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Research Article

**A CASE-CONTROL RESEARCH TO ASSESS THE
REOCCURRENCE RATE OF THYROID DYSFUNCTION DUE
TO INTERFERON- α TREATMENT AMONG CHRONIC
HEPATITIS C PATIENTS**¹Dr Hammad Sayyad Abbasi, ²Dr Junaid Nawaz, ³Dr Kiran Nayab¹Medical Officer, DHQ Bagh AJK, ²Medical Officer DHQ Hospital Lodhran, ³Islamic International Medical College, Riphah International University.**Article Received:** March 2019**Accepted:** April 2019**Published:** May 2019**Abstract:**

Objective: The point of this investigation was to survey the recurrence and kinds of thyroid dysfunction that creates amid IFN- α treatment in patients of Chronic Hepatitis C.

Methods: We carried this case-control study at Mayo Hospital, Lahore from October 2017 to November 2018. The investigation was done on an aggregate of 50 patients of constant hepatitis C on recombinant IFN- α treatment. What's more 50 patients with perpetual hepatitis C, not on any antiviral treatment, were incorporated as controls. After educated assent, clinical history was gotten, physical examination was done and discoveries recorded on a pre-structured Performa. Blood testing was accomplished for thyroid profile toward the start of interferon treatment, at 12 weeks lastly at 24 weeks.

Results: Thyroid dysfunction (TD) was seen in 14% (n=7) of the patients on antiviral treatment for CHC (n=50). Amongst these seven patients with TD, hypothyroidism was seen in 5 and hyperthyroidism in 2 patients. Conversely, the recurrence of thyroid dysfunction saw in charge group (n=50) was 2%.

Conclusion: The recurrence of thyroid dysfunction in patients of constant hepatitis C treated with interferon approaches 14%, with hypothyroidism being the more normally watched example.

Keywords: Interferon therapy, Hepatitis C, Thyroid dysfunction.

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INTRODUCTION:

Viral hepatitis remains a typical and considerable medical issue everywhere throughout the world influencing roughly 2% of the total populace [1]. Treatment of hepatitis C has advanced in the course of the most recent 15 years. Till today, it stays dependent on interferon as a safe modulator [2]. Interferons are a group of normally happening little protein particles that are delivered and discharged by cells in light of viral contaminations or to different manufactured and biologic inducers [1]. Immune system thyroid infection is one of the announced antagonistic impacts of interferon- α treatment in patients with endless hepatitis C. Through its immunomodulatory properties, IFN- α appears to act through significant histocompatibility complex class I antigens to create antithyroid antibodies and thyroid infection; a direct inhibitory impact on thyrocytes might be assumed in subjects who create hypothyroidism without autoimmunity [2,3]. The general pervasiveness of thyroid dysfunction in such patients is accounted for to be 3% to 15% in different universal investigations. Ruinous thyroiditis related to transient early thyrotoxicosis pursued by hypothyroidism has likewise been seen. Hazard factors for creating thyroid issue are the nearness of previous immune system thyroiditis, (for example, positive antimicrosome or hostile to thyroperoxidase (TPO) antibodies before treatment) and female sex; the last straightforwardly connected with expanding age [4, 5]. Blend treatment utilizing interferon and ribavirin isn't, for the most part, accepted to expand the danger of dysthyroidism contrasted with monotherapy with interferon [6]. So also pegylated interferon isn't accepted to be a hazard factor contrasted with standard interferon [7]. In spite of the fact that IFN- α actuated thyroid issue can more often than not be controlled with prescription these disarranges are not constantly reversible. Information with respect to the long haul result of this complexity to date anyway is rare [8].

Because of the lack of accessible information with respect to the improvement of TD in IFN- α treated incessant hepatitis C (CHC) patients in our populace and since we have a higher predominance of genotype III of hepatitis C infection in our populace, there is a need to do additionally concentrates to survey the example of thyroid dysfunction that creates in our unending hepatitis C patients, while they are accepting interferon treatment.

MATERIALS AND METHODS:

We carried this case-control study at Mayo Hospital, Lahore from October 2017 to November 2018. It involved 50 patients of incessant hepatitis C on

recombinant IFN- α treatment alongside 50 patients of endless hepatitis C, not on any antiviral treatment, included as controls, utilizing non-likelihood accommodation examining. Patients answering to AFIP group for PCR of HCV RNA and who were being animated for interferon treatment for ceaseless hepatitis C were incorporated into the examination though patients found to have thyroid dysfunction toward the start of interferon treatment, the individuals who were unfit to finish antiviral treatment for the span of a half year because of any reason, and the individuals who did not report back for continue testing at determined timespans were rejected. Every one of the members was clarified about the test methodology and the necessities/essentialness of continued inspecting amid the time of interferon treatment. Composed assent was acquired from each patient at this stage. The patients were altogether inspected. The nearness or nonattendance of clinical appearances of thyroid dysfunction was noted. Every one of the discoveries was noted in the patients' Proforma. Alongside that, the discoveries of hormonal examinations including serum TSH and T4 were additionally embraced for the patients for whom they were at that point accessible. Estimation of serum TSH levels was done toward the beginning of antiviral treatment to preclude prior thyroid dysfunction. The patients were told to report back at 12 and 24 weeks of interferon treatment to continue examining, the research facility demand shapes with indicated dates of the following visit were given over to every patient. The patients were situated serenely for around 15 minutes before examining for thyroid profile. Five ml of blood was gathered in a plain cylinder. Thyroid profile examination included serum TSH, Free T4 and Total T3. The cylinders were appropriately marked and the examples were transported to the handling room inside thirty minutes of group Ad permitted to clump at room temperature. Serum was isolated by centrifugation at a relative radiating power of 2000-3000 g for 15 minutes. Amid the 24 weeks treatment serum, TSH was utilized as the mainline test to screen patients with thyroid dysfunction. Patients found to have manifestations of thyroid dysfunction or strange TSH levels were assessed further by free T4 and all-out T3 estimation, as demonstrated. Hormonal investigation (Serum TSH, Free T4, and Total T3) was accomplished for the patients and the controls, selected for the examination. It was done in groups, using Chemiluminescence Immunoassay strategy, a kind of pointer named immunoassay, on Immulite 2000, a robotized, irregular access, immunoassay analyzer. The information was put away and arranged for factual examination utilizing Statistical Package for Social Sciences SPSS. Mean

and Standard deviation (SD) were determined for numerical information including age, and thyroid profile (Serum TSH). Recurrence and rate were determined for subjective information including thyroid status and the kinds of thyroid dysfunction.

RESULTS:

A sum of 64 patients of Chronic Hepatitis C on recombinant interferon- α treatment (Group A) was enrolled at first. Be that as it may, twelve patients did not report back amid the subsequent visits,

furthermor, two were found to have unhinged thyroid profile at the beginning, and in this way were avoided from the examination. In like manner out of the underlying 58 patients without interferon treatment, who filled in as controls (Group B, n=50), eight were dropped as they neglected to report at the predefined timespans. In group A (n=50), the mean age of the patients was 36 ± 16 years (mean \pm SD). With respect to dissemination, bunch A contained 40(80%) male patients and 10 (20%) female patients.

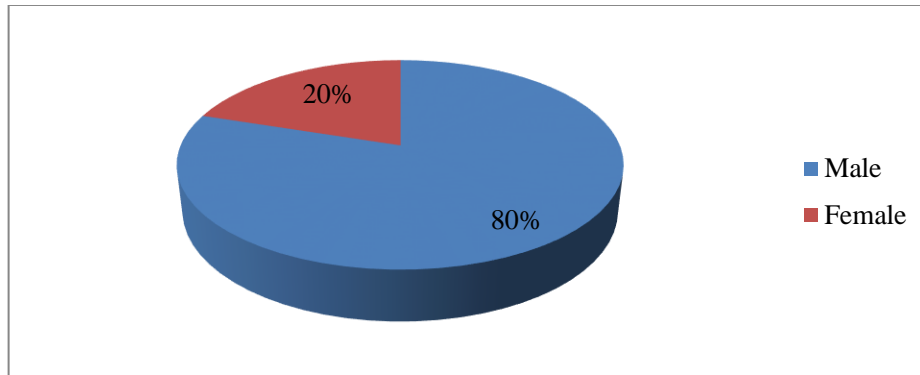


Figure – I: Gender distribution of group on interferon therapy (n=50)

The control group (n=50) comprised of 39 (78%) male and 11 (22%) female patients, with a mean age of the patients being 30 ± 10 years (mean \pm SD), an example of appropriation practically like that of the

patient group. Biochemical thyroid dysfunction (TSH < 0.4 or > 4.0 miU/L) was seen in 7 (14%) of the 50 patients.

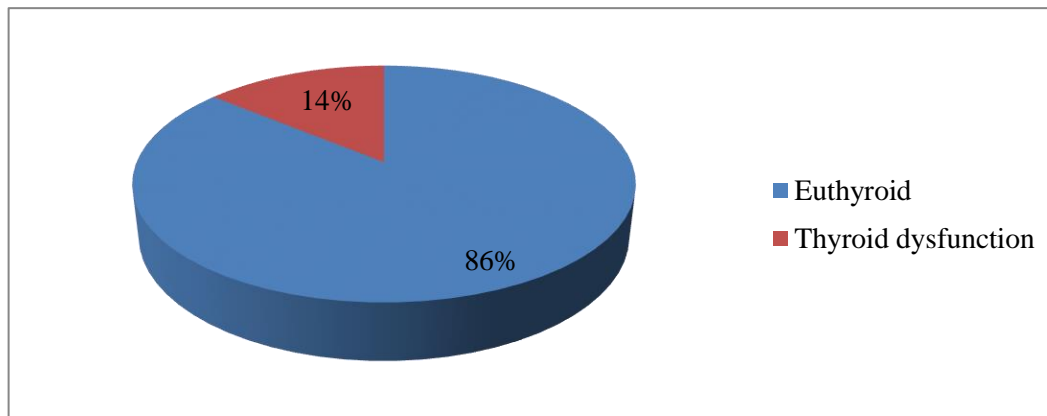
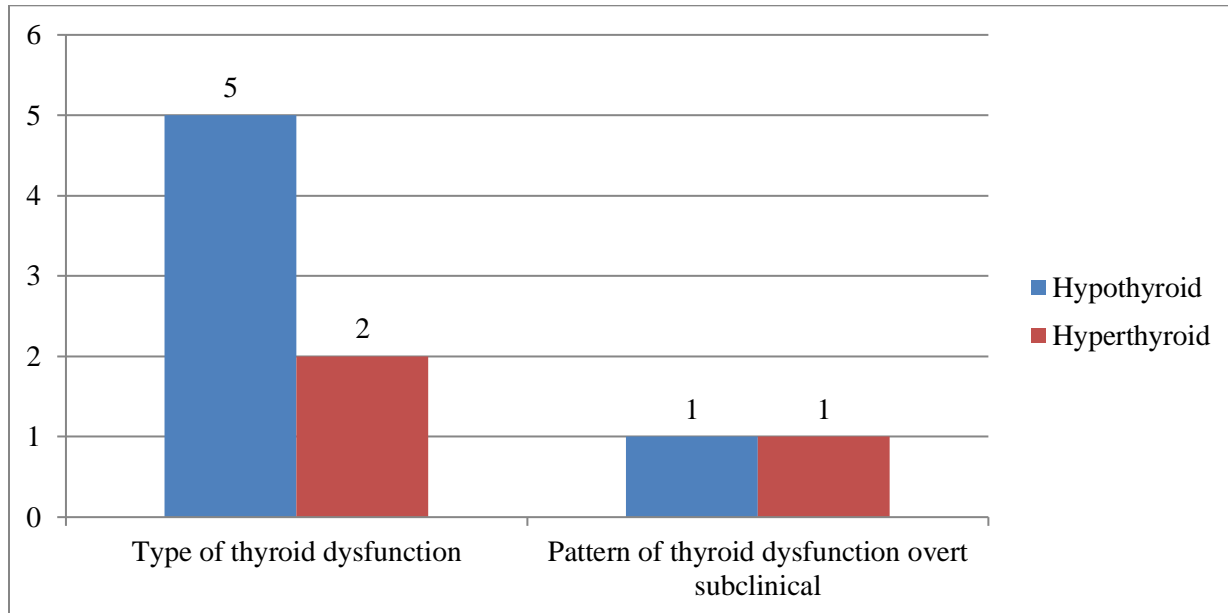


Figure – II: Frequency of thyroid dysfunction in chronic hepatitis C patients on interferon therapy (50) Among these seven patients, 3 were guys, and 4 were females. Hypothyroidism was found in 5 and hyperthyroidism in 2 patients.

Table: Thyroid dysfunction development in chronic hepatitis C patients on interferon treatment (7)

Category	Hypothyroid	Hyperthyroid
Type of thyroid dysfunction	5	2
The pattern of thyroid dysfunction overt subclinical	1	1
	4	1



Additionally, 2 out of these 7 patients created symptomatic thyroid illness, one female patient with trademark highlights of hypothyroidism (weight increase, cold narrow mindedness and drowsiness) and another male patient with ordinary manifestations of hyperthyroidism (fine tremors, palpitations, heat bigotry). Such unconventional highlights were not seen in the remainder of the patients. Albeit dubious indications like laziness and exhaustion were watched, yet they were just transient, regularly happening simply after the

portion of IFN. With respect to time to the beginning of thyroid dysfunction, 3 patients were found to have unsettled thyroid capacities 3 months after commencement of IFN treatment. The other 4 patients were distinguished at the last example (24 wks). Correlation of CHC patients in the two groups at 24 weeks uncovered improvement of thyroid dysfunction in just 1 understanding (2%) in control bunch in respect to the patient group (14%), showing a measurably noteworthy contrast in the watched qualities ($p < 0.027$).

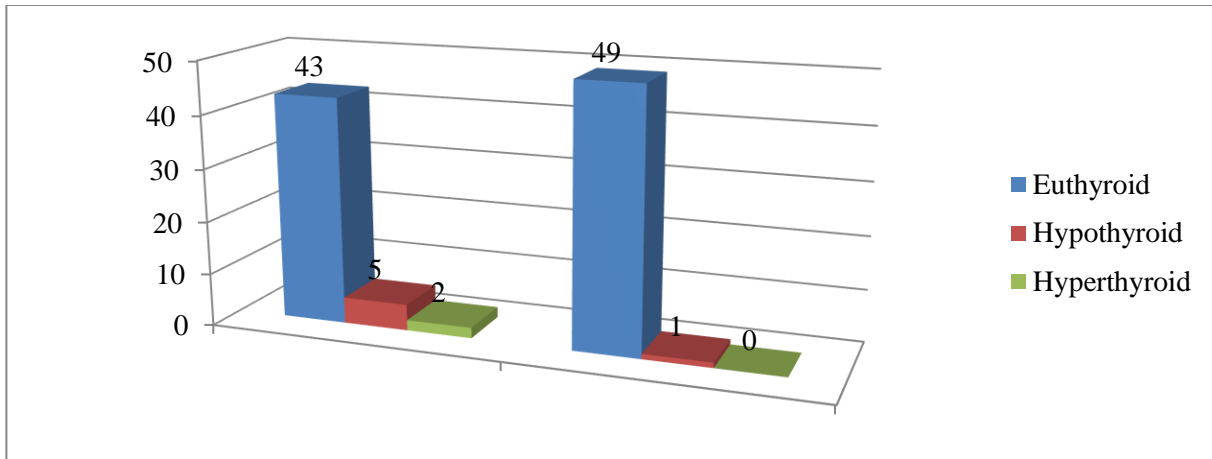


Figure – III: Comparison of thyroid dysfunction pattern in the patient group (50) and control group (50)

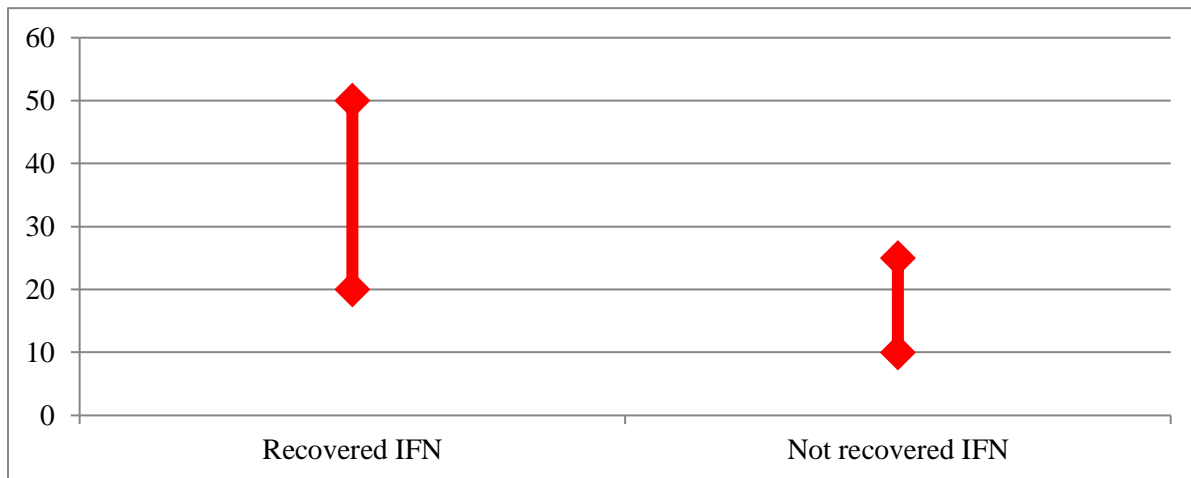


Figure – IV: Statistical Difference

DISCUSSION:

The improvement of thyroid dysfunction in patients on IFN- α treatment for ceaseless hepatitis C has been featured by various global examinations, in spite of the fact that the example and kind of the discoveries have been observed to be variable. A couple of neighbourhood considers have likewise focused on specific highlights of hepatitis C treatment, however nearby information on the example/recurrence of thyroid dysfunction in these patients is rare. In various examinations did around the world, the frequency of thyroid dysfunction created amid interferon- α treatment has been 6-15% roughly [9]. Recurrence of TD saw in IFN- α treated CHC tolerant in our investigation was 14%. This inconstancy can be clarified based on ethnic inception, age and sexual orientation proportion in the considered populaces and the length of interferon- α treatment. In one examination did on 225 patients, clear thyroid

dysfunction showed up in 6.7% of the patients [10]. In another investigation, 5.2% of patients were found to have created clinical/subclinical thyroid issue, while all over again the appearance of TPO antibodies was seen in 6% of subjects [9]. Antonelli and partners, in an examination on 630 back to back patients with perpetual hepatitis C, found that these patients are bound to have hypothyroidism (13%; n=82)10.

Dalgard and collaborators have appeared thyroid dysfunction to create in 11.8% of 254 patients in their investigation [11]. Hypothyroidism, in our examination, was plainly the more typical example (72%) of TD in patients on blend antiviral treatment. The frequency of hypothyroidism as a rule populace is around 2-5% [12]. It has been proposed by different investigations worldwide that the infection itself may likewise assume a casual job in the

improvement of hypothyroidism in IFN regarded patients as the commonness is higher than in the all-inclusive community [13]. To additionally add to the unpredictability of the circumstance, hypothyroidism is significantly more often seen in patients having blend treatment of IFN- α and ribavirin (RBV) (instead of IFN- α treated alone). While HCV itself, additionally, is not able to instigate a higher predominance of auto-immunizer, this may not really convert into hypothyroidism (either clinical or subclinical) [14]. To conquer this issue, we examined the example of thyroid dysfunction in HCV patients who did not get recombinant interferon treatment (Group B), in parallel with patients of HCV on antiviral treatment (Group A), for direct correlation. Hypothyroidism influenced just 2% (n=1) persistent in the control group, affirming the discoveries that IFN- α and ribavirin (RBV) treatment might be causative elements for the event of TD in the investigation group. The pathogenesis remains inadequately saw yet IFN- α is thought to have a direct inhibitory impact on thyrocytes anticipating hormonogenesis and discharge. Another propose is immunomodulation of the resistant framework brought about by recombinant interferon- α within the sight of hepatitis C contamination, which prompts the advancement of thyroid auto-antibodies with complete annihilation and thusly changeless hypothyroidism in hereditarily vulnerable people [15].

Albeit recombinant IFN- α treated hepatitis B patients additionally may create hypothyroidism, its predominance is much lower than that of the patients with constant hepatitis C. This proposes the hepatitis C infection or its genome itself additionally has a basic influence in the advancement of thyroid dysfunction. The infection has been hypothesized to incite thyroid auto-antibodies by producing high endogenous IFN levels activating off immune system thyroid malady in powerless people, like Cocksackievirus. This infection and others have been appeared to actuate a more elevated amount of endogenous IFN- α level which has likewise been related with other auto-insusceptible ailments, for example, type 1 diabetes. At the point when IFN- α is managed exogenously, this impact is emphasized. It is undoubtedly conceivable however absolutely theoretical that exogenous IFN- α synergizes with the endogenous source, overstating the impact on the thyroid hence causing extra hypothyroidism [16]. The nearness of hostile to TPO antibodies preceding interferon treatment and previous immune system issue has likewise been embroiled by different examinations to be another hazard factor for improvement of hypothyroidism. These tests ought to

be proposed before starting antiviral treatment in patients with interminable hepatitis C, anyway the autoantibody profile of the patient group s was not a piece of our investigation hence it is beyond the realm of imagination to expect to remark on the contributory part played by hostile to TPO antibodies in the causation of thyroid dysfunction or something else. In our investigation, the quantity of patients who created hyperthyroidism (n=2) in group A, is too little to even think about arriving at any complete resolution. Goitre was missing in both the cases and thyrotoxicosis looking like Graves illness was not watched. Hyperthyroidism in these patients was gentle and settled unexpectedly with IFN portion decrease. This was ventured to be IFN- α /immune system interceded. Radioactive iodine take-up sweeps are required in such cases for complete finding. Anyway, these tests were past the extent of our examination and, in this way, were not performed. Symptomatic treatment utilizing beta-blockers is for the most part demonstrated. Interference of the antiviral treatment ought to be talked about deliberately, adjusting the dangers and advantages for every individual patient.

CONCLUSION:

The examination means that patients with Chronic Hepatitis C have an unmistakable inclination to create thyroid dysfunction while on recombinant IFN- α treatment. The example of most regularly watched is hypothyroidism. Far-reaching longitudinal examinations are required if the long-haul result of the recombinant IFN- α treatment in perpetual hepatitis C patients is to be completely valued.

REFERENCES:

1. Delgard O, Bjoro K, Hellum K, Myrvang B, Bjoro T, Haug E, et al. Thyroid dysfunction during treatment of chronic hepatitis C with interferon alpha: no association with either interferon. Arch Intern Med 2002; 251-377-8. Woeber KA. The Year in Review: The Thyroid. Ann Intern Med 1999; 131: 959-62
2. Benelhadj S, Marcellin P, Castelnaud C, Colas-Linhart N, Benhamou JP, Erlinger S, et al. Incidence of hypothyroidism during interferon therapy in chronic hepatitis C. Horm Res 1997; 48: 209-14.
3. Berris B, Feinman SV. Thyroid dysfunction and liver injury following alpha-interferon treatment of chronic viral hepatitis. Dig Dis Sci 1991; 36: 1657-60.
4. Ward DL, Bing-You RG. Autoimmune thyroid dysfunction induced by interferon-alpha treatment for chronic hepatitis C: Screening and monitoring recommendations. Endocr Pract

- 2001; 7: 52-8.
5. Dayan CM, Daniels GH. Chronic autoimmune thyroiditis. *New Engl J Med* 1996; 335: 99-107.
 6. Obermayer-Straub P, Manns MP. Hepatitis C and D, retroviruses and autoimmune manifestation. *J Autoimmu* 2001; 16: 275-85.
 7. Lily S, Chuong B, Robert M, Diep N, Fotias A. Thyroid Dysfunction During Interferon Alpha Therapy for Chronic Hepatitis C. *Clinical Nuclear Medicine* 2005; 30 (8): 546-7.
 8. Fernandez-Soto L, Gonzalez A, Escobar-Jimenez F, Vazquez R, Ocete E, Olea N, et al. J. Increased the risk of autoimmune thyroid disease in hepatitis C vs hepatitis B before, during, and after discontinuing interferon therapy. *Arch Intern Med* 1998; 158: 1445-8.
 9. Bini EJ, Mehendaru 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: 2371-6.
 10. Antonelli A, Ferri C, Pampana A, Fallahi P, Nesti C, Pasquini M, Marchi S, Ferrannini E: Thyroid disorders in chronic hepatitis C. *Am J Med* 2004, 17:60-1.
 11. Monzani F, Caraccio N, Dardano a, Ferrannini E. Thyroid autoimmunity and dysfunction associated with type 1 interferon. *Arch Intern Med* 2002; 251: 377-8.
 12. Antonelli A, Ferri C, Pampana A, Fallahi P, Nesti C, Pasquini M, Marchi S, Ferrannini E: Thyroid disorders in chronic hepatitis C. *Am J Med* 2004, 17:60-1.
 13. Blatt LM, Davis J, Klein SB, Taylor MW. The biologic activity and molecular characterization of a novel synthetic IFN- α species, consensus interferon. *J Interferon Cytokine Res* 1996; 16: 489-99.
 14. Mazziotti G, Sorvillo F, Stornaiuolo G, Rotondi M, Morisco F, Ruberto M, et al. Temporal relationship between the appearance of thyroid autoantibodies and development of destructive thyroiditis in patients undergoing treatment with two different types I interferons for HCV related chronic hepatitis; a prospective study. *J Endocrinol Invest* 2002; 25: 625-30.
 15. Ming kee K, Mo Lee. C, Wang J, Tung H, Changchien C, Nan Lu S et al. Thyroid dysfunction in patients with chronic hepatitis C receiving a combined therapy of interferon and ribavirin: Incidence, associated factors and prognosis. *J Gastro Hep* 2008; 21(1):319 – 26.
 16. Rust M F, Theobald J, Zeuzem S, Bojunga J. Thyroid function and changes in ultrasound morphology during antiviral therapy with pegylated interferon and ribavirin in patients with chronic hepatitis C. *Journal of Viral Hepatitis* 2008;16 (3):168 – 77
 17. Kryezka W, Brojer E, Kowalska A, Michaluk D. Thyroid gland dysfunctions during antiviral therapy of chronic C. *Med Sci Monit* 2001; 7 [suppl 1]: 221-5.