune thyroid disease by changing the Thl/Th2 balance [5].

Possible factors predisposing to interferon-induced AITD include hepatitis C by itself. Female gender has also been suggested to be a risk factor for interferon induced AITD even though the risk ratio has not been determined [3]. Pretreatment presence of

Tab's is associated with thyroid dysfunction during Interferon (IFN) therapy [6-7]. Genetic factor represent risk factors that have been shown to predispose to AITD, one study from Japan found an association between HLA-A2 and the development of interferon induced AITD [8]. Therapeutic regimen-related factors may influence the development of thyroid disease. Patients with cancer treated with lymphoblastic IFN alfa had a higher frequency of early thyroid dysfunction than those treated with recombinant IFN[9].

Before patients undergoing IFN therapy, it is suggested that serum TSH, FT4, TgAb, and TPOAb concentrations and perhaps a thyroid echography be carried out to identify preexisting thyroid dysfunction and autoimmunity. IFN treatment should be started after adequate correction of the existing thyroid dysfunction. During IFN treatment, measurement of serum TSH concentrations should be carried out every 8-12 wk [10].

2. Methods

Sampling was performed after informed consent was obtained from each patient included in the study to use the samples and clinical data for research purposes after being informed about the nature of the study. The study protocol conforms to the most recent ethical guidelines of the Declaration of Helsinki as reflected in a priori approval by the National Liver Institute (NLI) human research committee.

This study included 50 patients with chronic hepatitis C (CH HCV) and 25 healthy persons as a control group. Patients attended to the outpatient clinics in The National Liver Institute of Menoufiya University during period from March 2011 to September 2011. All subjects were classified into three groups. The1st included 25 HCV treated patients with INF and ribavirin. This group was studied before therapy and 3, 6 months after starting therapy. All treated patients received peginterferon alfa- 2a (Pegasys, Hoffmann-La Roche, Nutely, NJ) at fixed dose of 180 mg/week given subcutaneously together with ribavirin 1000 mg to 1200 mg daily,1000 mg for those who weight less than 75 kg and 1200 mg for those who weight more than 75kg.the 2nd group including 25 untreated CH HCV patients. These patients did not receive IFN therapy as they were afraid of IFN side effects or due to financial. The 3rd included 25 healthy persons as control group. All included subjects underwent full medical history, with stress on symptoms of thyroid disorders, clinical examination with full hepatological examination and thought medical examination for thyroid disorders. Blood samples were drawn for testing liver function,fasting blood glucose, complete blood count, hepatitis markers(HCV Abs.HBs Ag & HBc Abs & quantitative HCV RNA by PCR for patients who have positive HCV Abs) and finally testing for Thyroid function tests (FT3, FT4,TSH, anti thyroglobuline Abs thyroid anti peroxidase).

Statistical analysis: Results were collected, tabulated, statistically analyzed by IBM personal computer and statistical package SPSS version 11. Two types of statistics were applied A-Descriptive: e.g. percentage (%), range, mean and standard deviation SD. B-Analytical: e.g.1)- Student's t-test was done to collectively indicate the presence of any significant difference between two groups for a normally distributed quantitative variable.2)- Mann-Whitney test used to collectively indicate the presence of any significant difference between two groups for a not normally distributed quantitative variable.3)- One a way ANOVA (F test): a single test used to collectively indicate the presence of any significant difference between several groups for a normally distributed quantitative variable.4)- Kruskal -Wallis test: It is the non-parametric version of ANOVA it is used to collectively indicate the presence of any significant difference between several groups for a not normally distributed quantitative variable.5)- Chi-Squared (χ^2): It is used to compare between two groups regarding one qualitative variable in 2x2 contingency table or r c complex (Table.6)- Fisher's exact test: It is used to compare between two groups or more regarding one qualitative variable in 2x2 contingency table or r c complex table when the count of any of the cells less than 5. 7)- Z test: used to compare between two proportions. 8) - Paired t test: used to collectively indicate the presence of any significant difference between different time sequences for a normally distributed quantitative variable.9) - Wilcoxon signed rank test: used to collectively indicate the presence of any significant difference between different time sequences for a not normally distributed quantitative variable. For all analysis *P* value <0.05 was considered statistically significant while *P* value >0.05 considered on statistically significant. *P* value < 0.001 highly significant difference.

3. Results

The study enrolled 50 patients diagnosed as chronic HCV genotype 4 classified into two groups. In the 1st group whom received IFN plus RBV therapy (25 patients) the following data were found: the mean age was 34.0 ± 6.76. Most of them were male (15/10). Most of these patients had no history of thyroid dysfunction (*P* value >0.05). There is an increase in the percentage of thyroid dysfunction after IFN therapy (40%= 10/25 patients).which was statistically significant (*P* value < 0.05) in comparison to healthy control patients (whom did not receive IFN therapy). Out of these ten patients 60% (6/10) were hypothyroid while 40% (4/10) were hyperthyroid after 24 weeks of therapy.

Table 1- Comparison between the levels of studied thyroid function tests regarding gender among group I patients (n=25):

GROUP I Patients	Gender		Mann-Whitney test	*P* value
	Males (n=15) Mean ± SD	Females (n=10) Mean ± SD		
Free T3	2.51 ± 0.53	1.81 ± 0.46	* 3.52	<0.01*
Free T4	1.26 ± 0.19	1.17± 0.13	* 1.37	>0.05
TSH	4.03 ± 0.95	4.99 ± 0.85	2.65	<0.05*
Anti TPO	34.47 ± 18.36	37.70 ± 24.51	0.14	>0.05
Anti TG	126.80 ± 59.66	128.0 ± 50.0	0.44	>0.05

* t test FT3 (Free Triiodothyronin), FT4 (Free Tetraiodothyronin), TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline).

Table 2- Comparison between the levels of studied thyroid function Tests regarding gender among group II patients (n=25):

Group II patients	Males (n=15) Mean ± SD	Females (n=10) Mean ± SD	Mann-Whitney test	*P* value
Free T3	3.76 ± 0.17	3.15 ± 0.17	* 7.27	<0.001
Free T4	1.35 ± 0.27	1.16 ± 0.33	* 1.47	>0.05
TSH	2.34 ± 1.20	2.50 ± 1.41	0.62	>0.05
Anti TPO	14.60 ± 5.49	21.0 ± 12.65	1.67	>0.05
Anti TG	53.0 ± 10.47	75.30 ± 31.93	2.17	<0.05

* t test FT3 (Free Triiodothyronin), FT4 (Free Tetraiodothyronin), TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline).

Table 3 - Comparison between the levels of studied thyroid function tests regarding gender among group III (n=25):

Group III	Males (n=13) Mean ± SD	Females (n=12) Mean ± SD	T Test	*P* value
Free T3	3.28 ± 0.48	3.26 ± 0.43	0.10	>0.05
Free T4	1.38 ± 0.19	1.23 ± 0.21	1.77	>0.05
TSH	2.60 ± 0.50	2.70 ± 0.93	* 0.62	>0.05
Anti TPO	18.54 ± 9.82	25.17 ± 5.54	* 1.88	>0.05
Anti TG	57.31 ± 13.28	62.50 ± 14.44	0.94	>0.05

* Mann-Whitney test FT3 (Free Triiodothyronin), FT4 (Free Tetraiodothyronin), TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline).

Table 4 Comparison between the levels of different thyroid tests after 3 months and 6 months among treated HCV patients:

Group I patients	Baseline Mean ± SD	After 3 months Mean ± SD	After 6 months Mean ± SD	Paired t test	*P* value
Free T3	3.40 ± 0.33	2.96 ± 0.72	2.23 ± 0.61	3.26 9.93 5.36	*P* >0.05
Free T4	1.42 ± 0.34	1.43 ± 0.18	1.22 ± 0.18	0.16 2.55 6.82	*P*>0.05
TSH	2.63 ± 0.84	3.53 ± 0.86	4.41 ± 1.02	6.49 8.40 4.67	P_1<0.001 P_2<0.001 P_3<0.001
Anti TPO	17.24 ± 7.99	27.28 ± 16.94	35.76 ±20.61	#4.10 #3.69 #1.48	P_1<0.001 P_2<0.001 P_3>0.05
Anti TG	53.36 ± 24.50	101.36 ± 58.53	127.28 ± 54.90	#4.26 #4.29 #2.14	P_1<0.001 P_2<0.001 P_3<0.05

Wilcoxon-Signed rank P1 = between baseline and after 3 months. P_2 = between baseline and after 6 months. P_3 = between 3 and after 6 months FT3 (Free Triiodothyronin), FT4 (Free Tetraiodothyronin), TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline).

There was found that there is an increase in the prevalence of Tabs in group I (40%) after 24 weeks of therapy. and there was a high statistical difference in the prevalence of Tabs in group I in comparison to the other groups. As regarding to the early effect of IFN treatment the current study showed that there was a statistically significant difference between 12 weeks and 24 weeks of interferone treatment in Anti TPO and Anti TG.

The 2nd group whom not received IFN therapy (25 patients) the following data were found: the mean age was 34.6 ± 6.33, Fiveten males and ten females and Most of these patients had no history of thyroid dysfunction. The present study found that there is an increasing in the percentage of thyroid disorders in group II patients than the control group (16% VS 0%). However there was no statistical significance in the occurrence of thyroid dysfunction between both groups. There is an increase in the percentage of hypothyroidism in untreated HCV patients than the control group (16% VS 0%). However there is no statistical significance in the occurrence of thyroid dysfunction between groups II and III. There is a slight increase in the prevalence of Tabs in untreated HCV patients (8%) than the control group. However, there was a decrease in the prevalence of Tabs in comparison to group I (8% vs. 40%).

The current study showed significant correlation between female sex and occurrence of thyroid disorder in TSH and FT4 in group I and in free T3 and anti TG in group II. No significant relationship between age and thyroid function tests in (TSH, FT3 or FT4) in both group I and group II.

No correlation between the viral load and thyroid dysfunction in (TSH, FT4 or FT3) in group I patients while in group II there was a correlation between viral load and anti TPO level.

Table 4 showed Comparison between the levels of different thyroid tests after 3 months and 6 months among treated HCV patients: showed that there was significant difference higher after 3 months and 6 months after the start of treatment with interferone and ribavirine as regarding TSH (Thyriod Stimulating Hormone), Anti TPO (Anti thyroidal peroxidase), Anti TG (Anti thyroglobuline). This was explained by interferone induced thyrioditis which produce anti thyroid antibodies and thyroid dysfunction, The pattern of which include autoimmune hypothyroidism, hyperthyroidism and thyroiditis explained by high Anti TPO and Anti TG. Table 5 showed (6/25=24%) cases of hypothyroidism, (4/25=16%) cases of hyperthyroidism.

Table 5- Mean values of studied thyroid function testes after 6 month treatment among group I patients with different thyroid dysfunction

Group I Patients	Clinical picture of thyroid			F test	Post hoc test
	Hyperthyroidism (n=4)	Hypothyroidism (n=6)	Normal (n=15)		
	Mean ± SD	Mean ± SD	Mean ± SD		
Free T3	2.30 ± 0.49	2.06 ± 0.70	2.27± 0.64	0.24	>0.05
Free T4	1.38 ± 0.20	1.12 ± 0.13	1.21 ± 0.15	3.51	<0.05(1,2- 1,3) >0.05 (2,3)
TSH	3.20 ± 1.40	5.08 ± 1.21	4.02 ± 0.83	4.56	<0.05 (1,2- 2,3) >0.05 (1,3)
Anti TPO	40.80 ± 22.64	47.0 ± 20.84	28.33 ± 12.73	* 3.23	>0.05
Anti TG	156.60 ± 54.28	100.60 ± 55.96	126.40 ± 53.56	* 3.75	>0.05

*Kruskal-Wallis 1 = group I 2= group II 3= group III

Table (5): showed that there was a statistical significant difference in the mean levels of TSH and free T4 in group I patients whom developed TD and the others whom did not, after 6 month treatment of IFN therapy

Table 6- Mean values of studied thyroid function testes among group II patients with different thyroid dysfunction

Group II pddatients	Clinical picture of thyroid		t test	*P* value
	Hypothyroidism (n=4)	Normal (n=21)		
	Mean ± SD	Mean ± SD		
Free T3	3.48± 0.26	3.57 ± 0.32	0.57	>0.05
Free T4	0.88± 0.49	1.15 ± 0.20	1.93	>0.05
TSH	4.73 ± 0.82	1.96± 0.73	6.79	<0.05
Anti TPO	27.13 ± 18.08	15.26 ± 5.72	* 0.87	>0.05
Anti TG	86.75 ± 48.62	57.19 ± 13.54	* 1.14	>0.05

* Mann-Whitney test

Table (6): showed that there was a statistical significant difference in the mean level of TSH in group II patients whom developed TD and the others whom did not.

Table 7- Comparison between groups according to thyroid function tests after 6 months treatment with IFN therapy

	Group I (6 months) (n=25) Mean ± SD	Group II (n=25) Mean ± SD	Group III (n=25) Mean ± SD	Kruskal-Wallis	Post hoc test
Free T3	2.23 ± 0.61	3.56 ± 0.31	3.27 ± 0.45	* 55.13	<0.01 (1&2 – 1&3) <0.05 (2&3)
Free T4	1.22 ± 0.18	1.27 ± 0.31	1.31 ± 0.21	* 0.78	>0.05
TSH	4.41 ± 1.02	2.40 ± 1.27	2.65 ± 0.72	35.71	<0.01 (1&2 – 1&3) >0.05 (2,3)
Anti TPO	37.76 ± 26.61	17.16 ± 9.37	21.72 ± 8.59	19.71	<0.01 (1,2) <0.05 (1,3) >0.05 (2,3)
Anti TG	127.28 ± 54.90	61.92 ± 23.88	59.80 ± 13.81	35.38	<0.001 (1,2) <0.001 (1,3) >0.05 (2,3)

*F test = ANOVA 1 = Group I 2= Group II 3= Group III

Table (7): showed that there was a statistical significant difference in TSH and FT3 levels among the studied groups while there were highly significant differences in Anti TPO and Anti TG levels between group I and other groups.

Table 8- Correlation between viral load and studied thyroid function tests after 3 months treatment

Thyroid tests Vs viral load	Viral load			
	Group I patients		Group II patients	
	r	*P* value	r	*P* value
T3	- 0.08	>0.05	- 0.14	>0.05
T4	- 0.13	>0.05	- 0.38	>0.05
TSH	- 0.12	>0.05	- 0.38	>0.05
Anti TPO	- 0.14	>0.05	- 0.49	<0.05
Anti TG	- 0.11	>0.05	- 0.03	>0.05

Table (8): showed that there was no a significant correlation between viral load and the occurrence of thyroid dysfunction in group I patients. While there was a significant correlation in group II patients regarding antiTPO level.

4. Discussion

Interferons are natural cytokines produced by the cells of the immune system of most vertebrates in response to challenges by foreign agents such as viruses, parasites and tumor cells. Interferon assist the immune response by inhibiting viral replication within host cells activating natural killer cells, increasing antigen presentation to lymphocytes, and inducing the resistance of host cells to viral infection. When the antigen is presented to matching T and B cells, those cells multiply and strategically and specifically wipe out the foreign substances [11]. The prevalence of thyroid disease during IFN treatment was extremely variable ranging between 1 and 35%. The low rates are likely an underestimation of the true prevalence because in some studies a careful evaluation of thyroid status was not carried out [12]. Prospective studies have shown that up to 15% of HCV patients receiving IFN develop clinical thyroid disease, and up to 40% become thyroid antibody positive. In some cases IFN-induced thyroiditis (IIT) may result in discontinuation of interferon therapy; thus, IIT represents a major clinical problem for hepatitis C patients receiving IFN therapy, IFN-α seems to acts through major histo-compatibility complex class I antigens to produce anti thyroid antibodies and thyroid dysfunction. The pattern of which include autoimmune hypothyroidism, hyperthyroidism and thyroiditis [3], These results was in agreement with our study. Also Foldes *et al.* (2004) and Mandac *et al.* (2008) stated that, many studies have explored that thyroid dysfunction can be induced by cytokine therapy. Every fifth patients with chronic hepatitis C showed thyroid dysfunction during interferon-alpha therapy, it is necessary therefore to control the hormonal status and the thyroid antibody titer. Treated patients have to be informed in advance

that as a "side effect" persistent hypothyroidism may develop [14, 20].

This study was to detect the presence and prevalence of thyroid gland dysfunction in patients with chronic hepatitis C virus before and after treatment with interferon and evaluate the effect of HCV itself on thyroid state.

In the 1st group There was an increase in the percentage of thyroid dysfunction after IFN therapy (40%= 10/25 patients). this was in concordance with many prospective studies that have shown up to 40% developed some kind of thyroid dysfunction in HCV patients receiving IFN. However there were higher incidences of TD in other studies as Kabbani *et al.* (2006) found 89% (556/ 625 patients) having thyroid dysfunction among HCV patients receiving IFN [13]. From studies that found lower incidence of TD were: Foldes *et al.* (2004) they detected thyroid dysfunction only in 21.7% of cases [14]. And also Tomer *et al.* (2007) who stated that 15% of HCV patients receiving IFN alpha developed clinical thyroid disease [15]. This variation between results may be due to difference in virus genotypes and /or duration of course of treatment [16].

The present study found there was an increase in the percentage of thyroid dysfunction in group I (40%= 10/25 patients) Out of these ten patients 60%(6/10) were hypothyroid while 40%(4/10) were hyperthyroid after 24 weeks of therapy.

In concordance with our study Dalgardo *et al.* (2002) found that the hypothyroidism more common than hyperthyroidism (67% and 66% vs. 33% and 34%) respectively during and after treatment with IFN [18]. On the contrary with our study Dio *et al.* (2005) in a study on 349 HCV patients found that thyroid disorders occurring after IFN therapy were 55% hyperthyroidism and 45 % hypothyroidism [19]

In concordance with our study both, Mandac *et al.* (2008) and Carella *et al.* (2007) detected Tabs in HCV patients receiving IFN (40% and 37% respectively) [20-21]. In concordance with our study both Metcalf *et al.* (2007) found 7.5% in the HCV non treated patients [22]. In concordance with our study is Moncoucy *et al.* (2007) who found that the autoimmune disease of thyroid gland is a more common side effect of the immunomodulating properties of IFN than non immune pathology [7]. accordance with this result, Kee *et al.* (2006) in a study on 461 patients found a significant association between female sex and occurrence of thyroid disorders in HCV patients treated with IFN (p value > 0.001) [6].

In the 2nd group the study found that there was an increasing in the percentage of thyroid disorders (hypothyroidism) in untreated HCV patients than the control group (16%=4/25 VS 0%). This in concordance with Huang *et al.* who found that the prevalence of thyriod dysfunction in chronic HCV patients VS healthy control persons (17% VS 0%) [17]. From data of all studies on HCV and thyroid autoimmunity was demonstrated a significant increase in the risk of thyroiditis in HCV patients**.** Therefore, HCV infection is infectious agent that is clearly associated with an increase risk for autoimmune thyroiditis [2].

The present study showed no correlation between the viral load and thyroid dysfunction in (TSH, FT4 or FT3) in group I patients while in group II there was a correlation between viral load and anti TPO level.

On the contrary with the present study, Tran *et al.* (1993) in a prospective study done in 201 patients founded that there was positive and significant association between thyroid disorder and HCV RNA level [23]. This difference may be due to small samqple size, virus genotype and short duration of follow up in our study.

Conclusion:

The frequency of thyroid disorders and anti-thyroid antibodies in HCV infected patients was higher than in healthy persons. Hypothyroidism (24%) was significantly more common than hyperthyroidism (16%) in thyroid disorders occurring during treatment of HCV with interferon. There was no significant association between presence of pretreatment antibodies, age or duration of treatment and occurrence of thyroid disorders. However, female gender represented a risk factor for occurrence of thyroid disorders in IFN treatment of HCV patients.

Recommendation:

Close observation should be done for risk factors, especially female sex and presence of pretreatment thyroid antibodies, for occurrence of thyroid disorders or autoimmunity. Cases of HCV infection that will be treated with interferon should be investigated for thyroid disorders+ and Tab's (FT3, FT4, TSH, Anti TPO and Anti TG) before treatment, during treatment and as a follow up**)** Treatment with IFN is contraindicated in patients with uncontrolled thyroid diseases**).**

Conflict of interest: Non to Declare

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References

1. *Antonelli A, Ferri C, Pampana A et al., (2011):* Thyroid disorders in chronic hepatitis C. Am J Med., 117: 20-23.

2. *Antonelli A, Ferri C, Ferrari SM et al., (2009):* Endocrinal manifestations of hepatitis C virus infection. Nat Clin Pract Endocrinal Metab, 5 (1): 26- 34.
3. *Yael M, Wong JB and Koff RS (2004):* Thyroid gland dysfunction during antiviral therapy of chronic hepatitis C. Med Sci Monit;7:233-4.
4. *Ward DL, Bing-You RG.(2007*):Autoimmune thyroid dysfunction induced by interferon-alfa treatment for chronic hepatitis C:screening and monitoring recommendation. J Clinl Endocrino and Metabol Vol; 86No.5:1925-1929
5. *Prummel MF and Lauberg P. (2008*): Interferon-and autoimmune thyroid disease. Thyroid; 13:547-51
6. *Kee KM, Lee CM, Wang JH, et al., (2006):* Thyroid dysfunction in patients with chronic hepatitis C receiving a combined therapy of interferon and ribavirin: incidence, associated factors and prognosis. J Gastroenterol Hepatol; 21: 319-26.
7. *Moncoucy X, Leymarie F, Delemer B, et al (2007)*: Risk factors and long term evolution of thyroid dysfunction during antiviral treatment in 221 patients with chronic hepatitis C. Gastroenterology:29;339-45.
8. *Oppenheim IY, Ban Y, and Tomer Y (2004*):Interferon induced autoimmune thyroid disease a model for human autoimmunity. Autoimmunity Rev; 3:388-93.
9. *Russo M and Fried W (2003*): Side effects of therapy for chronic hepatitis C.Gastroenterology 124:1711-9.
10. *Di Bisceglie AM and Hoofnagle JH (2006*): Optimal therapy of hepatitis C. Hepatology; 36:121-127.
11. *Louis* MO, Mosby, *Porterfield SP (2009)*:The thyroid gland. In: Endocrine Physiology. St., p. 57-81.
12. *Roti G and Keeffe EB (2009*): The management of chronic liver disease: selective rather than routine. Rev Gastroenterol Disord;5:195-205
13. *Kabbani MM, Godiva HE and Mohammed K (2006):* Thyroid disorders during interferon alpha therapy in 625 patients with CHC. Hepato-Gastro-Entrology; 57(4):343-7.
14. *Foldes I, Dávid K, Horváth G, et al., (2004):* Thyroid disorders in chronic hepatitis C. Am J Med; 117(1): 60-71.
15. *Tomer Y, Blackard JT and Akeno N (2007):* Thyroid dysfunctions in patients with viral hepatitis treated with interferon-alpha. J Hepatol; 145(23):1211-6.
16. *Gehring, S; Kullmer, U; Koeppelmann, S and Patrick, G. (2006):* Prevalence of autoantibodies and the risk of autoimmune thyroid disease in children with chronic hepatitis C virus infection treated with interferon-α. World J Gastroenterol; 12 (36): 787-792.
17. *Huang BY, Sheen IS, Yeh CT and Liaw, YF (1999):* Prevalence and significance of thyroid autoanti- bodies in patients with CHC during interferon therapy. J Endocrinology; 13(6): 547-51.
18. *Dalgardo O, Bjoro K and Hellum K. (2002):* Thyroid dysfunction during treatment of chronic hepatitis C with interferon alpha: no association with either interferon dosage or efficacy of therapy. J Intern Med; 251:400-6.
19. Doi F, Kakizaki S, Takagi H, Murakami M, Sohara N, et al. (2005) Long-term outcome of interferon-alpha-induced autoimmune thyroid disorders in chronic hepatitis C. Liver Int. 25(2): 242–6.
20. *Mandac JC, Chaudhry S, Lius G, et al (2008*):The clinical and physiological spectrum of interferon-alfa induced thyroiditis: toward a new classification. Hepatology; 43:661-72.
21. *Carella C, Mazziotti G, Amato G and Braverman LE. (2007*): IFN related thyroid disease: epidemiological, pathological and clinical aspects' Clin Endocrinal Metab; 88:3656-3661.
22. *Metcalfe RA, Ball G, Kudesia G and Weetman A P (2007):* Failure to find an association between hepatitis C virus and thyroid autoimmunity. Thyroid; 7: 421–4.
23. *Tran JF, Quadrant and Benzaken S. (1993*): High prevalence of thyroid autoantibodies in a prospective series of patients with chronic hepatitis C before interferon therapy. Hepatology; 18: 253–257.

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